

BRIEN ANTHONY HOLDEN OAM, PHD, DSC – HIS SIGNIFICANCE AND ROLE IN THE DEVELOPMENT OF CONTACT LENSES, THE INSTITUTIONS AND GLOBAL VISION CARE

Desmond Fonn, Dip Optom, M Optom

Distinguished Professor Emeritus
School of Optometry & Vision Science
University of Waterloo
Waterloo, Ontario, Canada

dfonn@uwaterloo.ca

Deborah F Sweeney, B Optom, PhD

Deputy Vice-Chancellor (Research
and Innovation)
Western Sydney University
Sydney, NSW, Australia

d.sweeney@westernsydney.edu.au

Gullapalli N Rao, MD, DSc

Chair, L V Prasad Eye Institute
Hyderabad, India

gnrao@lvpei.org

Kovin Naidoo, MPH, OD, PhD

African Vision Research Institute,
University of KwaZulu (UKZN)
South Africa

kovinn@gmail.com

Paul Erickson, BA, MS, OD, PhD

Retired R&D consultant
Wombarra, NSW, Australia

peri5nsw@gmail.com

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ABSTRACT

The purpose of this paper is to describe Brien Holden's enormous contributions to the science and development of soft contact lenses, the creation of associations and centers for research and how he was responsible for making Australia and, in particular Sydney, the epicenter of the contact lens research world for the better part of 40 years. His ingenuity with support of his co-workers generated hundreds of millions of dollars in royalties from co-development of contact lenses, which were ploughed back into research and funding of his humanitarian programs to provide eyecare services and spectacles for millions of underprivileged visually impaired people. His memorable achievements and awards are unsurpassed in our era but arguably the most significant is his research and fostering of education on contact lenses that contributed to the growth of contact lenses throughout the world.

Key Words

Soft contact lenses, uncorrected refractive error, myopia, BHVI, cornea, IACLE, ISCLR, history.

INTRODUCTION

There are many good reasons to celebrate the 50th anniversary of the approval by the Food and Drug Administration (FDA) in the United States for the commercialization of soft contact lens (SCL) use after classifying a SCL as a medical device. Certainly, 175 million contact lens wearers¹ (mostly SCL wearers) world-wide would cheer the discovery. Although the growth of the number of wearers in this timeframe is reasonable, it only represents about 3% of the population who require some form of vision correction.

Without describing the details of the historical development of the SCL as this has been recorded in a number of texts, it is worth recounting the sequence of events that led to the FDA approval in 1971. Otto Wichterle, a professor and director of the Macromolecular Chemistry at the Czechoslovak Academy of Sciences, with Drahoslav Lim developed the hydrophilic material 2-hydroxyethyl methacrylate (pHEMA) and realized the

advantage of this soft transparent material and patented it for use as a soft contact lens in 1953. The patent was bought from the Czechoslovak Academy of Sciences in 1964 by Robert Morrison an American optometrist and the patent rights were eventually acquired by Bausch & Lomb who marketed the Spin Cast Soflens.

