SINGAPORE EYE RESEARCH INSTITUTE

30 Years of Myopia Research

SINGAPORE EYE RESEARCH INSTITUTE

Singapore Eye Research Institute (SERI)

SERI is Singapore's national research institute for ophthalmic and vision research. SERI's mission is to conduct high impact eye research with an aim to prevent blindness, low vision and major eye diseases common to Singaporeans and Asians.

Serving as the research institute of the Singapore National Eye Centre (SNEC) and affiliated to the Duke-NUS Medical School and National University of Singapore, SERI undertakes vision research in collaboration with local clinical ophthalmic centres and biomedical research institutions, as well as major eye centres and research institutes throughout the world.

Today, SERI is recognised as a pioneering centre for high quality eye research in Asia, with breakthrough discoveries that have translated to a significant paradigm shift in eye care delivery.

Myopia research has been an important point of focus at SERI even before its establishment in 1997. In fact, the myopic eye is central to the SERI logo.

Myopia Research in Numbers

Total Investment in Myopia Research via Competitive Funding:

S$100 million

Research Groups with Myopia-related work:

9 groups

(Myopia, Glaucoma, Retina, Cornea & Refractive, Ocular Imaging, Ocular Genetics, Ocular Epidemiology, Health Services Research, Ocular Therapeutics & Drug Delivery)

Research Papers on Myopia:

1,645 publications

SERI's Myopia Research Breakthroughs and Achievements

High Prevalence and Incidence of Myopia in Singapore

THE PATTERN OF MYOPIA IN YOUNG SINGAPOREAN MEN

S J Chew, S C Chia, L K H Lee

SYNOPSIS

Prevalence and Risk Factors for Refractive Errors in Adult Chinese in Singapore

Tien Yin Wong,[1,2,3] Paul J. Foster,[1,4] Jocelin Hee,[1] Tze Pin Ng,[5] James M. Tielsch,[6] Seh Jin Chew,[1,2] Gordon J. Johnson,[4] and Steve K. L. Seah[1]

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IMPACT

SERI was the first to document the high prevalence of myopia in Singapore amongst young men enlisted in national service 30 years ago and conducted the first population-based study in Asia, the Tanjong Pagar Survey, on the prevalence of myopia in Chinese Singaporean adults, showing it was two times higher than similarly aged populations in whites and blacks in America. SERI then documented the high incidence and progression rates of myopia in Singaporean children through the Singapore Cohort Study of the Risk Factors for Myopia (SCORM) conducted between 1999 and 2000.

SERI also conducted the largest multi-ethnic study of myopia using the Singapore Epidemiology of Eye Disease (SEED) study, and in global efforts to estimate the number of people affected by myopia, projected a tsunami of myopia in 2040. This brought into sharp focus the myopia epidemic and a sense of urgency amongst health authorities and stakeholders to address the problem in Singapore and beyond.

[1]*Chew SJ, Chia SC, Lee LK. The pattern of myopia in young Singaporean men. Singapore Med J. 1988Jun;29(3):201-11.*

[2]*Wong TY, Foster PJ, Hee J, Ng TP, Tielsch JM, Chew SJ, Johnson GJ, Seah SK. Prevalence and risk factors for refractive errors in adult Chinese in Singapore. Invest Ophthalmol Vis Sci. 2000 Aug;41(9):2486-94.*

OTHER KEY PUBLICATIONS

Pan CW, Zheng YF, Anuar AR, Chew M, Gazzard G, Aung T, Cheng CY, Wong TY, Saw SM. Prevalence of refractive errors in a multiethnic Asian population: the Singapore epidemiology of eye disease study. Invest Ophthalmol Vis Sci. 2013 Apr 9;54(4):2590-8.

Seet B, Wong TY, Tan DT, Saw SM, Balakrishnan V, Lee LK, Lim AS. Myopia in Singapore: taking a public health approach. Br J Ophthalmol. 2001 May;85(5):521-6.

Saw SM, Tong L, Chua WH, Chia KS, Koh D, Tan DT, Katz J. Incidence and progression of myopia in Singaporean school children. Invest Ophthalmol Vis Sci. 2005 Jan;46(1):51-7.

