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# Tracing the twenty-year evolution of developing AI for eye screening in Singapore: A master chronology of SiDRP, SELENA+ and EyRis

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# Tracing the Twenty-Year Evolution of Developing AI for Eye Screening in Singapore: A Master Chronology of SiDRP, SELENA+ and EyRis

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## Abstract

This working paper is entirely comprised of a timeline table that begins in 2002 and runs through mid-2023. Across these two decades, this timeline traces the evolutionary development of the following:

- The early Singapore R&D efforts to apply software-based image analysis algorithms and methods to analyse eye retina images for diabetic retinopathy and other eye diseases. This was based on a collaboration between the Singapore Eye Research Institute (SERI) and its parent organization, the Singapore National Eye Centre (SNEC), with faculty from the School of Computing at National University of Singapore.
- The establishment and operation of the Singapore Integrated Diabetic Retinopathy Programme (SiDRP), which was a new approach at that time for standardizing and improving the way eye retina images from public healthcare facilities were evaluated by a centralized team of human readers at SNEC.
- The development of the 1st generation Singapore Eye LEsioN Analyzer (SELENA) for automatically evaluating eye retina images and the subsequent development of the 2nd generation SELENA+ software system that used a Deep Learning neural network architecture and convolutional neural network methods to substantially improve the ability of the software to detect diabetic retinopathy and several other eye diseases.
- The scientific evaluation of the performance of SELENA+ using SiDRP data as well as datasets from other parts of the world.
- The multi-step transition of incorporating SELANA+ into the SiDRP workflow through various testing phases and then into full-scale production usage. This involved strong partnerships across SERI, SNEC, several public healthcare institutions and Singapore's national healthtech agency, Integrated Health Information Systems (IHiS).
- The formation of a start-up company called EyRis to take on the responsibility for gaining regulatory approval for using SELENA+ in Singapore and elsewhere in the world as well. Additionally, EyRis would be responsible for packaging and supporting SELENA+ as a commercial product for use domestically within Singapore as well as internationally.
- The trajectory of EyRis as it gained regulatory approval in more countries and as it developed a growing network of partnerships and alternative approaches for bringing the SELENA+ solution to various markets.

## Purpose of this chronology

This detailed master chronology was created as a reference resource to support the drafting of a teaching case titled "EyRIS: AI FOR EYE-DISEASE SCREENING," co-authored by Steven M. Miller, David Gomulya, and Mahima Rao-Kachroo. This teaching case is a product of the Centre for Management Practice at Singapore Management University (SMU).

The "EyRIS: AI FOR EYE-DISEASE SCREENING" teaching case will be publicly released sometime in the July to August 2023 time frame. Once it is publicly released, it can be found and purchased at the following two teaching case distribution websites:

- SMU's Centre for Management Practice: https://cmp.smu.edu.sg/cases/all
- Harvard Business Publishing: https://hbsp.harvard.edu/cases/

A very substantially abridged version of this full master chronology appears as an exhibit in the teaching case.

## Acknowledgements related to creating this chronology

The following people have reviewed this chronology and have attempted to make it as complete and accurate as possible.

- From the clinical research and application aspects (from Singapore National Eye Centre (SNEC) and Singapore Eye Research Institute (SERI)): Dr Wong Tien Yin, Dr Daniel Ting, and Haslina Hamzah
- From the AI technical aspects (from NUS School of Computing): Prof Wynne Hsu and Prof Lee Mong Li
- From the commercial aspects (from the start-up company EyRIS): Lai Teck Kin, Steven Ang, and Jasmine Goh

As author of this chronology, I bear all responsibility for any errors, omissions, or misrepresentations.

## A convenient overview of the SiDRP, SELENA+ and EyRis story to provide context for this chronology

Please see the article, "Two Singapore public healthcare AI applications for national screening programs and other examples," published in the journal Health Care Science in August 2022. The first example highlighted in this article summarizes the origins of SiDRP, SELENA+ and EyRis, and how this lead to Singapore's national level screening of eye retina images for diabetes related eye diseases.

In addition, the forthcoming teaching case, "EyRIS: AI FOR EYE-DISEASE SCREENING" will also provide context for understanding this chronology, and will also provide additional interview-based content beyond what is found in the article referred to above or in the master chronology.

## Master chronology of SiDRP, SELENA+ and EyRis

| Date | Event | Comment | Theme |
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| Starting in early 2002 | Early SERI/SNEC/NUS School of Computing efforts to use software-based image analysis algorithms and methods to analyse retina images.<br><br>WONG Tien Yin is an eye researcher and clinician from the NUS Medical School Department of Ophthalmology and also part of Singapore Eye Research Institute (SERI) and the Singapore National Eye Centre (SNEC). Both SERI and SNEC are both part of Singapore Health Services (SingHealth), a large public healthcare cluster of hospitals and other health facilities and national speciality centres that is part of Singapore's public healthcare system under the Ministry of Health. SERI is a research unit under SNEC.<br><br>Wynne HSU and LEE Mong Li are both computer science faculty members in the NUS School of Computing (SoC).<br><br>NUS School of Computing undergraduate, and PhD students, and research staff actively contributed to the computer science/automated image analysis aspects of this work. | The earliest joint efforts led to the development of new techniques to segment retina vessels.<br><br>The earliest publications from the NUS School of Computing Team (Wynne Hsu, Lee Mong Li and colleagues) based on this collaboration with SERI/SNEC were:<br><br>Bin Fang, Wynne Hsu and Mong Li Lee. Reconstruction of Vascular Structures in Retinal Images, in Proceedings of the IEEE International Conference on Image Processing (ICIP), Barcelona, Spain, September 2003.<br><br>Huiqi Li, Wynne Hsu, Mong Li Lee and Hongyu Wang. A Piecewise Gaussian Model for Profiling and Differentiating Retinal Vessels (Poster), in IEEE International Conference on Image Processing (ICIP), Barcelona, Spain, September 2003. | Research |
| 2004 | Wynne Hsu and Lee Mong Li collaborated with Wong Tien Yin to apply for an ASTAR SERC grant to explore how computer-science based image analysis algorithms can be applied to analysing eye retina images.<br><br>ASTAR = Singapore's Agency for Science, Technology and Research.<br><br>SERC = the Science and Engineering Research Council under ASTAR. | NUS School of Computing received a three-year funding award for the research. | Research |
| 2005 February | NUS School of Computing developed a web-based REtinal VEssel Analysis and Linkage system called REVEAL, that incorporates robust image analysis algorithms, to facilitate the grading of retinal images and automatically quantify the degree of narrowing of retinal blood vessels.<br><br>The degree of narrowing is computed based on the arteriolar-to-venular diameter ratio (AVR) measure.<br><br>SERI used REVEAL to grade 100 retinal photographs taken from the Blue Mountains Eye Study, a population-based study of eye diseases in Australia.<br><br>" Experiment results show that REVEAL is able to achieve an average correlation of 0.91 on arteriolar-to-venular diameter ratio (AVR) of the retina image with the human graders." | Supporting publications led by the NUS School of Computing team (Wynne Hsu, Lee Mong Li and colleagues), also including Wong Tien Yien:<br><br>Jiong Gao, Xinyu Guo, Wynne Hsu, Mong Li Lee, Colleen Koh, Paul Mitchell, Jie Jin Wang, Tien Yin Wong. Computer-based Automated Grading of Retinal Vessel Diameters: Validation of a New Software, 2nd SERI-ARVO meeting on Research in Vision and Opthalmology, Singapore, February 2005.<br>• Included in abstracts under "free paper/poster presentations", presentation #RE407<br><br>Huiqi Li, Wynne Hsu, Mong Li Lee, Tien Yin Wong. Automatic Grading of Retina Vessel Caliber, in IEEE Transactions on Biomedical Engineering, Vol 52, No. 7, 2005. | Research |

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| 2006 January | SNEC opens an ocular reading centre, a centralised facility for reviewing various types of ophthalmology images.<br><br>In the initial years, this centralised ocular reading centre was primarily supporting SERI/SNEC research studies, particularly the start of the 10,000 cohort Singapore Epidemiology Eye Study (SEED). It was also used for some operational image review for images obtained as part of SNEC eye exams.<br><br>External facilities (e.g., Singapore polyclinics) were not initially connected via a network to this centralised ocular reading centre. | Provided centralized evaluation and interpretation (grading) services within SERI and SNEC of ocular pathology from fundus photographs, fluorescein angiograms, Optical Coherence Tomography (OCT) scans or other imaging modalities, using advanced and standardised grading protocols. | Research and Clinical Practice |
| 2007 | NUS School of Computing developed a more sophisticated and comprehensive semi-automated vessel measurement system called SIVA (the Singapore Eye Vessel Assessment system).<br><br>Background on SIVA is described in the chapter, "The Singapore Eye Vessel Assessment System" by Qiangfeng Peter Lau, Mong Li Lee, Wynne Hsu, Tien Yin Wong that appeared in the 2014 book, "Image Analysis and Modeling in Ophthalmology." | Over the years, over 20 international end-user licenses have been signed related to SIVA (and follow-on work built on top of SIVA )– to develop AI algorithms to measure the vessel calibre. | Research |
| 2009 January | Wong Tien Yin becomes Executive Director of SERI. | Dr Wong had previously been an eye doctor involved in SERI, SNEC and National University of Singapore Hospital (1992 – 2002), as well as NUS Medical School and Duke-NUS Medical School.<br><br>He had left Singapore in 2003 to become a professor at University of Melbourne and its affiliated Centre for Eye Research Australia.<br><br>He returned to Singapore to assume this position at SERI. | Research |
| 2009 April | A five-year project agreement is signed between SERI and NUS to facilitate joint work between SERI and NUS School of Computing related to software for automated analysis of retina images.<br><br>Principle investigators of agreement:<br>• From Seri, Wong Tien Yin<br>• From NUS School of Computing Wynne Hsu<br>• From NUS School of Computing Lee Mong Li<br><br>The project agreement work plan was titled "Retinal Image Analysis."<br><br>"The goal of this project is to develop new accurate and reliable machine vision and pattern recognition methods for automatic fundus image analysis. The methods will be applied to | The funding came from two national sources for retina image analysis effort: 1) from the Ministry of Health National Medical Research Council via a Singapore Translational Investigator Award, and 2) from ASTAR's Biomedical Research Council.<br><br>Via this new SERI/NUS project agreement, SERI would use some of these recently awarded grant funds to support the ongoing collaboration with NUS School of Computing on software for eye retina image analysis. | Research |