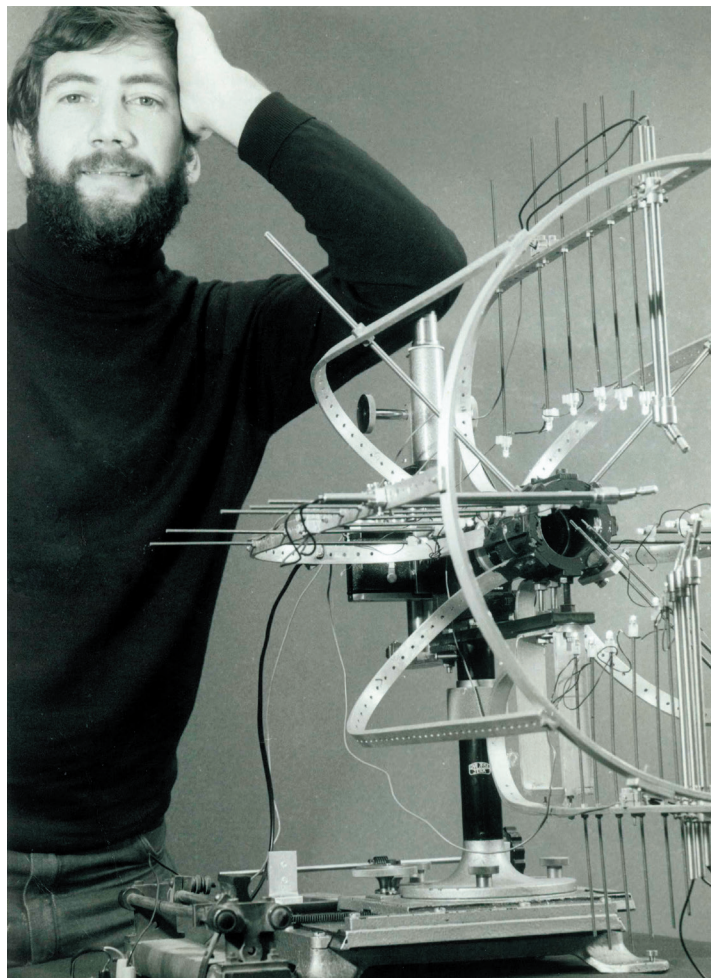
SCL use preceded the FDA's 1971 historic approval in a number of countries such as Czechoslovakia, Japan, United Kingdom (UK), Canada and Australia who sourced Bionite and Hydron lenses. John de Carle, a British ophthalmologist is credited with developing the first high water hydrophilic lens dedicated to extended wear. Reports from his practice of patients wearing these lenses in some cases for up to six months of continuous wear without complications spurred research in Australia and elsewhere in the seventies on this topic.

There are many other luminaries who deserve special recognition for the early soft lens development in the seventies,

but with justification (as this paper will demonstrate), the person who has had the greatest impact on the understanding of the ocular response to contact lens wear, its development over the next 45 years and all associated initiatives that spawned societies, associations, education and globalization of our field is Professor Brien Anthony Holden. Brien passed away prematurely at the “young” age of 73 on July 27, 2015, and over the years a number of glowing tributes have been written about him²⁻⁴ and others that have not been published in journals.

THE EARLY YEARS

Brien graduated from the University of Melbourne as an Optometrist in 1964, practiced for a year then set sail for the UK with his wife, Yvonne. His intention was to further his clinical contact lens knowledge. Following some encouragement from another Aussie mate and Optometrist, Dr. Ian Bailey, he enrolled as a PhD student at the City University in London. Dr. Charles McMonnies has written an amusing account of Brien’s years in London which provides a glimpse of his social conscience.² The subject of his thesis was orthokeratology (using PMMA lenses) and its effect on refractive error, and 40 years later he returned with vigor to the subject of myopia and its control.



Brien Holden with his construction to measure corneal topography (PhD thesis).

After five years of London life, a PhD and two children, the Holdens returned to Australia in 1971 and Brien joined the Department of Optometry in the School of Applied Physics and Optometry at the University of New South Wales (UNSW) in Sydney and immediately immersed himself in contact lens research. By this stage SCLs were available in Australia and Holden seized the opportunity of establishing himself as a leading researcher on this new modality. This was the beginning of the Holden empire, commandeering space, what little there was in the small building housing the Optometry school, acquiring equipment and searching for funds. He established a rapport with the Australian contact lens manufacturers and the Optometric profession soon became aware of his presence. What really set the stage for great things to come was the establishment of the Optometric Vision Research Foundation (OVRF) by Holden, Brian Layland and a few other Optometrists which raised funds for research at UNSW through donations from Optometric practices Australia wide. One of his earliest papers⁵ provides insight of his unmatched understanding of contact lenses in those early years and set the stage for building a research program on hydrogel contact lenses. This quite remarkable paper highlighted some of the limitations of lens wear: limbal hyperemia, hypoxia, discomfort and discontinuation of lens wear (primarily hard lenses) and the need for extended wear. These were to become the research cornerstones over the next four decades.