Dirani M, Chan YH, Gazzard G, Hornbeak DM, Leo SW, Selvaraj P, Zhou B, Young TL, Mitchell P, Varma R, Wong TY, Saw SM. Prevalence of refractive error in Singaporean Chinese children: the strabismus, amblyopia, and refractive error in young Singaporean Children (STARS) study. Invest Ophthalmol Vis Sci. 2010 Mar;51(3):1348-55.

Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, Wong TY, Naduvilath TJ, Resnikoff S. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016 May;123(5):1036-42.

Pathological Myopia and Myopic Choroidal Neovascularization

PERSPECTIVE

Epidemiology and Disease Burden of Pathologic Myopia and Myopic Choroidal Neovascularization: An Evidence-Based Systematic Review

TIEN Y. WONG, ALBERTO FERREIRA, ROWENA HUGHES, GEMMA CARTER, AND PAUL MITCHELL

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Retina

Is Choroidal or Scleral Thickness Related to Myopic Macular Degeneration?

Chee Wai Wong,[1,2] Val Phua,[1] Shu Yen Lee,[1,2] Tien Yin Wong,[1,2] and Chui Ming Gemmy Cheung[1,2]

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IMPACT

A key consequence of high myopia is pathological myopia. In this field, SERI continues to be a leader in initiating breakthrough studies to understand the adverse effects on the eye. SERI led research into retinal and choroidal changes in pathological myopia, including the classification, pathophysiology, clinical features, epidemiology and disease burden. It also led an international consortium to propose a grading scheme for pathological myopia and showed that the pattern of degeneration changes over time with age, suggesting that the impact of myopia in children may not be noticed until decades later.

[1]*Wong TY, Ferreira A, Hughes R, Carter G, Mitchell P. Epidemiology and disease burden of pathologic myopia and myopic choroidal neovascularization: an evidence-based systematic review. Am J Ophthalmol. 2014 Jan;157(1):9-25.e12.*

[2]*Wong CW, Phua V, Lee SY, Wong TY, Cheung CM. Is Choroidal or Scleral Thickness Related to Myopic Macular Degeneration? Invest Ophthalmol Vis Sci. 2017 Feb 1;58(2):907-913.*

OTHER KEY PUBLICATIONS

K, Kawasaki Y, Yamazaki M, Meuer S, Ishibashi T, YasudaM, Yamashita H, Sugano A, Wang JJ, Mitchell P, Wong TY. META-analysis for Pathologic Myopia (META-PM) Study Group. International photographic classification and grading system for myopic maculopathy. Am J Ophthalmol. 2015 May;159(5):877-83.e7.

Wong CW, Teo YCK, Tsai STA, Ting SWD, Yeo YSI, Wong WKD, Lee SY, Wong TY, Cheung CMG. Characterization of the Choroidal Vasculature in Myopic Maculopathy with Optical Coherence Tomographic Angiography. Retina. 2018 Jun 26.

Chang L, Pan CW, Ohno-Matsui K, Lin X, Cheung GC, Gazzard G, Koh V, Hamzah H, Tai ES, Lim SC, Mitchell P, Young TL, Aung T, Wong TY, Saw SM. Myopia-related fundus changes in Singapore adults with high myopia. Am J Ophthalmol. 2013 Jun;155(6):991-999.e1.

Risk Factors Associated with Myopia

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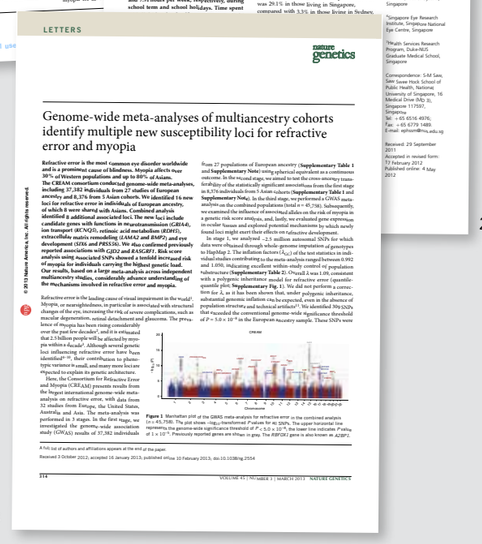

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IMPACT

Questions that needed to be addressed, in our attempts to fight myopia, were the causes and risk factors. Why are Singaporeans and Asians afflicted with high incidence and prevalence of myopia, and children in Asia have high progression rates of myopia? With groundbreaking studies, SERI established the correlation between near work and myopia in young children. Closely related to this risk factor is that outdoor time and light levels affect myopia and its progression, which we have established.