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| | automatic screening system, monitoring of disease progress and support for medical decision making." | | |
| 2009 October | An international patent application on "Platform for non-invasive Observation of Cardiovascular disorders using retina image analysis." is official published by the World Intellectual Property Organization.<br><br>The application for the patent was made by ASTAR Exploit, ASTAR's licensing and technology transfer unit.<br><br>The applicant named in the patent filing document was National University of Singapore (NUS).<br><br>The named inventors listed in the patent application were Wynne HSU and LEE Mong Li (NUS School of Computing) and WONG Tien Yin (listed under NUS). | International publication date of application: 15 October 2009<br>WO 2009/126112 A1<br><br>The patent application was initially filed on 3 February 2009<br>PCT/SG2009/000040<br><br>The abstract reads as follows:<br>"A platform is proposed for automated analysis of retinal images, for obtaining from them information characterizing retinal blood vessels which may be useful in forming a diagnosis of a medical condition. A first aspect of the invention proposes that a plurality of characteristics of the retina are extracted, in order to provide data which is useful for enabling an evaluation of cardiovascular risk prediction, or even diagnosis of a cardiovascular condition. A second aspect uses fractal analysis of retinal images to provide vascular disease risk prediction, such as, but not limited to, diabetes and hypertension." | Research |
| 2010 | ASTAR Exploit awarded Flagship grant to bring SIVA to a product.<br><br>A description of this effort from NUS Soc Prof Lee Mong Li's website (listed under completed projects):<br><br>**Flagship Project on Ocular Imaging:**<br>The project is funded by ASTAR Exploit Technologies to fully automate the Singapore Eye Vessel Assessment System (SIVA). This system brings together various technologies from image processing and artificial intelligence to construct vascular models from retinal images. Subsequently, these models of blood vessels can be queried for a variety of measurements which have been shown to be correlated to diseases such as stroke, diabetes, hypertension etc. This project is a collaboration between Singapore Eye Research Institute (SERI) and NUS School of Computing. | A non-exclusive license was signed with TOPCON for clinical SIVA. | Research to Commercial Translation |
| 2010 July | A pilot version ( early-stage interim version) of the Singapore Integrated Diabetic Retinopathy Programme (SiDRP) is started by SNEC, the Tan Tock Seng Hospital (TTSH) Eye Institute (TEI) and Singapore Ministry of Health.<br><br>At the July 2010 start of this effort, one polyclinic (Outram Polyclinic) was connected via a tele-ophthalmology network enabling retina images from that polyclinic to be transmitted to the SNEC centralised ocular reading centre for review and reporting. Subsequently, a year later, TEI | This initiation of the SiDRP effort, starting with this interim pilot phase, played a very important role in starting the accumulation of the Singapore data sets of high-quality labelled retina images taken under real-world clinical conditions.<br><br>Gradually, over the 12-year period from mid-2010 through end of 2022, the tele-ophthalmology network for linking diabetic retinopathy (DR) screening centres to SiDRP is expanded to include all 20+ | Clinical Practice |

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| | started operations and received images from their first polyclinic.<br><br>Integrated Health Information Systems (IHiS), the national healthtech agency, played a key implementation-focused role in setting up this pilot of the tele-ophthalmology network and in the early version of the information systems for managing the image workflow and image data within the SNEC ocular reading centre. | polyclinics (23 as of mid-2022) and some other designated DR screening facilities across the public, non-private and private sectors. | |
| 2010 November | Wong Tien Yin is awarded Singapore's President's Science Award "For the development and use of novel retinal imaging to understand pathways in cardiovascular and metabolic diseases."<br><br>The award announcement specifies his affiliations as Singapore Eye Research Institute, Singapore National Eye Centre, and National University Health System.<br><br>"Professor Wong Tien Yin's pioneering research over the past 10 years has resulted in the development of a suite of advanced computing imaging software and diagnostic platforms, which allows scientists, doctors and clinicians to assess a patient's cardiovascular disease and diabetes risk through a simple retinal photograph. This simple eye scan is a unique and non-invasive way to understand, screen and detect early cardiovascular and metabolic diseases." | Singapore's "President's Science & Technology Awards" – which include the Science and Technology Medal, the Science Award and the Technology Award – are the highest national honours for science and technology achievements deemed to be of great national significance.<br><br>See the web page for the history of recipients of these awards.<br><br>Note that in 2014 November, Dr Wong Tien Yin and Professors Wynne Hsu and Lee Mong Li of NUS School of Computing win the 2014 President's Technology Award for "the development of novel ocular image analysis technology for the screening and evaluation of significant clinical problems in eye and vascular diseases." See this entry for 2014 November (below). | Research |
| 2012 April | The Singapore Integrated Diabetic Retinopathy Programme (SiDRP) – a national diagnostic screening effort - is officially started and publicly announced by Ministry of Health.<br><br>When officially launched, SiDRP is a partnership between SNEC and Tan Tock Seng Hospital Eye Institute (National Healthcare Group). The Ministry of Health and IHiS are also involved.<br><br>Three polyclinics spanning two of the national healthcare clusters (SingHealth and NHG) are now participating.<br><br>SingHealth April 2018 April summary on SiDRP providing background. | Officially launching and expanding SiDRP strengthens and accelerates effort to accumulate the Singapore data set of high-quality labelled retina images taken under real-world clinical conditions.<br><br>SiDRP, which unofficially started in 2010, was not one of the earlier national level diabetic retinopathy screening programmes to be established. However, it was one of the very largest such national screening programmes to be created, in fact, the largest one outside of any of the UK entities.<br><br>Note: this point about the relative timing and size of the SiDRP national screening effort is derived from the information in Table 1 in the 2020 July study on "The Evolution of Diabetic Retinopathy Screening Programmes: A Chronology of Retinal Photography from 35 mm Slides to Artificial Intelligence" published in Clinical Ophthalmology (led by a UK author team.) | Clinical Practice |

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| 2012 April | Study on "The Lab, the Clinic, and the Image: Working on Translational Research in Singapore's Eye Care Realm" is published in Science, Technology and Society journal (led by faculty and staff from NUS Sociology and from SERI).<br><br>"…we first describe how retinal photographs became associated with cutting-edge research in Singapore, and despite this, why it remains hard to translate such research into broad clinical practice. We then examine the work that goes on in the Singapore Advanced Imaging Laboratory for Ocular Research (SAILOR), and in particular the small-scale testing of a new tele-ophthalmology service to support the screening for eye disease associated with diabetes." | "…we investigate how translational research trajectories are built in present-day Singapore, through a case study pertaining to the use of retinal photography for disease screening. The circulation of such images in the context of a tele-ophthalmology pilot service designed to support the early detection of eye disease related to diabetes, helps attune research to clinical practice and vice versa, in ways that open possibilities for future medical innovation. Our case study points to an inversion of the typical characterization of translational research as a process that begins at the 'bench' and then moves downstream (to the 'bed') in a linear fashion…. Everyday clinical practice, rather than being understood as the last 'hurdle' for medical innovation, is actively aligned with the pursuit of research and in this way gradually configured for the uptake of novel diagnostic tests." | Research and Clinical Practice |
| 2013 to 2014 | Wynne Hsu and Lee Mong Li worked with PhD student Gilbert Lim to explore the use of deep learning for the automated detection of Diabetic Retinopathy.<br><br>SERI team do their first trials of using deep learning methods for retina image analysis.<br><br>This put the NUS/SERI team on the pathway to development of SELENA+ – a deep learning software system for detecting diabetic retinopathy.<br><br>Note that prior to this, there was a SELENA software system (version 1.0) which did not use a deep learning convolutional neural network (CNN) to detect DR.<br><br>The earlier (pre-deep learning CNN-based) SELENA software system used other types of computer image based pattern analysis methods and supporting computer aided technology. | First joint NUS School of Computing/SERI publication on using deep learning methods for analysing eye retina images appears in July 2014:<br><br>Gilbert Lim, Mong Li Lee, Wynne Hsu, Tien Yin Wong. Transformed Representations for Convolutional Neural Networks in Diabetic Retinopathy Screening, in AAAI Workshop on Modern Artificial Intelligence for Health Analytics (MAIHA), Quebec, Canada, July 2014. | Research |
| 2013 December | A joint Project Management Office involving SNEC (SingHealth), National Healthcare Group Eye Institute (Tan Tock Seng Hospital) and IHiS was set up to manage the development of the features and functions of the SiDRP Tele-Ophthalmology to improve the efficiency of SiDRP workflow and reporting and to further standardize grading standards.<br><br>Note: In some entries below, the National Healthcare Group Eye Institute is referred to as TEI, referring to the Tan Tock Seng Hospital Eye Institute. | The objectives of this joint included:<br>• Improve the level of screening standards and turnaround time<br>• Provide uniform assessment and referral guidelines for diabetic retinopathy reporting at the national level<br>• Provide standardized training and audit governance for SiDRP reporting<br><br>IHiS role: continue expanding and improving the IT backbone, continue getting more polyclinics onboard the national tele-ophthalmology network, improve the information systems supporting the reading centre workflow, | Clinical Practice |

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| | | and enhance the data repository and associated data management. | |
| 2014 January through December and into 2015 | Across 2014 and 2015, SingHealth (SNEC) ophthalmology chief resident and SERI researcher - Dr Daniel TING was invited to lead the clinical research study using SELENA (a pre-cursor to SELENA+) under the mentorship of Wong, in collaboration with Hsu/Lee research partnership to automatically analyse retina images for diabetic retinopathy.<br><br>The DEEP EYE STUDY commenced, with invitation to 4 international collaborators to develop and test the AI for DR detection (SELENA). The development, validation and testing datasets were conducted on SiDRP datasets between 2010 and 2015.<br><br>The SiDRP datasets, previously graded by human graders, were re-graded once more by Dr Daniel Ting using International Clinical Diabetic Retinopathy Severity Scales to train SELENA (now SELENA+), and the ground truth was also used to serve as the reference standard for SiDRP 2014/2015 datasets published in JAMA 2017 (Ting et al).<br><br>See Dec 2017 entry for the resulting work published in top tier medical journals. | For technical training, Ting/Lim explored different options of CNNs (Yip et al, ACCV, 2018), pre-trained vs untrained models, different coding programs, use of cross validation and ensemble models.* The final CNN model chosen was VGG architecture with ensemble model and a gradeability model. This is also one of the first AI deep learning medical system at that time that incorporated the gradeability model into the overall AI operational system in addition to CNN.<br><br>*The technical paper (Yip et al, ACCV 2018; Yip et al, Nature Digital Medicine 2020) were published after the clinical paper (Ting et al, JAMA 2017) as the team felt the importance of sharing the research and development effort that has led to the birth of SELENA (now SELENA+).<br><br>**Yip et al.** Enhanced Detection of Referable Diabetic Retinopathy via DCNNs and Transfer Learning. ACCV, 2018. URL: **https://link.springer.com/chapter/10.1007/978-3-030-21074-8_23** | Research and Clinical Practice |
| 2014 August | Dr Wong Tien Yin is appointed as the 5th Medical Director of SNEC in 2014. | He relinquishes his prior role as Executive Director of SERI and transitions to Medical Director of SNEC and concurrently Chairman of SERI. | Clinical Practice |
| 2014 November | Wong Tien Yin, Wynne Hsu and Lee Mong Li are awarded Singapore's President's Technology Award "for their outstanding contributions to the development of novel ocular image analysis technology for the screening and evaluation of significant clinical problems in eye and vascular diseases."<br><br>The award announcement specifies the affiliations as follows:<br>• For Wong Tien Yin: Singapore Eye Research Institute, Singapore National Eye Center, and Duke-NUS Graduate Medical School of the National University of Singapore<br>• For Wynne Hsu and Lee Mong Li: School of Computing, National University of Singapore<br><br>"The core technology is the Platform for Ocular Image Screening and Evaluation (POISE) that encompasses a suite of advanced image analysis algorithms and innovative integration of these methods. These include programmes that have been developed for large-scale clinical use for | Also from the 2014 President's Technology Award announcement:<br><br>". The technology has been licensed to and used by several academic and medical centres and research institutions, including University College London, University of Wisconsin-Madison, University of Melbourne, University of Sydney, the Centre for Eye Research Australia, the Commonwealth Scientific and Industrial Research Organisation, Moorfields Eye Hospital and Topcon Inc. Several joint research labs such as SAILOR - the SERI-I2R-NUS Joint Lab, and the ATLANTIA Topcon-I2R Joint Lab have been established to drive the next generation of advanced ocular imaging technologies."<br><br>"This work has resulted in more than 30 patents, and 20 end-user licenses with companies, institutions and hospitals | Research |