Under-graduate and post graduate students became vital members of the Holden research programs. He built metrology systems to measure SCLs, the envy of most contact lens manufacturers. Most of the metrology work on SCLs was performed by optometry students who worked in his laboratory part time. Brien’s first two PhD students, Steve Zantos and Lewis Williams, helped him establish his international reputation and leadership position in contact lens research. Their observations of the effects of the SCLs on the corneal endothelium ultimately captured the imagination of the contact lens world and set Holden off on world-wide tours of conferences and presentations at the major international contact lens corporations. Lewis’ PhD was on the transient endothelial changes of the in-vivo human cornea. There was considerable skepticism about John de Carle’s claim of complication free extended wear which prompted Steve Zantos to study the ocular response to continuous wear of contact lenses as his PhD thesis. Brien’s international travel began in earnest in the early/mid-seventies. Brien was invited by Dr. Raymond Myers (Manager of Professional Affairs) to visit to Bausch & Lomb (B&L) in Rochester, New York as he had been very critical of B&L’s Soflens.⁶ His visits to B&L were legendary because of his outspoken opinions but in spite of his criticisms the management realized his capabilities resulting in him establishing long lasting relationships with the researchers and upper management. Dr. George Mertz was one of the optometrists in the research clinic that Brien befriended. In 1984 Dr. Paul Erickson joined B&L and soon after met Brien. They became good friends and worked together for many years. Paul eventually left B&L to work with Brien from 1998-2002 and again from 2010 until Paul’s retirement in 2017.

Besides B&L having the early sales monopoly in the US, they understood the value of education of eye care practitioners so they initiated an annual National Research Symposium in the US and the European Research Symposium on CLs in the mid-to-

late seventies which continued for about 20 - 30 years. Brien was invited to be a moderator and speaker at these symposia and became a standard fixture. To their credit B&L never used these meetings to promote their products but with the help of the moderators invited prominent scientists/clinicians to present the latest research in the field. Brien's interaction with the company in research and education, arguably did as much to establish his prominence and leadership in the world of contact lenses as any other factor.

CORNEA AND CONTACT LENS RESEARCH UNIT

Holden established the Cornea and Contact Lens Research Unit (CCLRU) in 1976 within the School of Optometry. He was astute in writing a constitution giving the CCLRU autonomy within the University system. This arrangement served him and the CCLRU well and the University capitalized from his research and financial contribution in later years as his operation expanded. After a period of six years the Unit needed to move to a larger building off campus because of growth in the number of post graduate students, researchers employed by the CCLRU and auxiliary personnel. Needless to say, the CCLRU attracted considerable funding from the major contact lens corporations and Australian grants to the extent that at its peak, employed about 100 individuals. Many of the researchers became internationally renowned scholars.



Brien (top right) with CCLRU personnel and graduate students (early eighties).

It became customary for the CCLRU to host many visiting scientists. Two who must be mentioned were Ophthalmologists that Brien met during his formative years. Antti Vannas from the Department of Ophthalmology University of Helsinki in Finland was a corneal specialist with interest in endothelial function and contact lenses and Gullapalli Nageswera (Nag) Rao, an Indian academic ophthalmologist and corneal specialist who spent 10 years in the US as a professor at the University of Rochester before returning to Hyderabad in India to establish the LV Prasad Eye Institute. Both of these were encounters at conferences and the common theme was endothelium. They became life- long friends and collaborators.

The CCLRU became the mecca for studying corneal function in response to wearing contact lenses, in particular the understanding of corneal swelling when wearing contact lenses

during open and closed eye conditions. The seminal paper by Carney and Bailey⁷ and others in the early seventies which showed that hydrophilic lenses caused corneal swelling troubled Holden. He thought that it was due to poor tear exchange under a SCL but soon changed his mind to thinking that hypoxia was the real cause. He may have been influenced by Mertz who demonstrated that reducing the thickness of a HEMA lens decreased corneal swelling.⁸ It set off a wave of experimentation beginning in 1980 when Mertz left B&L to join the CCLRU and, with John McNally from California, they published a number of papers in the early eighties, the most famous of which is the Critical Oxygen transmission of a soft lens to avoid corneal swelling in open and closed eye conditions by Holden and Mertz.⁹



Brien and George Mertz, 1980.