These findings, along with SNEC and SERI's participation in the Ministry of Health's National Myopia Prevention Programme and proactive engagement with the Health Promotion Board, Ministry of Education and schools, have shaped public health and school policies and practices, resulting in a downward trend in myopia and associated healthcare cost. The debate on the causes of myopia then moved to 'Nature verse Nurture'. SERI discovered the genetic factors that caused myopia and charted the molecular pathways of myopia development in animal models.

[1]*Saw SM, Hong CY, Chia KS, Stone RA, Tan D. Near work and myopia in young children. Lancet. 2001 Feb 3;357(9253):390.*

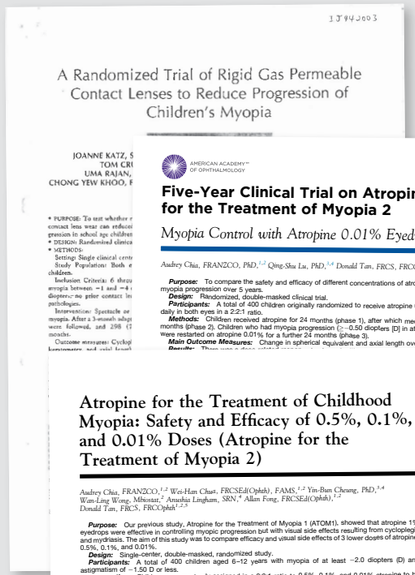
[2]*Dharani R, Lee CF, Theng ZX, Drury VB, Ngo C, Sandar M, Wong TY, Finkelstein EA, Saw SM. Comparison of measurements of time outdoors and light levels as risk factors for myopia in young Singapore children. Eye (Lond). 2012 Jul;26(7):911-8.*

[3]*Verhoeven VJ, et al. Genome-wide meta-analyses of multiancestry cohorts identify multiple new susceptibility loci for refractive error and myopia. Nat Genet. 2013 Mar;45(3):314-8.*

OTHER KEY PUBLICATIONS

Barathi VA, Kwan JL, Tan QS, Weon SR, Seet LF, Goh LK, Vithana EN, Beuerman RW. Muscarinic cholinergic receptor (M2) plays a crucial role in the development of myopia in mice. Dis Model Mech. 2013 Sep;6(5):1146-58.

Prevention of Myopia



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IMPACT

SERI's research efforts on myopia are not purely academic. The ultimate goal is to 'cure' myopia, to prevent and treat myopia or slow its progression. Studies on intervention and treatment for myopia are thus critical. SERI conducted one of the first randomised trial on contact lens and myopia in the 1990s. SERI performed a series of landmark clinical trials that showed that 0.01% atropine can slow down myopia by 60% in young children compared with untreated children through a five-year trial. This led SNEC to develop and produce the Myopine™ eye drop. Commercially available in Singapore and other parts of the world, it slows down the progression of myopia, with minimal side effects, in children.

Drawing on the findings of risk factors of near work and outdoor time, researchers at SERI and NUS developed a myopia-related fitness tracker (FitSight) to encourage children to increase time spent outdoors. This device goes hand-in-hand with schools allocating more outdoor and play time for students, and facilitates parents in managing near work and outdoor activities of their children.