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| | eye diseases such as glaucoma, diabetic retinopathy and age-related macular degeneration as well as systemic vascular diseases such as stroke, heart disease, dementia, diabetes and hypertension."<br><br>Note:<br>This is a precursor of what later evolves into SELENA+ and SIVA+. | globally full commercial licenses with multinational companies) ;more than 300 publications and multiple international prizes and awards." | |
| 2015 | SNEC celebrates its 25th anniversary for the years 1991 to 2015.<br><br>See the commemorative SNEC 25th Anniversary booklet | SiDRP is highlighted as one of the many major accomplishments of SNEC. | Clinical Practice |
| 2015 September | Dr Ting submitted a SingHealth Foundation (SHF) grant for SELENA to continue the AI research, under the Wong's mentorship, in collaboration with Lim/Hsu/Lee. | Daniel Ting completes his PhD at University of Western Australia in Sept 2015 on the topic of Retinal Imaging in Diabetic Retinopathy. | Research |
| 2016 April to June | Staff at the Infocomm and Media Development Authority of Singapore (IMDA) suggests that SiDRP/SELENA team should talk to the Singapore IT entrepreneur Lai Teik Kin—and gets his advice on how to proceed with commercialisation. | While Teik Kin was in the process of being appointed as a business mentor to SNEC Ophthalmic Technologies Incubator earlier in 2016, he had not previously engaged in mentoring discussions focused with how to commercialise the SELENA deep learning effort for eye disease screening. | Commercial |
| 2016 June | LAI Teik Kin – co-founder of Nova MSC Berhad Malaysia and Nova Health Pte Ltd Singapore was officially appointed Business Mentor to the Singapore National Eye Centre (SNEC) Ophthalmic Technologies Incubator to provide business insights and guidance.<br><br>Through his companies Nova MSC (Malaysia) and Nova Health (Singapore), Teik Kin had prior experience with IT applications in healthcare and e-government in Singapore and Malaysia. He did not have prior experience with machine learning-based AI systems. | Teik Kin starts advisory interactions with SNEC to provide inputs on commercialisation of various SNEC and SERI initiatives. At this point, his advisory work with the SNEC incubator is not specifically focused on SiDRP or SELENA as there are many other potential commercialisation projects to be considered within SNEC's overall portfolio. | Commercial |
| 2016 October | Study on "Cost-effectiveness of a National Telemedicine Diabetic Retinopathy Screening Program in Singapore" is published in Ophthalmology journal of Amer Academy of Ophthalmology (led by SERI, SNEC, and TEI, and including other Singapore and international collaborators). | Compares Singapore data on SiDRP screening to standard family practice-based screening. Shows cost and other advantages of the SiDRP screening approach compared to the prior family-practice-based approach. The study concludes that data provide a strong economic rationale to expand the telemedicine-based DR screening program in Singapore and elsewhere.<br><br>Impacts of using the SELENA AI system for SiDRP related eye screening are not considered in this analysis as these research evaluations are still underway and major results have not yet been published. | Research |
| 2016 November | After nearly 2 years' worth of multiple iterations between Ting/Lim ( with input from senior PIs (Wong/Hsu/Lee), the final manuscript was submitted to the Lancet. | | |

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| 2016 December | Study on "Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs" is published in JAMA (led by Google with collaborators from US and India).<br><br>Deep learning system trained on 128,175 images from the US and India.<br><br>Validation based on 11,711 images from US and French data sets. | The study concludes that an algorithm based on deep machine learning had high sensitivity and specificity for detecting referable diabetic retinopathy, and that further research is necessary to determine the feasibility of applying this algorithm in the clinical setting and to determine whether use of the algorithm could lead to improved care and outcomes compared with current ophthalmologic assessment.<br><br>First published paper in a major international medical journal demonstrating the ability to use deep learning methods for evaluating referable retina scans for diabetic retinopathy and referable diabetic macular edema. | Research |
| 2017 January | 1st rejection of the manuscripted submitted to the Lancet on 2016 November.There were over 200 comments from 5 different reviewers. | The editor at The Lancet claimed this is no longer "novel" as the Singapore team was pre-empted by the Google-led team. | |
| 2017 January | The study team appealed to the Lancet senior editor based on the following: As compared to the Google paper, the submitted manuscript from Singapore had larger datasets, pre-dominantly Asian, presence of independent testing datasets from several sites (4 sites) | The appeal was granted by the Lancet Senior Editor. The Singapore team was invited to re-submit, though only given 1-week turnover time to rebut more than 200 comments from all reviewers<br><br>Ting/Lim/Alfred (study team statisticians) spent almost every night and stayed past mid night (averaging at 3 to 4 hours sleep per night) to rebut, with input from senior PIs and co-investigators.<br><br>The Lancet editorial board made the decision to reject the resubmitted paper 1 week after its resubmission. | |
| 2017 Feb to June | Dr Ting and the Singapore research team attempted to submit their their research results to different Tier 1 medical journals (NEJM, Nature, Nature Medicine, Nature Biotechnology, BMJ, Annals of Internal Medicine and a few others) with no luck.<br><br>Most of these journals sent the research manuscript out to external reviewers, but most external reviews came back with similar concerns related to the precedence of the Google paper. | No other medical journal editors would take the Singapore team paper, claiming the precedence of the Google team paper.<br><br>A related challenge in getting this research work published was a lack of understanding of deep learning in the clinical fields. Most highly qualified and experienced senior academic clinicians/reviewers had very limited AI expertise and did not understand the difference between the new generation of | Research |

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| | Some reviewers thought the Singapore team's deep learning approach was very similar to the previous feature-based machine learning approach and did not understand the contribution of developing and using the new deep learning methods.<br><br>Dr Ting attempted to apply for new research grants in Singapore (NMRC New Investigator Grant) over a 6 months period in order to continue this research work, but was rejected initially, and then a second time after a 6 month rebuttal and resubmission.<br><br>The comments of the Singapore grant evaluation committee and their external reviews were largely similar to the reasons The Lancet and other medical journals had rejected the work: precedence of Google paper, and a lack of the understanding of the novelty and importance of using and validating the new deep learning AI approach as compared to the older types of machine learning techniques. | deep learning methods vs the prior generation of machine learning methods that used manually-crafted feature models. | |
| 2017<br>July to Oct | SERI/SNEC/NUS team quickly mobilized and expanded the international collaborative effort – The Deep Eye Study – to include two additional blinding eye diseases (i.e., glaucoma suspect and age-related macular degeneration) in addition to diabetic retinopathy resulting in a new deep learning system called SELENA+. They also substantially expand the size and diversity of the data sets to train and validate the performance of SELENA+ - the total sample size tested for 3 conditions increased from approximately 200K to nearly 500K, with inclusion of 2 new eye conditions and more datasets from five additional countries (China, Hong Kong, Australia, US and Mexico). | Super intensive, rapid mobilization effort to expand scope of study to three eye diseases and expand sources of validation data in order to give reason for a new publication that goes beyond what was reported in the Google-led JAMA publication.<br><br>Drs Ting/Wong submitted a pre-submission inquiry to Dr Howard Bauchner, immediate past JAMA Editor-in-Chief, who then expressed interest in taking in the article as afollow-up piece on the prior Gulshan et al, Google 2017 publication. | Research |
| 2017<br>December | Publication of the Ting et al, JAMA 2017 (in December)<br><br>Study on "Development and Validation of a Deep Learning System for Diabetic Retinopathy and Related Eye Diseases Using Retinal Images From Multiethnic Populations With Diabetes," published in JAMA (led by SERI and NUS School of Computing with other Singapore and international collaborators).<br><br>The SELENA+ deep learning system was trained on 274,169 images from the Singapore National Diabetic Retinopathy Screening Program (SIDRP) obtained between 2010 and 2013 from people in Singapore of Chinese, Malay and Indian ethnicity.<br><br>Validation based on 220,492 images from 2014 and 2015 SiDRP data as well as from 10 additional external (non-SiDRP) multiethnic cohorts of participants with diabetes from | More diverse data sets for validation.<br>More observations for both training and validation.<br>A wider range of real world, clinical conditions for both the training and validation data.<br>Diabetic retinopathy plus two other eye diseases (Glaucoma and Age Related Macular Degeneration)<br><br>The study concludes the deep learning system had high sensitivity and specificity for identifying diabetic retinopathy and related eye diseases using retinal images from multiethnic populations with diabetes, and that further research is necessary to evaluate the applicability of the deep learning systems in health care settings and their utility to improve vision outcomes. | Research |

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| | different settings (community, population-based, and clinic based) including from other Singapore eye studies, from China and Hong Kong, from Australia, from the US (African Americans) and from Mexico.<br><br>A summary of the key papers related to SELENA+<br>1. https://jamanetwork.com/journals/jama/fullarticle/2665775 - JAMA<br>2. https://www.thelancet.com/journals/landig/article/PIIS2589-7500(19)30004-4/fulltext - Lancet Digital Health<br>3. https://www.thelancet.com/journals/landig/article/PIIS2589-7500(20)30060-1/fulltext - Lancet Digital Health<br>4. https://www.nature.com/articles/s41746-019-0097-x (see this paper - AI generated DR grading for large scale epidemiology studies use) - Nature Digital Medicine<br>5. https://www.nature.com/articles/s41746-020-0247-1 - Nature Digital Medicine | This was also one of the landmark AI papers for medical imaging that illustrated several important points:<br>i. Inclusion of gradeability (a.k.a diagnosibility) of an AI system into the overall AI operational system<br>ii. Creating independent testing datasets (with no overlap of unique patients) to avoid overfitting<br>iii. To state importance of AI biases and test for AI generalizability on external independent testing datasets for different ethnicities, clinical settings with varying of prevalence rate (or pre-test probabilities), countries, reference standards and retinal cameras<br>iv. To utilize a visualization technique to illustrate the AI explainability (XAI) | |
| 2017, 2nd half of year, while working on their JAMA paper | SERI/SNEC/NUS SoC team start thinking about how to make practical clinical use of their results for using deep learning to screen for DR and the other eye diseases.<br><br>They start thinking about a "start-up" – though they do not really understand what is required for this type of start-up for a medical AI device.<br><br>This was prior to the release of US FDA SaMD guidelines. | The very beginning of the journey of attempting to translate the most current version of the software for analysing the retina images - the SELENA+ deep learning system - from research to clinical practice. | From Research to Commercial Translation |
| During 2017, while working on JAMA paper | SERI/SNEC team has initial discussions with Singapore's Health Sciences Authority (HSA) to inquire about making use of deep learning diagnostic screening ability for Diabetic Retinopathy and other eye diseases. | SERI/SNEC team is informed by Singapore HSA that to make use of the SELENA+ deep learning system for clinical practice:<br>1) regulatory approval would be required (will first need a peer-reviewed article that illustrates robust clinical validation and testing based on the clinical intended use in a reputable journal), and<br>2) A 3rd party independent entity as a PRODUCT OWNER (not SERI or SNEC as their were public healthcare institutions) would have to officially make the submission.<br><br>This leads to the realisation that in order to obtain regulatory approval and make use of this new deep learning screening capability in practice, either<br>• a start-up must be formed, or<br>• the technology must be licensed to an existing commercial business. | Regulatory and Commercial |
| 2017 Oct | SiDRP/SELENA+ core team members (from SERI, SNEC and NUS SoC) explored various possibilities and pathways for commercialisation, including | This included very early-stage exploratory conversations with several potential CEO candidates for a startup. | Commercial |