[1]*Katz J, Schein OD, Levy B, Cruiscullo T, Saw SM, Rajan U, Chan TK, Yew Khoo C, Chew SJ. A randomized trial of rigid gas permeable contact lenses to reduce progression of children's myopia. Am J Ophthalmol. 2003 Jul;136(1):82-90.*

[2]*Chia A, Lu QS, Tan D. Five-Year Clinical Trial on Atropine for the Treatment of Myopia 2: Myopia Control with Atropine 0.01% Eyedrops. Ophthalmology. 2016 Feb;123(2):391-9.*

[3]*Chia A, Chua WH, Cheung YB, Wong WL, Lingham A, Fong A, Tan D. Atropine for the treatment of childhood myopia: safety and efficacy of 0.5%, 0.1%, and 0.01% doses (Atropine for the Treatment of Myopia 2). Ophthalmology. 2012 Feb;119(2):347-54.*

OTHER KEY PUBLICATIONS

Verkicharla PK, Ramamurthy D, Nguyen QD, Zhang X, Pu SH, Malhotra R, Ostbye T, Lamoureux EL, Saw SM. Development of the FitSight Fitness Tracker to Increase Time Outdoors to Prevent Myopia. Transl Vis Sci Technol. 2017 Jun 16;6(3):20.

Chia A, Chua WH, Wen L, Fong A, Goon YY, Tan D. Atropine for the treatment of childhood myopia: changes after stopping atropine 0.01%, 0.1% and 0.5%. Am J Ophthalmol. 2014 Feb;157(2):451-457.e1.

Chua WH, Balakrishnan V, Chan YH, Tong L, Ling Y, Quah BL, Tan D. Atropine for the treatment of childhood myopia. Ophthalmology. 2006 Dec;113(12):2285-91.

Tan DT, Lam DS, Chua WH, Shu-Ping DF, Crockett RS; Asian Pirenzepine Study Group. One-year multicenter, double-masked, placebo-controlled, parallel safety and efficacy study of 2% pirenzepine ophthalmic gel in children with myopia. Ophthalmology. 2005 Jan;112(1):84-91.

Intervention for Myopia


Clinical science

Eighteen-year prospective audit of LASIK outcomes for myopia in 53 731 eyes

Daniel Chua, Hla Myint Htoon, Li Lim, Cordelia ML Chan, Jodhbir S. Mehta, Donald T H Tan, Mohamad Rosman

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IMPACT

SERI and SNEC's corneal and refractive teams conducted pivotal research to improve new surgical and laser methods to correct myopia. The impact on Singaporean patients has been tremendous. SNEC was amongst the first to introduce LASIK and other refractive surgeries in the public sector, giving spectacle-free lifestyles and 'restored vision' to thousands of Singaporeans. It was also the first to introduce SMILE and ReLEx SMILE - femtosecond laser-assisted myopia correction with lenticule extraction, an alternative to LASIK.

[1] *Chua D, Htoon HM, Lim L, Chan CM, Mehta JS, Tan DTH, Rosman M. Eighteen-year prospective audit of LASIK outcomes for myopia in 53 731 eyes. Br J Ophthalmol. 2018 Oct 24. pii: bjophthalmol-2018-312587.*

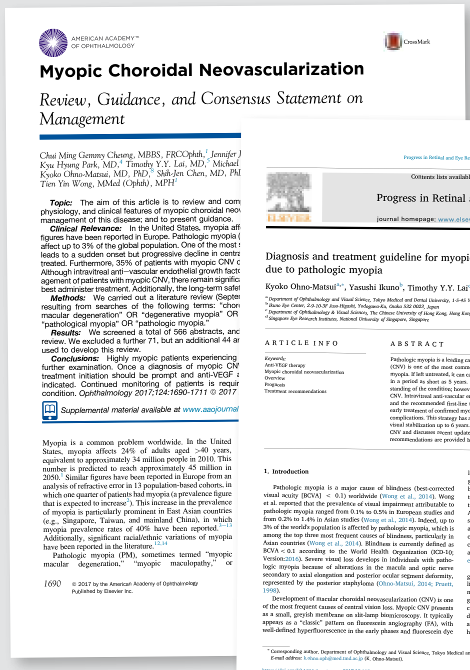
OTHER KEY PUBLICATIONS

Ang M, Mehta JS, Rosman M, Li L, Koh JC, Htoon HM, Tan D, Chan C. Visual outcomes comparison of 2 femtosecond laser platforms for laser in situ keratomileusis. J Cataract Refract Surg. 2013 Nov;39(11):1647-52.