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| | but not limited to the earliest discussions with Lai Teik Kin. | | |
| 2017<br>From October thru early 2018 | Lai Teik Kin starts focused effort on mentoring the SiDRP/SELENA/NUS SoC team and the SNEC incubation office on how to move forward with the commercialisation effort for the SELENA+ deep learning system for eye disease screening.<br><br>After doing his "homework" per SiDRP and the SELENA+ deep learning system, Teik Kin informs the key medical/technology team (SERI/SNEC and NUS SoC) that he would be interested in being the founding CEO.<br><br>This is the start of Teik Kin's focused interactions with the SERI/SNEC/NUS SoC team per commercial pathways for SELENA+. | This is the very beginning of what would become EyRIS- though prior to the actual formation of EyRIS.<br><br>The SERI/SNEC/NUS SoC team that were core to SiDRP/SELENA+ liked the fact that Lai Teik Kin had prior experience with Healthcare IT and that he had the machinery, experience and financial backing of Nova Group behind him.<br><br>As part of the evaluation, the SERI/SNEC/NUS SoC team had inetrviews/meetings with Teik Kin and also had him submitting a business plan. | Commercial |
| 2018<br>February | EyRIS is officially incorporated as a business in Singapore.<br><br>Administratively, EyRIS is under Nova Health Pte Ltd (Singapore), the ongoing technology company the Lai Teik Kin was already heading. Nova Health Pte Ltd is under Nova MSC Berhad Malaysia, also run by Teik Kin. | 7 EyRIS co-founders:<br>• Three Clinicians from SNEC and SERI: Dr WONG Tien Yin, Dr Daniel TING, Haslina HAMZAH<br>• Three NUS SoC researchers: Prof Wynne HSU, Prof LEE Mong Li, Gilbert LIM<br>• CEO: LAI Teik Kin<br><br>One Advisory Board Member:<br>• SNEC Ocular Reading Centre former Clinical Director Dr Gavin TAN (who is currently – as of January 2023 - Head of the SNEC Ocular Diagnostics Dept, which oversees 3 other functions including the Reading Centre). | Commercial |
| 2018<br>February thru 2019 October<br><br>~ 20 months | **Step 1:**<br>**2018 Feb to 2019 Jul:**<br><br>EyRIS does all the necessary work to<br>• Meet all preconditions for being able to submit a Singapore regulatory approval request including obtaining ISO 13485 certification – quality management system requirements for medical devices.<br>• Prepare all documentation needed as part of the regulatory request.<br>• Make the actual regulatory request submission on 2019 July.<br><br>**Step 2:**<br>**From just after this first regulatory submission (2019 July) till the time regulatory approval was received (2019 October):**<br><br>Singapore HSA reviews the EyRIS regulatory submission. EyRIS has to respond to many inquiries related to the submission.<br><br>During both Step 1 and Step 2 of this 20 month period, EyRIS co-founders from SERI/SNEC and from NUS provide supporting inputs on medical matters (research and clinical) and on deep | As per this summary on Medical AI device regulatory submissions in the US, in the 2016, 2017, 2018 time period, there were still very few AI medical devices (Software as a Medical Device) that had been approved by the US FDA.<br><br>As such, this type of request for an AI medical device regulatory review and approval was very new to Singapore's HSA, and was a first of its type request.<br><br>Worldwide, very few medical device regulatory consultants had experience with submissions based on deep learning AI software systems.<br><br>See 2018 April item announcing US FDA gives its first time approval for an AI medical device to analyse eye images for diabetic retinopathy.<br><br>Five "big things" were happening in parallel this 20-month period:<br>1. Figuring out how to "productize" the R&D version of SELENA+. | Regulatory and Commercial |

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| | learning/AI matters to EyRIS so company can prepare the regulatory submission (Step 1) and respond to all inquiries from HSA post-submission (Step 2).<br><br>EyRIS employs the services of several consultants to support these two steps as well.<br><br>One consulting firm EyRIS worked with in a major way was TUV Sud, the international standards and compliance organisation that also does consulting for medical device approval.<br><br>Seeking ISO 13485 approval and Singapore HSA approval for an AI medical device (AI software as a medical device) was entirely new to the TUV Sud consulting team supporting EyRIS so even the consultant was not familiar with this specific situation. | 2. Building the start-up team and the capabilities of the team.<br>3. Understanding and navigating the regulatory space, starting with Singapore.<br>4. Completing all requirements to make EyRIS' very first regulatory submission to Singapore HAS.<br>5. Continuing effort on the validation process needed for regulatory approval and commercialisation—(following up on the results of the 2017 Dec JAMA paper). This required SERI to seek additional grant support, and also support from EyRIS. | |
| 2018<br>April | US Food & Drug Administration (FDA) issues news release stating "FDA permits marketing of artificial intelligence-based device to detect certain diabetes-related eye problems."<br><br>"The device, called IDx-DR, is a software program that uses an artificial intelligence algorithm to analyze images of the eye taken with a retinal camera called the Topcon NW400."<br><br>"IDx-DR is the first device authorized for marketing that provides a screening decision without the need for a clinician to also interpret the image or results, which makes it usable by health care providers who may not normally be involved in eye care."<br><br>IDx-DR webpage<br><br>IDX was founded in 2010 as a spin-off from the University of Iowa Medical School.<br>The company changes its name from IDx to Digital Diagnostics in January 2022.<br><br>The Digital Diagnostics webpage | "IDx-DR was reviewed under the FDA's De Novo premarket review pathway, a regulatory pathway for some low- to moderate-risk devices that are novel and for which there is no prior legally marketed device. IDx-DR was granted Breakthrough Device designation, meaning the FDA provided intensive interaction and guidance to the company on efficient device development, to expedite evidence generation and the agency's review of the device." | Regulatory and Commercial Competition |
| 2018<br>Early year thru Mid-year | Singapore Smart Nation and Digital Government Office (SNDGO) has discussions with the SiDRP/SELENA team to learn more about the deep learning AI system and its potential clinical application.<br><br>Sometime around 2018 mid-year, SNDGO encourages IHiS (national healthtech agency) to start looking into how SELENA+ can be incorporated into the everyday operations of SiDRP.<br><br>This is also the time period during which the SNDGO is in the early stage of their effort to conceptualise and formulate a national AI policy so they are looking for good examples. | EyRIS was still in the process of preparing to submit SELENA + to Singapore's HSA for regulatory approval. The submission had not been done yet, so this discussion with Singapore's Smart Nation Office was a preliminary discussion. | Clinical Practice |

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| 2018 September | SERI/SNEC and NUS SoC officially licence intellectual property for SELENA+ to EyRIS. | Now EyRIS is the official licence holder of SELENA+. | Commercial |
| 2018 Nov to 2019 Nov 12 months: | SiDRP (SNEC + NHG Eye Institute) + SERI + NUS SoC plus IHiS team to do Phase 1 Proof of Concept to test viability of using SELENA+ within SiDRP.<br><br>EyRIS is not directly involved is this Phase 1 Proof of Concept. The extent of EyRIS involvement was<br><br>mainly providing vendor services to IHIS to install SELENA+ on the national Business Research Analytics Insights Network (BRAIN) platform that IHiS created to support analytics and AI efforts for Singapore's public healthcare institutions.<br><br>As SELENA+ has not yet received regulatory approval from the Singapore HSA, this is still a research study. Data on SELENA+ results is collected, but SELENA+ is not used for any clinical diagnostic decision support or decision making.<br><br>All usage of SELENA+ is still in research mode for the purpose of research studies, SiDRP patients had to sign a consent form to have their eye image be used as part of a research study in order for their retina image to be additionally analysed by SELENA+ (off-line, in batch mode) in addition to the SiDRP human graders doing their regular SiDRP evaluation. | The SiDRP Level 1 and Level 2 human graders do their regular everyday image evaluation work as per their standard processes and protocols.<br><br>At the end of each day, in batch mode, the retina images from 6 of the polyclinics (across SingHealth, NHG, NUHS) are additionally run through SELANA+ for automatic evaluation.<br><br>Then for that day's retina images additionally run through SELENA+, the SELENA+ evaluations are compared against the SiDRP human grader evaluations to compare the human grader results vs the SELENA+ results.<br><br>This is done on a daily basis for the duration of this Phase 1 pilot in order to test how SELENA+ performs relative to human graders under actual clinical conditions. | Research and Clinical Practice |
| 2019 January | EyRIS company news story on "SELENA+, the Intelligent Deep Learning System to Prevent Diabetic Blindness." | First time EyRIS announces that the SELENA+ is their product offering.<br><br>News story states "Our team has developed a state-of-the-art artificial intelligence (AI) system to automatically perform primary assessment of retinal photographs, thus significantly reducing the public health care cost while maintaining its standard."<br><br>The news release mentions the "test results" reported in the 2017 December JAMA paper.<br><br>The press release does not make any mention of the role of SERI/SNEC and NUS played in publishing the 2017 December JAMA paper or in the development of SELENA+. | Commercial |
| 2019 January | Ping An Insurance Group (China) announces that the Ping An Voyager Fund has invested in Airdoc, a Chinese company also with an office in the US that specializes in medical AI solutions.<br><br>Beijing Airdoc Technology's product portfolio also includes a deep learning AI solution for analysing | As of Dec 2022, Airdoc's market capitalisation is HK$1.55 billion, equivalent to US$200 million.<br><br>This is an example of the type of competition that EyRIS is facing from other international efforts. | Commercial Competition |

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| | eye retina images to screen for diabetic retinopathy.<br><br>Two other major global competitors providing a deep learning based AI system for analyzing retina images for diabetic retinopathy include:<br><br>Eyenuk (EyeArt product)<br>See 2020 August item on Eyenuk<br>See 2022 October item on Eyenuk<br><br>Digital Diagnostics (IDx-DR product)<br>See 2018 April item on IDX-DR/Digital Diagnostics<br>See 2022 August item on Digital Diagnostics | As part of its automatically generated report, the Airdoc deep learning system for analysing eye retina images also provides a heat map visualisation showing the location of the detected lesions.<br><br>The EyRIS autogenerated report does not provide this type of heat map visualisation showing the location of the detected lesions.<br><br>However, EyRIS has the advantage of trust associated with growing out of Singapore public sector R&D and strong supporting scientific publications (e.g., the JAMA Dec 2017 paper). | |
| 2019<br>May | Study on "AI Deep Learning to Screen for Vision Threatening DR in Africa: Clinical Validation Study," published in Lancet Digital Health (lead by SERI/SNEC and NUS SoC and other Singapore and international collaborators).<br><br>Key implication of study:<br>Even in a low resourced country like Zambia, it is possible to use SELENA+ to do eye screening, and this can be done without having a SiDRP-like central ocular reading centre to confirm judgements. In essence, the ability of SELENA+ to do fully automated retina image evaluations is of sufficient quality that it is better than the alternative of no screening at all.<br><br>Study also provides additional validation and benchmarking of SELENA+ performance using one additional external population. | From the conclusion of the paper:<br>"In conclusion, our study shows a clinically acceptable AI system in detection of referable diabetic retinopathy, vision-threatening diabetic retinopathy, and diabetic macular oedema for the Zambia population. Future research is needed to evaluate the cost-effectiveness of such sophisticated technology for diabetic retinopathy screening worldwide, especially for those countries with little access to health-care services." | Research |
| 2019<br>July | SERI and National University of Singapore (NUS) sign a Technology Development Agreement on 24th July 2019.<br><br>One important clause of this agreement is that the commercial spin-off EyRIS would not charge any licensing fees for using SELENA+ to Singapore public sector healthcare institutions, | | Commercial |
| 2019<br>September | SiDRP receives the National Clinical Excellence Team category Award that was one of the categories of the 2019 Ministry of Health National Clinical Excellence Awards announced 05 Sept 2019<br><br>Importance of receiving this national award:<br>It was an acknowledgement from Singapore's Ministry of Health that the SiDRP approach to eye disease screening and image evaluation via a centralized ocular reading centre (vis-a-viz the prior approach) changed and improved the model of care. | National Healthcare Group (NHG) Centre for Healthcare Innovation summary document on SiDRP and its impacts-related to SiDRP winning the 2019 MOH team award for clinical excellence – based on SiDRP background from 2013 through most of 2019.<br><br>Note: document includes mention that there are plans to further enhance efficiency of SiDRP by making use of SELENA+ in the future. | Clinical Practice |
| 2019<br>Sept | Study on "Artificial intelligence for diabetic retinopathy screening: a review," is published in Nature Eye (led by international researchers from Poland with SERI and NUS SoC co-authorship. | The paper concludes:<br>"A number of systems for automatic detection of DR are already available commercially, with others in the pipeline | Research And Commercial Competition |

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| | A summary of international work and progress in this area. The following major international efforts that have published results are highlighted in detail:<br>• IDx-DR (from Digital Diagnostics)<br>• RetmarkerDR<br>• EyeArt (from Eyenuk)<br>• Google<br>• Singapore SERI-NUS (the origins of EyRIS)<br>• Bosch DR algorithm<br>• Retinalyze<br>• And several other systems are mentioned<br><br>They note "…However, only a few of these are currently commercially available."<br><br>They note, "One of the biggest hurdles to overcome in the development of such systems is the acquisition of a sufficiently large set of retinal images on which to train and validate those algorithms. Confidentiality, data protection and other regulations are just some of the difficulties in obtaining a sufficiently large dataset. In addition, such images need to be human-graded and labelled as a reference standard, which is a significant time and cost sink." | and others still in early development. Nevertheless, regardless of development phase, most of those systems are still being actively developed with changes and improvements to detection algorithms, user interface, scalability, better detection of DMO, etc. in progress.<br><br>"A head-on comparison of the available systems has so far proven very difficult, for multiple reasons. Depending on the system, the output may be tuned for a different outcome—DR present/absent, referable DR present/absent, no DR/referable DR/Sight-threatening DR outcome, or others. Sensitivity and specificity data between detecting any DR and referable DR are not directly comparable for multiple reasons, such as differences in reference standards and grader capabilities; the cut-off for referable DR for example, may not always correspond with the same ETDRS grading level between two studies. In real-world situations, the cut-off for referable DR may be different between regions, depending on available resources."<br><br>Per the Singapore SERI-NUS effort, the article states:<br>"This is one of the few AI systems described that could also detect non-DR pathologies. It may therefore be used in a DR screening setting to detect non-DR related, but potentially sight-threatening conditions (e.g. glaucoma suspect and AMD) that may require intervention in tertiary settings." | |
| 2019 October | Nova Group announces that EyRIS obtained regulatory approval from the Singapore HSA for the company's first medical device, "an effective assistive tool in the diagnosis of 3 eye diseases, diabetic retinopathy (DR), Glaucoma and Age-Related Macular Degeneration (AMD). " | The SELENA+ deep learning system is now approved for regular clinical usage in Singapore as a medical device for eye disease diagnostic screening (DR, Glaucoma, AMD). Using SELENA+ for screening retina images for these eye diseases is now recognized as being part of the "standard of care."<br><br>This regulatory approval means SiDRP can now make use of SELENA+ to analyse SiDRP retina images without having to obtained signed consent from a patient to participate in a research trial study to evaluate SELENA+. Prior to this approval, all usage of SELENA/SELENA+ related to Singapore's SiDRP effort required the participating patients to sign a consent form for participating in a research study.<br><br>Similarly, EyRIS can now offer the services of using SELENA+ to private sector | Regulatory and Commercial |

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| | | practitioners without patients having to sign a consent form. Also, SELENA+ can be used as an eye disease screen tool independently of SiDRP. As in, with this regulatory approval, private sector or non-profit entities can make use of SELENA+ for eye screening without having to go through the SiDRP programme. (Though there are some differences in the nature of the report generated of using SELENA+ in the SiDRP context vs using it stand-along outside of the SiDRP context). | |
| 2019 October through 2020 September<br><br>About 12 months | In-depth discussions and contract negotiations directly between EyRIS and IHiS to work out the commercial contract terms for SiDRP to licence the use of SELENA+ from EyRIS (as EyRIS is the official party that received the Singapore HSA regulatory approval and is the entity that owns the licence for using the SELENA+ IP).<br><br>SiDRP staff from SNEC and from TEI provide inputs on requirements to IHiS which IHiS uses as part of determining contract requirements.<br><br>Based on this finalized contract, SELENA+ is integrated into the national BRAIN platform managed by IHIS.<br><br>The SNEC/SiDRP clinicians who are also co-founders of EyRIS (Wong Tien Yin, Daniel Ting, Haslina Hamzah and Dr Gavin (Advisor)) were not allowed to participate in these discussions to avoid conflicts of interest.<br><br>Other members of SNEC/SiDRP including Dr. Fang Xiaoqin and Mr Lee Kai Yin representing the interests of SiDRP and SNEC. | These were complex and protracted discussions that took about one year as the contract completion was not announced till September 2020. | Commercial |
| 2019 November | Singapore Smart Nation and Digital Government Office (SNDGO) releases National Artificial Intelligence Strategy document.<br><br>SELENA+ is highlighted as a key national AI application initiative in the public healthcare sector in order to improve disease prediction and management.<br><br>The SNDGO National AI Strategy document. See mention of SELENA+ on page 30 of this document. | This gives SELENA+ further expanded national and international visibility as it is one of the few specifically named "products" mentioned in this National AI Strategy document.<br><br>Deputy Prime Minister Heng Swee Kiat highlights the usage of SELENA+ as national AI strategy public healthcare use case example during his opening speech for the Singapore FinTECH Festival in November 2019. | Clinical Practice and Commercial |
| 2020 January | The Say No to Vision Loss collaboration is launched in Singapore by Zero Vision Loss ("ZVL"), a collaborative initiative between the Singapore Optometric Association and EyRIS to provide eye screening services using EyRIS's SELENA+ product at dedicated EyRIS-partnered participating optometrists.<br><br>This is the first customer revenue for EyRIS for its SELENA+ product. | This partnership introduced a Zero Vision Lost Eye Screening Package for S$25, a 10 minute scan.<br><br>The Package includes the following services:<br>• Acquisition of fundus images of your left eye and right eye by an Optometrist using a fundus camera; | Commercial |

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| | This very first contract for customer revenue comes from private sector optometrists in Singaore and not from the Singapore public sector.<br><br>While agreements with private sector entities like the Singapore Optometric Association (SOA) and its member optometrists does not have the scale of public sector contracts, such contracts with other private sector entities are less cumbersome and therefore faster to put into place. | • Evaluation of fundus images using SELENA+ with a view to identifying the following possible health concerns:<br>  ○ Diabetic Retinopathy;<br>  ○ Glaucoma Suspect; and<br>  ○ Age-Related Macular Degeneration;<br>• Amsler Chart Test; and<br>• Objective Refraction Test.<br><br>Any other services or consultations required or rendered may be subject to further charges by the Optometrist or other healthcare professionals | |
| 2020 March | EyRIS receives notification of its SELENA+ product passing the European Union conformity assessment giving EyRIS approval to use the EU's CE mark on its product.<br><br>EyRIS' SELENA+ Medical IA device is now approved for usage within the EU.<br><br>This submission and review process goes much faster than the initial regulatory submission to Singapore's HSA for the following reasons:<br><br>1. The submission was largely based on all the prior documentation already used to obtain regulatory approval from Singapore's HSA.<br>2. EyRIS is now more familiar with regulatory processes and submission requirements.<br>3. By this time, regulatory authorities in more countries around the world have more experience with submissions for AI medical devices.<br>4. By now there are precedents in other countries (e.g. Singapore, US) for approved AI medical devices using deep learning methods to screen for diabetic retinopathy and other eye diseases.<br><br>EyRIS co-founders from SERI/SNEC and from NUS provide supporting research, clinical and deep learning/AI related knowledge and inputs to EyRIS regulatory team (including EyRIS regulatory consultants) to support preparation and submission of regulatory documents.<br><br>Same points on regulatory efforts moving more quickly – relative to the very first submission – made above also apply to al other concurrent and subsequent EyRIS regulatory submissions and approvals. | From https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices<br><br>Manufacturers can place a CE (Conformité Européenne) mark on a medical device once it has passed a conformity assessment.<br><br>The conformity assessment usually involves an audit of the manufacturer's quality system and, depending on the type of device, a review of technical documentation from the manufacturer on the safety and performance of the device. | Regulatory |
| 2020 April | EyRIS receives approval from the Malaysia Medical Device Authority (MDA) for its SELENA+ product.<br><br>EyRIS' SELENA+ Medical IA device is now approved for usage within Malaysia | https://portal.mda.gov.my/industry/overview-of-regulatory-medical-device.html | Regulatory |

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| 2020<br>April | Study on "Artificial intelligence for teleophthalmology-based diabetic retinopathy screening in a national programme: an economic analysis modelling study" published in Lancet Digital Health (led by SERI, SNEC, NUS, and Tan Tock Seng Hospital Eye Institute).<br><br>While SELENA+ is not specifically mentioned in this publication, the deep learning system referred to is SELENA+. | From the conclusion:<br>"This study presents one of the first health economic evaluations of competing models for implementing a DLS (deep learning system) designed to screen for referable diabetic retinopathy… We showed that a semi-automated model combining the deep learning system with human assessment could achieve the best economic return in screening for diabetic retinopathy… Although the fully automated model completely removes human grading, the semi-automated model, which lowers grading costs by only 74%, yields greater savings. This is because of a higher rate of false positives, and therefore more unnecessary specialist visits, under the fully automated model. The higher costs of graders in the semi-automated model is more than offset by the lower consultation costs. However, this is again based on the wages in Singapore, and might not apply to other settings. | Research |
| 2020<br>April | Dentist and oral surgeon Steven ANG becomes joins Nova Group (under LAI Teik Kin) as Vice President of Business Development. | Steven Ang starts to work with Lai Teik Kin on business development for Nova Group, focusing on business development for healthcare applications.<br><br>Later on, in Jan 2021, Steven Ang becomes Senior Vice President of Business Development for EyRIS and focuses full time on EyRIS business development and the SELENA+ product as well as plans for future EyRIS products. | Commercial |
| 2020<br>April | Study on "A Human-Centered Evaluation of a Deep Learning System Deployed in Clinics for the Detection of Diabetic Retinopathy" is published in Proceedings of 2020 ACM SIG-HCI conference (led by Google health and a Thai collaborator).<br><br>" Through field observations and interviews at eleven clinics across Thailand, we explored the expectations and realities that nurses encounter in bringing a deep learning model into their clinical practices."<br><br>This study was done in partnership with the Ministry of Public Health in Thailand to conduct field research in 11 rural clinics across the provinces of Pathum, Thani and Chiang Mai.<br><br>The authors note:<br>"Given that the deep learning system was deployed in an observational, prospective study, it was critical for nurses to obtain patient consent prior to using the system. The informed consent process was the first challenge we observed, and was made more complicated by the need to explain the deep learning system." | From their concluding discussion<br>"Our research highlights that end-users and their environment determine how a new system will be implemented; that implementation is of equal importance to the accuracy of the algorithm itself, and cannot always be controlled through careful planning.…<br><br>…Complexity across factors (e.g., medical conditions treated, organizational structure) increased the likelihood of non-adoption. When introducing new technologies, planners, policy makers, and technology designers did not account for the dynamic and emergent nature of issues arising in complex healthcare programs. The authors argue that attending to people—their motivations, values, professional identities, and the current norms and routines that shape their work—is vital when planning deployments.<br><br>… Our findings suggest that even when a deep learning system performs a relatively straightforward task (e.g., focuses on | Research on clinical practice challenges |