Liu YC, Rosman M, Mehta JS. Enhancement after Small-Incision Lenticule Extraction: Incidence, Risk Factors, and Outcomes. Ophthalmology. 2017 Jun;124(6):813-821.

SMILE Procedure

Medical Innovations to Treat Myopic-CNV


Myopic Choroidal Neovascularization

Review, Guidance, and Consensus Statement on Management

1


Progress in Retinal and Eye Research

Diagnosis and treatment guideline for myopic choroidal neovascularization due to pathologic myopia

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IMPACT

SERI led research diagnosis and management of myopic choroida neovascularization (CNV). SERI was a site for major randomised trials on treatment of myopic CNV, and was the reading centre that graded the retinal images for the pivotal MYRROR trial for CNV.

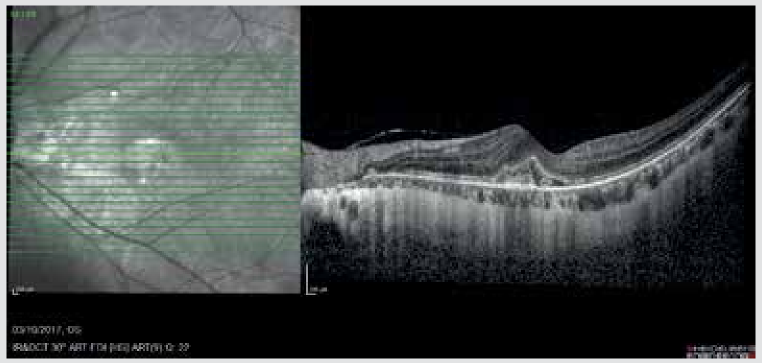
[1] *Cheung CMG, Arnold JJ, Holz FG, Park KH, Lai TYY, Larsen M, Mitchell P, Ohno-Matsui K, Chen SJ, Wolf S, Wong TY. Myopic Choroidal Neovascularization: Review, Guidance, and Consensus Statement on Management. Ophthalmology. 2017 Nov;124(11):1690-1711.*

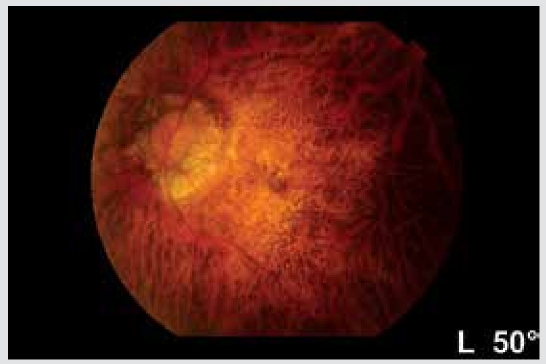
[2] *Ohno-Matsui K, Ikuno Y, Lai TYY, Gemmy Cheung CM. Diagnosis and treatment guideline for myopic choroidal neovascularization due to pathologic myopia. Prog Retin Eye Res. 2018 Mar;63:92-106.*

OTHER KEY PUBLICATIONS

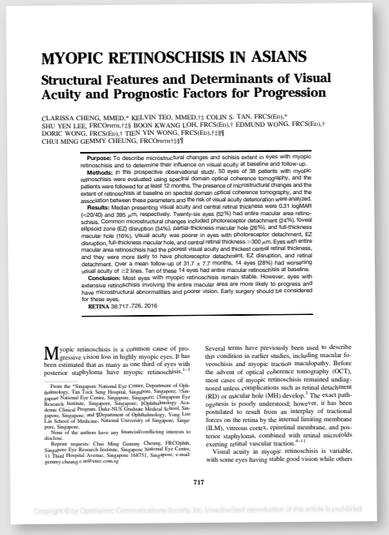
Ikuno Y, Ohno-Matsui K, Wong TY, Korobelnik JF, Vitti R, Li T, Stemper B, Asmus F, Zeitz O, Ishibashi T; MYRROR Investigators. Intravitreal Aflibercept Injection in Patients with Myopic Choroidal Neovascularization: The MYRROR Study. Ophthalmology. 2015 Jun;122(6):1220-7.

Myopic CNV presented on OCT and retinal images





Surgical Intervention for Myopia-related Retinal Complications



MYOPIC RETINOSCHISIS IN ASIANS

Structural Features and Determinants of Visual Acuity and Prognostic Factors for Progression

CLARISSA CHENG, MMED,* KELVIN TEO, MMED,†‡ COLIN S. TAN, FRCS(Ed),* SHU YEN LEE, FRCOphth,†‡§ BOON KWANG LOH, FRCS(Ed),† EDMUND WONG, FRCS(Ed),† DORIC WONG, FRCS(Ed),† TIEN YIN WONG, FRCS(Ed),†‡¶‖ CHUI MING GEMMY CHEUNG, FRCOphth‡§¶

Purpose: To describe microstructural changes and schisis extent in eyes with myopic retinoschisis and to determine their influence on visual acuity at baseline and follow-up.

Methods: In this prospective observational study, 50 eyes of 38 patients with myopic retinoschisis were evaluated using spectral domain optical coherence tomography, and the patients were followed for at least 12 months. The presence of microstructural changes and the extent of retinoschisis at baseline on spectral domain optical coherence tomography, and the association between these parameters and the risk of visual acuity deterioration were analyzed.

Results: Median presenting visual acuity and central retinal thickness were 0.31 logMAR (=20/40) and 395 μm, respectively. Twenty-six eyes (52%) had entire macular area retinoschisis. Common microstructural changes included photoreceptor detachment (54%), foveal ellipsoid zone (EZ) disruption (84%), partial-thickness macular hole (26%), and full-thickness macular hole (16%). Visual acuity was poorer in eyes with photoreceptor detachment, EZ disruption, full-thickness macular hole, and central retinal thickness >300 μm. Eyes with entire macular area retinoschisis had the poorest visual acuity and thickest central retinal thickness, and they were more likely to have photoreceptor detachment, EZ disruption, and retinal detachment. Over a mean follow-up of 31.7 ± 7.7 months, 14 eyes (28%) had worsening visual acuity of ≥2 lines. Ten of these 14 eyes had entire macular retinoschisis at baseline.

Conclusion: Most eyes with myopic retinoschisis remain stable. However, eyes with extensive retinoschisis involving the entire macular area are more likely to progress and have microstructural abnormalities and poorer vision. Early surgery should be considered for these eyes.

RETINA 36:717–726, 2016

Myopic retinoschisis is a common cause of progressive vision loss in highly myopic eyes. It has been estimated that as many as one third of eyes with posterior staphyloma have myopic retinoschisis.[1–3]

Several terms have previously been used to describe this condition in earlier studies, including macular foveoschisis and myopic traction maculopathy. Before the advent of optical coherence tomography (OCT), most cases of myopic retinoschisis remained undiagnosed unless complications such as retinal detachment (RD) or macular hole (MH) develop.[1] The exact pathogenesis is poorly understood; however, it has been postulated to result from an interplay of tractional forces on the retina by the internal limiting membrane (ILM), vitreous cortex, epiretinal membrane, and posterior staphyloma, combined with retinal microfolds exerting retinal vascular traction.[2–11]

Visual acuity in myopic retinoschisis is variable, with some eyes having stable good vision while others

IMPACT
SNEC's Surgical Retina Department led studies to improve understanding of surgical management of retinal complications of high myopia, including myopic macular holes and myopic foveoschisis.

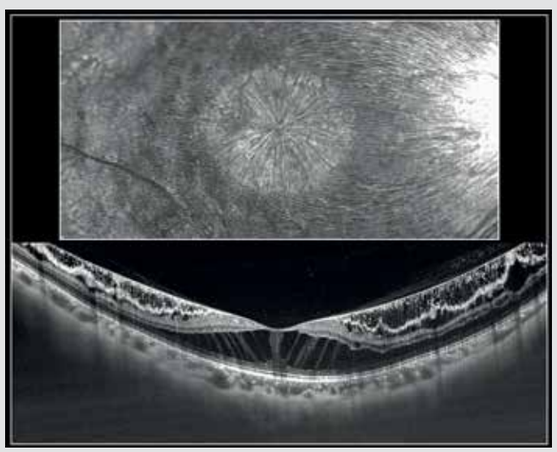
[1] *Cheng C, Teo K, Tan CS, Lee SY, Loh BK, Wong E, Wong D, Wong TY, Cheung CM. MYOPIC RETINOSCHISIS IN ASIANS: Structural Features and Determinants of Visual Acuity and Prognostic Factors for Progression. Retina. 2016 Apr;36(4):717-26.*