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| | | retinal images and does not cross into multiple domains, organizational implementation challenges, or policy challenges), socio-environmental factors are likely to impact system performance. “ | |
| 2020 May | Study on “A deep learning algorithm to detect chronic kidney disease from retinal photographs in community-based populations” published in Lancet Digital Health (led by SERI, Duke-NUS Medical School, NUS, other Singapore and international collaborators).<br><br>“In this study, we developed and validated a DLA for predicting chronic kidney disease from retinal images and compared this with two DLA (deep learning algorithm) models, one using classic clinical risk factor (RF) data and another using both retinal and RF data.”<br><br>Note:<br>This is a different deep learning system developed by the SERI and NUS team. It is a separate from the SELENA+ deep learning system.<br><br>The size of the data sets used to train and validate this model were much smaller than those used to train and validate SELENA+.<br><br>“We developed and internally validated the DLAs using data from the Singapore Epidemiology of Eye Diseases (SEED) study (5,188 patients to develop, 1297 to internally validate ), and externally tested the DLAs on two independent datasets: the Singapore Prospective Study Program (3,735 patients) and the Beijing Eye Study (1,538 patients).” | From the interpretation:<br>“A retinal image DLA (deep learning algorithm) shows good performance for estimating chronic kidney disease, underlying the feasibility of using retinal photography as an adjunctive or opportunistic screening tool for chronic kidney disease in community populations.”<br><br>From the discussion:<br>“…Our results indicate that chronic kidney disease can be accurately detected from retinal images without knowledge of specific retinal signs (eg, retinopathy).”<br><br>“The major strengths of this study are the development and validation of an algorithm based on retinal image only, which is simple and easy to obtain at primary care or community level. We were also able to have two independent population-based cohorts with similar imaging and chronic kidney disease protocol to validate our algorithm.” | Research<br><br>Expanded use of eye retina image analysis |
| 2020 June | Commentary on “Three Insights From Google's 'Failed' Field Test To Use AI For Medical columnist” published in Forbes (by David Talby).<br><br>Talby’s comments are based on his reading of the Google Health paper (2020 April) "A Human-Centered Evaluation of a Deep Learning System Deployed in Clinics for the Detection of Diabetic Retinopathy."<br><br>The combination of the Google Health field study and this Forbes column by David Talby provide a deeper understanding of the “on-the-ground” implementation and deployment issues encountered, especially in – but not limited to - developing countries. | The main points made in the column:<br><br>First, there is a difference between research and engineering, and research studies like this one should be heralded for the progress they enable.<br><br>Second, there must be an understanding of what it takes to get an AI system from idea to production.<br>• Science<br>• Engineering<br>• Process change<br><br>The third insight from this new study is based on the major differences between the 11 clinics that took part in it. The researchers reported major differences between them — from how the physical rooms at each clinic were laid out to the personalities and background of the nurses who worked there. Asa result, the trained model could not successfully operate at each of these distinct environments… | Commercial per clinical practice challenges |

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| | | Medical AI models generally perform poorly across locations. This not only applies to models deployed in Thailand versus Nigeria but also models deployed in two clinics that are 5 kilometers apart and serve essentially the same population. This happens in both first-world and third-world countries and across just about every medical specialty that's taken the time to measure it. | |
| 2020 July | Study on "The Evolution of Diabetic Retinopathy Screening Programmes: A Chronology of Retinal Photography from 35 mm Slides to Artificial Intelligence" published in Clinical Ophthalmology (led by a UK author team.)<br><br>SERI/SNEC/NUS participants in SiDRP and SELENA+ are not involved in this publication.<br><br>SiDRP is one of the main worldwide diabetic retinopathy national screening efforts highlighted.<br><br>Data in this paper shows the Singapore SiDRP national diabetic retinopathy screening programme to be the 2nd largest effort in the world, with only the UK's national screening effort involving more screening exams per year.<br><br>This article implicitly provides information on EyRIS potential addressable markets (other national-level diabetic retinopathy eye screening programmes) as well as other international competitors (other automated image analysis systems being used). | Summarises national diabetic retinopathy screening programmes in 7 seven countries (UK + 6 others):<br>• England (UK)<br>• Scotland (UK)<br>• Wales (UK)<br>• Northern Ireland (UK)<br>• Singapore<br>• Iceland<br>• Australia<br>• Finland<br>• USA<br>• Spain<br><br>Also summarises use of various automated image analysis systems for diabetic retinopathy screening – both before and after machine learning AI systems – in use in seven countries:<br>• UK<br>• Denmark<br>• Portugal<br>• USA<br>• Singapore<br>• Netherlands<br>• India | Research |
| 2020 August | News release from Eyenuk, a competitor to EyRIS:<br>"Eyenuk Announces FDA Clearance for EyeArt Autonomous AI System for Diabetic Retinopathy Screening."<br><br>The news release states, "EyeArt is the First FDA Cleared AI Technology for Autonomous Detection of Both More than mild and Vision-Threatening Diabetic Retinopathy."<br><br>Eyenuk website<br>Eyenuk was founded in 2010 in the US. | | Commercial Competition |
| 2020 September | EyRIS new release announcing "EyRIS was awarded a 5-year contract for the deployment of SELENA+, an deep learning system to detect diabetic retinopathy, glaucoma and age-related macular degeneration in the Singapore Integrated Diabetic Retinopathy Program (SiDRP)."<br><br>The contracting on behalf of Singapore's public healthcare system and SiDRP was done by IHiS, the national healthtech agency. This IHiS contract | The EyRIS news release also states<br>• "This award is not only a milestone for EyRIS **but also a world first in showcasing real world adoption of an artificial intelligence medical device in a national screening program."**<br>And<br>• EyRIS's SELENA+ is also deployed in 23 private optometric practices in | Commercial |

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| | with EyRIS gives options for annual renewal for up to five years and enables SiDRP to use the EyRIS product SELENA+ for eye screening.<br><br>The contract specifies that Singapore's public healthcare system (represented contractually by IHiS) would pay usage fees to EyRIS to cover a maximum of 120,000 SiDRP patients processed per year by SELENA+. | Singapore on the "Say No To Vision Loss" platform. | |
| 2020 Sept thru November | SiDRP, IHiS and EyRIS work together to make the necessary IT system and data management upgrades to make it possible to start incorporating the EyRIS SELENA+ product into the regular SiDRP operational workflow. | | Clinical Practice and Commercial |
| 2020 October | EyRIS receives approval from the Brazil Medical Device Regulatory Authority (ANVISA) for its SELENA+ product.<br><br>EyRIS' SELENA+ Medical AI device is now approved for usage within Brazil. | | Regulatory |
| 2020 November | EyRIS announces partnership with Topcon Health Solutions to roll out SELENA+ together with Topcon's Harmony RS eye screening product across 18 Asian Countries.<br><br>Topcon is a Japanese headquartered multinational focused on products based on optics, mechatronics and electronics. Topcon Healthcare is their business unit focusing on high performance retinal imaging products for eye examinations and screening. | | Commercial |
| 2020 December to 2021 December<br><br>12 months | SiDRP (SNEC + NHG Eye Institute) + SERI + NUS + plus IHiS team plus EyRIS do Phase 2 testing and piloting of integrating SELENA+ within SiDRP operational workflow.<br><br>Infrastructure is now in place for all SiDRP retina screening images taken at polyclinics and transmitted to the central ocular reading centre via the national tele-ophthalmology network to be processed by SELENA+ as part of the workflow – prior to being viewed by a human grader.<br><br>At this point in time, there are now two central ocular reading centres: the initial one at SNEC (on the SingHealth campus) and a second one at the National Healthcare Group's Eye Institute located at Tan Tock Seng Hospital (though the second reading centre at the Tan Tock Seng Eye Institute started Phase 2 SiDRP operations with SELENA+ one year after the first reading centre at SNEC<br><br>At start of this Phase 2 testing and piloting, 12 polyclinics (out of 20) are participating in the SiDRP screening effort.<br><br>Over this 12-month period, the remaining eight existing poly clinics plus three new poly clinics (for a total of 23) are gradually brought on board to the SiDRP screening program via the national tele-ophthalmology network. | Now every image obtained through SiDRP is initially automatically evaluated by SELENA+.<br><br>SiDRP still retains a Level 1 human grader to do a real-time check on all (100%) of SELENA's image evaluations, including those that are assessed as neither requiring referral nor requiring clarification.<br><br>As per the prior SiDRP workflow, any retina image assessed as requiring referral for any of the three eye diseases, or that requires special clarification, additionally goes to the Level 2 human grader.<br><br>Data continues to be gathered on SELENA+ evaluation accuracy compared to human grader assessments.<br><br>Even though SiDRP still retains the human Level 1 grader for checking all SELENA+ outputs, time taken for image evaluation for the Level 1 graders is reduced because of SELENA+'s pre-processing and results to aid the assessment<br><br>Clinical staff involved in SiDRP (from SNEC and SERI and the two central ocular | Clinical Practice and Research and Commercial |

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| | Both SNEC and TEI internally funded the integration cost of SELENA+ to SIDRP, without any external grant funding or support. | reading centres) hold periodic review discussions with MOH policy makers to review performance of SELENA+ and its impact on overall SiDRP performance, operations and cost.<br><br>Also, clinical staff involved in SiDRP continue to do fine tuning of SELENA+ system, including regular calibration studies and fine-tuning refinements- and other workflow improvements. | |
| 2021 January | EyRIS receives approval from the Malaysia Medical Device Regulatory Authority (RAMS) for its SELENA+ product.<br><br>EyRIS' SELENA+ Medical IA device is now approved for usage within Indonesia. | | Regulatory |
| 2021 January | EyRIS signs MOU to partner with Diabetes Singapore to offer eye screening for diabetic retinopathy.<br><br>In Singapore, a significant number of private sector Primary Care Network (PCN) groups send diabetic patients to Diabetes Singapore for diabetic screening.<br><br>This agreement with Diabetes Singapore was a milestone for EyRIS for two reasons:<br>1) Working with Diabetes Singapore gave EyRIS large coverage (and correspondingly large market share) for eye screening across the private sector PCNs within Singapore.<br><br>2) It demonstrated the adoption of SELENA+ by an important national non-profit organization. | The MOU with Diabetes Singapore (DS) is to collaborate on several key objectives:<br>• Improving the productivity, competency and cost-effectiveness of Diabetes Singapore through using Artificial Intelligence (AI) for the screening of retinal diseases<br>• Promoting the importance of eye screening for detection of early-stage diabetes to prevent vision impairment<br>• Increasing awareness of diabetic patients to have their eyes screened annually | Commercial |
| 2021 May | Study on "Multicenter, Head-to-Head, Real-World Validation Study of Seven Automated Artificial Intelligence Diabetic Retinopathy Screening Systems" published in Diabetes Care (led by University of Washington Medical School team).<br><br>No Singapore affiliated researchers from SERI/SNEC or other Singapore are involved in this publication.<br><br>This University of Washington Medical School study evaluates of the performance of AI-based diabetic retinopathy screening algorithms from five international companies:<br>• two in the United States (Eyenuk, Retina-AI Health),<br>• one in China (Airdoc),<br>• one in Portugal (Retmarker)<br>• and one in France (OphtAI) | According to January 05 2021 University of Washington press release summarizing this forthcoming article:<br>"The researchers found that the algorithms don't perform as well as they claim….Three of the algorithms performed reasonably well when compared to the physicians' diagnoses and one did worse. But only one algorithm performed as well as the human screeners in the test."<br><br>Key point:<br>• The press release and related journal article also conveys a sense of scepticism from some in the medical community of using AI/ML/deep learning trained algorithms for this type of screening—because of the difference between using carefully curated and controlled and "clean" clinical data vs using the types of images that are generated and | Research<br><br>And<br><br>Commercial Competition |

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| | This list gives examples of five other international competitors to EyRIS.<br><br>The SERI team (which therefore would mean EyRIS) was invited to participate in this evaluation but chose not to submit their model to be used for evaluation. The EyRIS decision not to participate (in consultation with SERI) was based on various commercial, practical and competition related considerations. | evaluated under more real-world clinical practice conditions across various national settings. | |
| 2021 May | EyRIS announces partnership with Eyeviser to support home-based eye examinations.<br><br>Eyeviser is a network of network of experienced optometrists and ophthalmologists in Singapore and Malaysia.<br><br>This partnership between Eyeviser added to the EyRIS partnership's with private entities in Singapore.<br><br>Strategically, it demonstrated SELENA+'s capability for supporting mobile screening.<br><br>Until this point in time, eye screening for diabetic retinopathy, glaucoma and AMD had always been done by bringing patients to clinics or hospitals. This new approach allowed EyRIS to explore the possibility of bringing the eye screening to patients.<br><br>COVID has also highlighted the need to move screening out from hospitals and into the community and home, and during the Covid peak periods, more home based care scenarios were developed.<br><br>This partnership also allowed EyRIS to test a new business model based on supporting home based screening. | The MOU with Eyeviser is to collaborate on several key objectives:<br>• Improve productivity and competency of Eyeviser in conducting home-based/mobile retinal screening program<br>• Scale up home-based/mobile services through the use of EyRIS' products<br>• Promoting the importance of eye screening for detection of early-stage diabetes to prevent vision impairment<br>• Increasing awareness of patients to have their eyes screened annually | Commercial |
| 2021 July | MIRXES, a Singapore biotech company that developed technology to analyze mRNA samples for diagnostic disease screening, announces US$77m in new funding, raising the company's valuation to ~ US$500 million.<br><br>MiRXES is in a totally different area of medical technology than EyRIS as MIRXES analyses mRNA samples to screen for multiple types of disease.<br><br>The reason for mentioning MIRXES is that they illustrate a "new model" of using a common diagnostic approach (in this case based on mRNA analysis) to screen for multiple types of diseases as part of one consolidated analysis effort based on a single sample of an individual person's mRNA data. | Steven Ang, the EyRIS SVP for Business Development, points to this MIREX example as a vision for future EyRIS products and services - where one day a person provides their retina image--- and a common AI platform - with multiple types of appropriately trained deep learning AI models - screens for multiple types of diseases-<br>• Eyes (DR, glaucoma, AMD), and also in an desired future:<br>• Chronic Kidney Disease<br>• Some aspects of chronic heart disease<br>• Some aspects of brain disease (e.g., Alzheimers).<br><br>The EyRIS clinical co-founders Dr Wong and Dr Ting and the EyRIS commercial team | Commercial<br><br>Related to venture funding environment |

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| | The MiRXES example also demonstrates that some segments of medical diagnostic testing are attracting large sums of investment money to help fund new R&D, scaling and further market expansion. | knows this is in the realm of the possible. At the same time, they fully acknowledge the very difficult institutional and cultural challenges of getting multiple areas of medical clinical practice to agree on clinical practices for this type of unified screening using eye retina images.<br><br>At the same time, the concept of using blood and now mRNA as "data" to do a consolidated screening for multiple types of disease has become accepted medical practice. So maybe in the future, a similar concept of using eye images to scan for multiple types of medical diseases will become more widely accepted. | |
| 2021 Sept With an update on 2022 January | US Medicare (through the Center for Medicare and Medicaid Services) announces a new billing code for "Remote Imaging of the Retina to Screen for Retinal Diseases."<br><br>This means the US Medicare system has approved the ability to bill for a the type of diabetic retinopathy diagnostic screening procedure – as per the day it is done by the EyRIS SELENA+ product – as per the conditions stated above.<br><br>This strengthens ability for EyRIS and for other companies in this area to pursue commercial opportunities in the US. | The Center for Medicare and Medicaid Services notification states:<br>"Noridian (a Medicare contracts 3rd party administrator) allows coverage for CPT® Code 92227 Imaging of Retina for detection or monitoring of disease; with remote clinical staff review and report, unilateral or bilateral, for the early detection of diabetic retinopathy in patients with Type I diabetes for greater than five years or Type II diabetes at the time of diagnosis on an annual basis until such time as such retinopathy is detected. CPT® 92229 allows coverage for Imaging of retina for detection or monitoring of disease; point-of-care automated analysis and report, unilateral or bilateral. Once retinopathy is detected the patient should be under the direct care of an ophthalmologist but on occasion a need may arise where remote acquisition of retinal images is medically necessary. For those times 92228 or 92229 is billed. | Commercial Related to opportunity in the US market |
| 2021 October | SingHealth announces an upcoming leadership change of Singapore National Eye Centre (SNEC) as of 01 January 2022.<br><br>Wong Tien Yin will be stepping down as Chair and Medical Director of SNEC and also relinquish his role as chairman of SERI. | As of 01 January 2022, Dr Wong will transition to being a Senior Advisor for SingHealth and a senior consultant ophthalmologist (part-time) at the Singapore National Eye Centre.<br><br>He will retain his academic affiliations with NUS Medical School and with Duke-NUS Medical School. | Research and Clinical Practice |
| 2021 October | EyRIS announces "New Deep Learning Algorithm To Detect Chronic Kidney Disease." | "EyRIS is excited to introduce another Deep Learning Algorithm (DLA), this time to detect Chronic Kidney Disease (CKD). Jointly developed by the clinicians and scientists from the Singapore Eye Research Institute and the National University of Singapore (NUS) School of Computing, this new DLA can detect early stages of CKD through automated analysis of fundus retinal images."<br><br>This is a follow up on the 2020 May Lancet Digital Health publication by the | Commercial<br><br>Expanded use of eye retina image analysis |

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| | | SERI/SNEC/NUS team with other collaborators. | |
| 2021 November | Tsinghua University (China) announces formation of a new academic system, Tsinghua Medicine which includes a new medical school. As of 01 January 2022, the Founding Head will be Professor Wong Tien Yin who is appointed University Professor at Tsinghua. | As of 01 January 2022, Dr Wong assume his new role as Founding Head of Tsinghua Medicine and Tsinghua University Professor.<br><br>The Tsinghua announcement states: "Professor Wong will also be developing new international networks and partnerships with top medical schools and academic healthcare systems in the US, Europe, Asia and Singapore." | Research and Clinical Practice |
| Jan 2022 thru Dec 2022<br><br>12 months | SiDRP is running at full scale with all 23 polyclinics participating in SiDRP screening. There are also other designated locations across Singapore's public, private and non-profit healthcare sector also offering SiDRP screening (as has been the case for several years already).<br><br>All (100%) of all SiDRP images are initially evaluated automatically by SELENA+ and results are shown to aid Graders in their assessments.<br><br>In this one-year period, 110,000 patients' visits are processed by SiDRP using SELENA+. Each patient visit produces a minimum of four eye retina images to be analysed.<br><br>This demonstrates that EyRIS' SELENA+ product has effectively been adopted as a screening evaluation tool on a national level on a production basis.<br><br>This approach of using SELENA+ on a large-scale production basis within SiDRP showed improvements both in efficiency and scalability towards Singapore's standard of care for diabetics per eye related disease screening and treatment. | SiDRP continues to retain a human Level 1 grader to do a real time check of every SiDRP image evaluation. Role of human Level 2 grader continues unchanged.<br><br>Data continues to be gathered on SELENA+ evaluation accuracy compared to human grader assessments.<br><br>Clinical staff involved in SiDRP (from SNEC and SERI and the two central ocular reading centres) continue to hold periodic review discussions with MOH policy makers to review performance of SELENA+ and its impact on overall SiDRP performance, operations and cost.<br><br>Possibility of eliminating need for human Level 1 review of every image analysed by SELENA+ is raised and reviewed. Decision is made to still retain human Level 1 "assurance" check of all SELENA+ images through this period as part of ongoing performance validation and benchmarking.<br><br>SiDRP team and EyRIS continue to periodically do calibration checks and work on various fine-tuning refinements to keep incrementally and steadily optimize SELENA+ performance- though without making any major changes to the model. | Clinical Practice and Commercial |
| 2022 January | EyRIS is named winner in the MOST PROMISING INNOVATION category of Singapore's Techblazer Awards. | The Techblazer Awards is Singapore's nation's highest accolade for commercial tech innovation and aims to provide recognition and endorsement to Singapore-based organisations that have exemplified the spirit of innovation in their development of tech products and services, or their use of tech to achieve excellence. | Commercial<br><br>National level recognition |
| 2022 Feb | EyRIS announces partnership with National Healthcare Group's Centre For Medical Technologies & Innovations To Develop AI To Detect Melanoma. | "The planned deep learning algorithm will leverage big data and advanced clinical assessment techniques to accurately evaluate skin lesions based on the dermatological standard known as the ABCD's of Melanoma (Asymmetry, | Research and Clinical Practice |

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| | National Healthcare Group is one of the three large Singapore public healthcare clusters.<br><br>The partnership to develop a new proprietary AI that detects melanoma using a mobile phone camera.<br><br>This is the first effort by the company EyRIS to develop an AI-based diagnostic support tool that is not based on using eye retina images. | Borders, Colour and Dermatoscopic features)." | |
| 2022 February | Nova Group (Malaysia), as the exclusive distributor of EyRIS products in Malaysia, signed a Memorandum of Understanding with the Association of Malaysian Optometrists (AMO) and Rhazes Consultancy Services Sdn Bhd (RHAZES), a tele-pharmacy platform provider, to bring its AI Deep Learning Technology, SELENA+ to mainstream adoption in Malaysia.<br><br>Even though Malaysia in the neighboring country is only just "across the causeway" from Singapore, this agreement represents a significant international expansion for EyRIS outside of Singapore.<br><br>Via this agreement and the resulting increasing EyRIS adoption through the AMO membership, it has opened up over 2000 optometric practices spread across Malaysia as potential touchpoints for expanding the EyRIS user base. | Under the collaboration, EyRIS' AI deep learning technology, SELENA+, will be deployed to AMO's more than 1,000 members across Malaysia via RHAZES Telehealth. RHAZES Telehealth is Malaysia's first knowledge-based telehealth service provider through its brand Rhazes TeleOpto. | Commercial |
| 2022 March | EyRIS receives approval from the South Africa Medical Device Regulatory Authority (SAHPRA) for its SELENA+ product.<br><br>EyRIS' SELENA+ Medical AI device is now approved for usage within South Africa. | | Regulatory |
| 2022 June | SNEC announces that "Scientists from the Singapore Eye Research Institute (SERI) have developed two novel screening tools for detecting chronic kidney disease (CKD) and predicting one's biological age. These tools, dubbed RetiKid and RetiAge respectively, use artificial intelligence-based deep learning algorithms to scan photos of patients' retina."<br><br>"RetiKid has been licensed to health tech start-up EyRIS for further productisation, regulatory clearance, commercialisation and market expansion to benefit more patients."<br><br>"Both RetiKid and RetiAge can potentially be integrated with the Singapore Eye Lesion Analyser Plus (SELENA+) – a retinal image-based deep learning system also developed by SERI and licensed to EyRIS – which is currently available at all polyclinics for patients to screen for diabetic eye diseases, glaucoma and age-related macular degeneration. This enables patients to be screened for more diseases with one image. " | "Developed by SERI and the National University of Singapore's School of Computing in 2019, RetiKid was tested with over 23,000 retinal images from close to 12,000 study participants from Singapore and China. Results of the study were published in The Lancet Digital Health in May 2020."<br><br>"The RetiAge algorithm, developed by SERI and South Korean healthcare start-up Medi Whale Inc. in 2021, was trained using more than 129,000 retina photos from over 40,000 participants from South Korea to predict the probability of a person having an "older" retina. The researchers then further evaluated RetiAge's ability to predict a person's 10-year risk of systemic disease and death, among some 56,000 participants in the UK Biobank. Results of the study showed that compared to people with the "youngest" retinas (the 1st quartile), those with "oldest" retinas (the | Research and Commercial<br><br>Expanded use of eye retina image analysis |