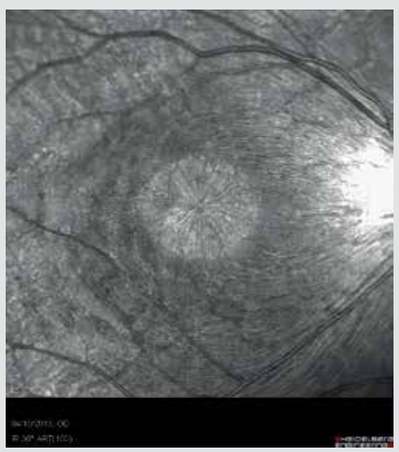
OTHER KEY PUBLICATIONS

Lim LS, Ng WY, Wong D, Wong E, Yeo I, Ang CL, Kim L, Vavvas D, Lee SY. Prognostic factor analysis of vitrectomy for myopic foveoschisis. Br J Ophthalmol. 2015 Dec;99(12):1639-43.

Lim LS, Tsai A, Wong D, Wong E, Yeo I, Loh BK, Ang CL, Ong SG, Lee SY. Prognostic factor analysis of vitrectomy for retinal detachment associated with myopic macular holes. Ophthalmology. 2014 Jan;121(1):305-310.

Myopic faveoschisis showed on OCT images





Socio-Economic Impact of Myopia

IJ2009034

The Impact of Corrected and Uncorrected Refractive Error on Visual Functioning: The Singapore Malay Eye Study

Elvanie L. Lamoureux, Saw-Mei Saw, Julian Thumboo, Hee Lin Wee, Aung Tin, Paul Mitchell, and Tien Y. Wong

Investigative Ophthalmology & Visual Science

Clinical and Epidemiologic Research

The Economic Cost of Myopia in Adults Aged Over 40 Years in Singapore

Ying-Feng Zheng, Chen-Wei Pan, Junxing Chay, Tien Y. Wong, Eric Finkelstein, and Seang-Mei Saw

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IMPACT
SERI's health economics studies established that myopia affects patients' quality of life and has substantial economic impact, with significant out-of-pocket expenditure imposing considerable economic burden on patients. This brought to new light the potential adverse socio-economic impact shortsightedness presents, something which is often overlooked or given little regard.