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| | "As imaging, cloud computing and mobile technologies advance, RetiKid also has the potential to be integrated into smart phones in the future. A point-of-care diagnosis can be given using a cloud-based RetiKid algorithm, from which healthcare providers can receive reports instantly."<br><br>From the Singapore Straits Times newspaper article on this topic (2022 June 17):<br>"Both RetiKid and RetiAge are pending clinical trials and approval by the Health Sciences Authority, and will be available to patients in about two years."<br><br>Adding RetiKID to the EyRIS product pipeline increases the company's services offerings, expanding from just retinal diseases detection to a much wider net of chronic disease detection.<br><br>This also brings EyRIS closer to their vision of being a game-changer in first-stage medical diagnostics based on the analysis of eye retina images. | 4th quartile) had double the risk of 10-year all-cause mortality, triple the risk of cardiovascular disease mortality and 1.7 times higher risk of cancer mortality, even though the two groups of people have the same chronological age." | |
| 2022 August | Digital Diagnostics, an EyRIS competitor (formerly named IDx), announces closing a US$75 million Series B Funding Round led by KKR. | News wire article states that Digital Diagnostic's total company investment raised now tops US$130 million. | Commercial Competition |
| 2022 August | EyRIS signs collaborative agreement with Remidio, a manufacturer of easy to use ophthalmic devices including fundus cameras.<br><br>Remedio website | EyRIS secures collaboration with Remidio to introduce a more seamless experience for users from image acquisition to uploading of images to receiving of results on an iPhone.<br><br>EyRIS devises plan to OEM cameras from Remidio and package AI image analysis for diagnostic screening as a single unified hardware-software product.<br><br>In the Singapore market, EyRIS introduces new strategy of giving the cameras away for free when a customer signs on for an annual package. | Commercial |
| 2022 September | Study on " A deep learning model for detection of Alzheimer's disease based on retinal photographs: a retrospective, multicentre case-control study" is published in Lancet Digital Health (led by team from Chinese University of Hong Kong with Singapore collaborators from SERI, NUS Medical School and Duke-NUS Medical School and other Singapore institutions).<br><br>5598 retinal photographs from 648 individuals with Alzheimer's disease and 7351 retinal photographs from 3240 people without the disease (for a total of 12,949 images) were used to train, validate, and test the deep learning models. | From interpretation:<br>"A retinal photograph-based deep learning algorithm can detect Alzheimer's disease with good accuracy, showing its potential for screening Alzheimer's disease in a community setting."<br><br>From discussion:<br>"Our deep learning algorithm showed consistently accurate performance for differentiating between patients with Alzheimer's disease-dementia and individuals with no dementia. In particular, the performance was similar for differentiating between people who were amyloid β positive from those who were | Research<br><br>Expanded use of eye retina image analysis |

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| | This is a different deep learning system developed by primarily by the Chinese University of Hong Kong team, though with strong collaboration from Singapore researchers. It is a separate from the SELENA+ deep learning system. | amyloid β negative. In addition, our deep learning algorithm had good performance in the presence of concomitant eye diseases (eg, age-related macular degeneration), thus allowing screening in optometry and ophthalmology settings."<br><br>"To the best of our knowledge, this is the first deep learning model to detect Alzheimer's disease from retinal photographs alone.<br><br>Our proof-of-concept study provides a unique and generalisable model that could be used in community settings to screen for Alzheimer's disease." | |
| 2022 October | EyRIS receives approval from the Thailand Medical Device Regulatory Authority (FDA) for its SELENA+ product.<br><br>EyRIS' SELENA+ Medical AI device is now approved for usage within Thailand. | | Regulatory |
| 2022 October | EyRIS signs distributor agreement with Intega, a pharmaceutical distribution company for 5 countries, primarily Malaysia, Indonesia, Thailand, Cambodia and Myanmar. | It is the first time a distributor sells the newl packaging of the EyRIS integrated AI software - hardware solution. | Commercial<br><br>Expansion |
| 2022 October | Eyenuk, a US-based competitor to EyRIS, secures US$26 Million Series A funding to accelerate global access to AI-powered eye-screening technology. | The newswire article states this brings Eyenuk's total funding to over US$43 million. | Commercial<br><br>Competition |
| 2022 November | EyRIS is named as one of the awardees for the Frontiers category in the inaugural edition of the AsiaStar 10×10 campaign. The award recognizes Southeast Asia startups that are developing deeply technical products for users in the region that are making an impact. | The inaugural edition of the AsiaStar 10×10 campaign, launched by Alibaba Cloud, is part of its Project AsiaForward initiative to foster and advance digitalization talents, digital entrepreneurs, and digital technologies across Southeast Asia. | Commercial<br><br>Regional recognition |
| 2022 December | EyRIS plans to announce product offering of using deep learning analysis of retina images to do diagnostic screening for Chronic Kidney Disease (CKD).<br><br>RetiKid is EyRIS' first vertical beyond diabetes, and demonstrates progress towards the EyRIS goal to take on a bigger role in screening for chronic disease detection.<br><br>Expanding into using retina images for CKD screening allows for a significant expansion of the potential user base for EyRIS. Patients who are more susceptible to CKD are not just diabetics, but also people with high blood pressure (hypertensive), and people with cardiac problems.<br><br>EyRIS views expanding into CKD diagnostic screening using retina images as just the beginning to achieving the changes in community | This is mentioned in the EyRIS marketing deck (slide 17), the 2nd slide on "Our Future."<br>This builds on<br>• 2020 May research publication in Lancet Digital Health by SERI/SNEC/NUS/International team paper on using deep learning for Chronic Kidney Disease screening using retina images and EyRIS' licensing of this technology from SNEC and NUS, and<br>• 2021 October EyRIS announcement about a new AI deep learning algorithm to screen for Chronic Kidney disease using eye retina images.<br>• 2022 June announcement by SNEC on RetiKid and its licensing to EyRIS. | Commercial<br><br>Expanded use of eye retina image analysis |

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| | and home based screening they want to see that will lead towards first stage medical diagnostics. | | |
| 2022 December | EyRIS signs MOU with Republic Power, a software development, technology solutions, robotics, and peripheral hardware company based in Singapore, to co-develop a fully automated unmanned tabletop fundus camera.<br><br>This is aligned with Republic Power's strategy of creating different types of unmanned medical booths.<br><br>https://www.straitstimes.com/singapore/health/self-service-medical-booths-to-measure-vital-signs-can-help-cut-waiting-times-at-clinics<br><br>EyRIS targets to roll out this new product prior to the end of 2023. This will make it possible for a fundus image of the interior of the eye to be acquired in a fully automated fashion. The image would be uploaded to the EyRIS cloud and analyzed by the AI software. The analysis report would be returned to the user seamlessly via a mobile phone app or via a message. | Prior to the end of 2023, EyRIS is targeting to demonstrate and market test the service delivery strategy of a fully automated unmanned medical booth to screen for eye disease using the unmanned eye fundus camera within a self-service medical booth. This allows for the possibility of the consumer doing a self-service eye disease screening test and directly receiving the screening results, bypassing the need to visit a health care provider for either doing the screening test or receiving the report of the results. | Commercial<br><br>Alternative mode of image acquisition enabling different approach to Go-To-Market |
| 2022 December | EyRIS has regulatory approval submissions under review in the following counties:<br><br>• China – NMPA<br>• US – FDA<br>• India – CDSCO<br>• Philippines - CDRRHR | Regulatory approval in any one or more of these five countries would substantially expand the addressable market for EyRIS.<br><br>Each of these countries presents very different types of challenges per 1) business model, and 2) making the necessary inroads with the ecosystem of "touchpoints" 3) local and/or international competitors operating in the country, | Regulatory and Commercial<br><br>Future expansion |
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| 2023 May | EyRis receives regulatory approval from the Ministry of Health and Prevention of the United Arab Emirates (UAE). | This enables EyRIS to bring their suite of products to the healthcare industry across the UAE. This also provides a first step towards EyRis eventually expanding into other Gulf Cooperation Council (GCC) countries in the Middle East. | Regulatory and Commercial<br><br>Future expansion |
| 2023 May | EyRis and VUNO announce a partnership with VUNO supplying their Med-Fundus AI solution used for detection of 12 fundus abnormalities to EyRis's SELENA+ platform to provide a more innovative and holistic AI solution to the eye screening community. | VUNO and EyRis claim that the combination of their respective Med-Fundus AI solution and SELENA+ solution provides an improved interpretation of fundus image and AI analysis results.<br><br>Under the partnership, the combined and integrated AI solutions will be deployed to multiple geographic markets. | Commercial<br><br>Future expansion and capability enhancement |
| 2023 June | EyRis announces a partnership with Optometrist Warehouse, part of the Chemist Warehouse Group in Australia, to do a large-scale, multi-year test of the practical business effectiveness of using AI-based methods to screen for diabetic retinopathy. | The study will span a period of 36 months and involve a large sample size of diabetic patients across various regions in Australia.<br><br>EyRIS provides the AI-based screening algorithms and product for the eye retina image analysis. Optometrist Warehouse | Commercial<br><br>Future expansion |

| Date | Event | Comment | Theme |
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| | This is a large-scale market validation of the extent to which this AI-based screening approach can enhance the accessibility and affordability of early screening in a commercially viable way.<br><br>https://mivision.com.au/2023/06/optometrist-warehouse-diabetic-retinopathy-ai-study/ | provides their extensive network of Chemist Warehouse pharmacies across Australia, as well as their expertise to evaluate the effectiveness of AI-driven screening for diabetic retinopathy. | |
| 2023 June | EyRIS announces collaboration with Sao Rafael Hospital, part of the Rede D'Or São Luiz healthcare network in Brazil.<br><br>SELENA+ has also received regulatory approval for use in Brazil. | Rede D'Or São Luiz, Brazil's largest integrated healthcare network, operates across multiple states, including Rio de Janeiro, São Paulo, Minas Gerais, Pernambuco, Bahia, Maranhão, Sergipe, Ceará, Paraná, Mato Grosso do Sul, Alagoas, Pará, and the Federal District. | Commercial<br><br>Future expansion<br><br>and Regulatory |
| 2023 June | EyRIS is selected to participate in a tripartite partnership with the International Centre for Eye Health at the London School of Hygiene and Tropical Medicine, U. of London, and the Tanzanian Ministry of Health to validate the use of Artificial Intelligence in screening for diabetic retinopathy in Tanzania, which is a low-resource setting for eye care with a very low ratio of ophthalmologist and allied ophthalmic personnel relative to the country's population size. | In the International Diabetes Federation Diabetes Atlas 10th edition published in 2021, Tanzania was noted to have the highest age-adjusted prevalence of diabetes in Africa.<br><br>This will lead to the first deployment of EyRIS SELENA+ for diabetic eye screening in an African country.<br><br>This also provides a first step towards EyRis eventually expanding into other African countries. | Commercial<br><br>Future expansion |