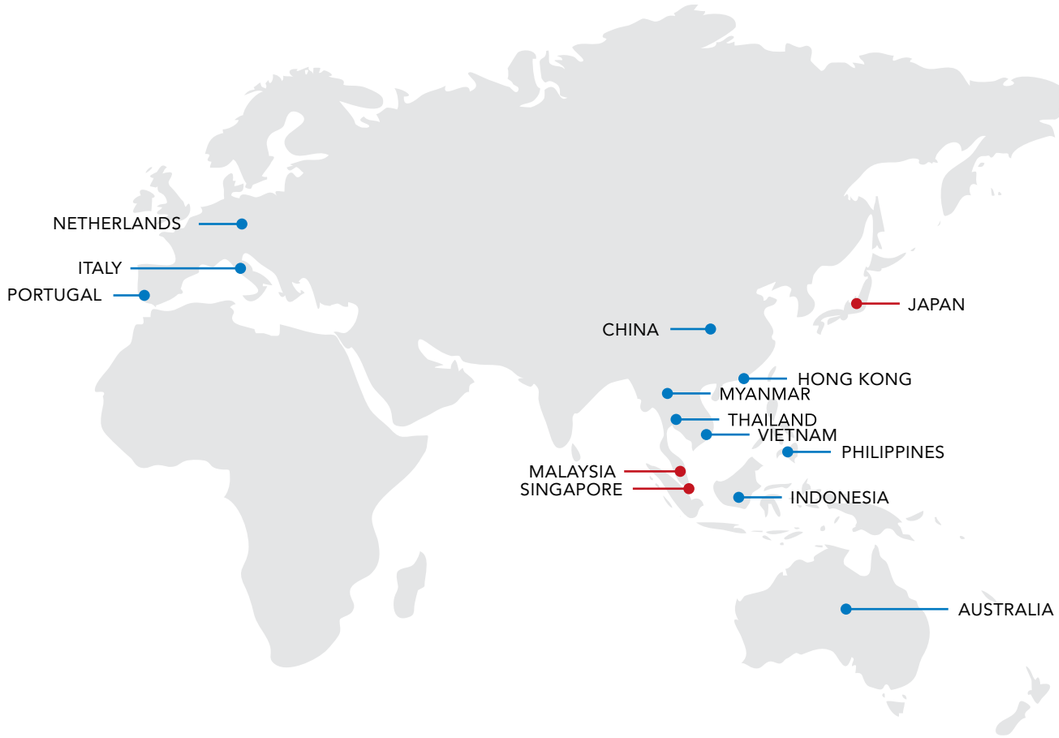
[1] *Lamoureux EL, Saw SM, Thumboo J, Wee HL, Aung T, Mitchell P, Wong TY. The impact of corrected and uncorrected refractive error on visual functioning: the Singapore Malay Eye Study. Invest Ophthalmol Vis Sci. 2009 Jun;50(6):2614-20.*

[2] *Zheng YF, Pan CW, Chay J, Wong TY, Finkelstein E, Saw SM. The economic cost of myopia in adults aged over 40 years in Singapore. Invest Ophthalmol Vis Sci. 2013 Nov 13;54(12):7532-7.*

Bringing High Impact R&D in Myopia to the International Market

MYOPINE™

A leading low-dose atropine treatment for childhood myopia developed at SERI-SNEC over the past two decades under a series of clinical trials has demonstrated up to a 60% reduction in myopia progression. Myopine™ is currently licensed to companies in 12 countries in Asia and Europe, with negotiations for several more. Myopine™ is available for patients in Singapore and overseas.



- Licensed and in use (name patient basis)
- Licensed (in the process of getting regulatory approval)

PLANO®

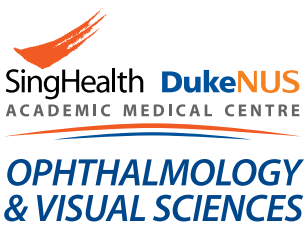
An innovative parental management application that aims to encourage healthy and safe smart device use in children worldwide. Following its foundation in 2017, the company has raised S$1 million in private funding from local-based angel investors. It is currently raising its Series A funding round and moving to expand geographically. This is the third spinoff company from SERI and the first from the SERI-SNEC ophthalmic technologies incubator.

SNEC - SERI - Johnson & Johnson Vision Strategic Partnership on Myopia First-of-its-Kind Public-Private Partnership in Asia

On 12 November 2018, SNEC, SERI and Johnson & Johnson Vision announced and inked a S$36 million research collaboration to tackle myopia. This is the first-of-its-kind public-private partnership in Asia on myopia.

This multi-year, multi-disciplinary programme will focus on three important areas:
1. Understanding the causes of myopia and why the condition progresses
2. Developing disease management frameworks to prevent its onset
3. Creating new myopia control and treatment products to slow or entirely stop the progression of myopia

LEFT TO RIGHT
***Christoph Vonwiller** - Regional Vice President, Surgical (Asia Pacific & Japan), JJV, **Ashley McEvoy** - Worldwide President, Medical Devices, J&J*
***Prof Wong Tien Yin** - Medical Director, SNEC, **Peter Shen** - Global Head of R&D, Medical Devices, J&J, **Prof Aung Tin** - Executive Director, SERI*
***Bebe Teo** - Managing Director of South Asia & Developed Markets, Vision Care, JJV, **Jorge Pinedo** - Area Vice President, Vision Care (Asia Pacific), JJV*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