The paper that superseded the one on critical oxygen transmissibility was "Effects of long-term extended contact lens wear on the human cornea"¹⁰ which ranks as the most cited paper in the contact lens literature other than a few on the subject of corneal infection associated with contact lens wear. Holden collaborated with a Swedish Optometrist, Klaus Nilsson and they used his large database of contact lens patients who were unilateral extended wearers of the Scanlens, (a high-water SCL). Their conclusions were that these lenses when used for extended wear induced changes to all layers of the cornea that could be minimized by using lenses with greater oxygen transmissibility, removing from the eye more frequently during extended wear, and replacing more frequently.

The expansion of the contact lens industry in the eighties is reflective of the diversified research that occurred at the CCLRU. That included presbyopic contact lens corrections, toric lens designs and substantial interest in extended wear and the etiology of infections and inflammation associated with hydrogel lenses. The CCLRU had been conducting clinical trials but Holden felt that their expertise should be enhanced so he recruited Dr. Michel Guillon from the UK with whom he had been collaborating with for years. Michel added rigour and structure to the protocols for

clinical trials which became such a huge component of their research. Clinical trials necessitated standardization of clinical assessment in order to record and monitor clinical changes to the ocular tissue. Photographic scales were developed from the extensive database of clinical images from conditions observed in their clinical studies. These grading scales were used internally to standardise inter-observer grading procedures. The standardised scales were first published in 1993¹¹ and are now used extensively and routinely in clinical practice and teaching institutions providing an effective means of charting changes that can occur during lens wear.

Another important collaborative effort between the CCLRU and the LV Prasad Eye Institute (LVPEI) resulted in the production of the "Guide to Corneal Infiltrative Conditions in Contact Lens Practice" that was released in 2001. The guide characterises adverse responses associated with contact lens wear detailing information on the signs, symptoms, appearance, laboratory findings, treatment and management of the range of adverse events.

INSTITUTE FOR EYE RESEARCH (IER)

In 1982 the CCLRU relocated to a new dedicated facility off the main University campus. At the inauguration Professor Holden gave a stirring address to a gathering of international visitors, university dignitaries, politicians and international and Australian representatives of the contact lens industry and CCLRU personnel. He acknowledged that the CCLRU had become the elite and world recognized contact lens research institution but they were capable of so much more. Vision research was going through a rapidly expanding phase that included diagnostic instrumentation and new devices for the treatment of ocular conditions. The CCLRU and its members were very well placed to enter this new space of investigation. It was clear to Holden that it was necessary to establish a new organization because of their diversified interest in eye research and in 1985 the IER was established as an independent university affiliated non-profit organization dedicated to the advancement of eye care research and education. Over the next few years the CCLRU became enmeshed within the IER to the extent that the CCLRU in effect became nonexistent. The IER was accredited by the Australian Government's National Health and Medical Research Council (NHMRC) as an independent Research Institute.

INTERNATIONAL ASSOCIATION OF CONTACT LENS EDUCATORS (IACLE)

The B&L sponsored European Research Symposium on Contact Lenses (ERS) was held in Monte Carlo, Monaco in 1979. Holden was a moderator and invited speaker. He along with a group of contact lens educators from Europe and North America, South Africa and Australia were invited by B&L to attend an informal meeting to discuss aspects of contact lens education.¹² Coincidentally George Mertz was the B&L facilitator and it was one of his last duties at B&L before departing to join Brien in Sydney at the CCLRU. It was decided at this informal gathering to form an international association of contact lens educators and at the next meeting in 1980 in London the organization of IACLE was formalized with an executive committee that included Holden as the Vice President. This group of educators continued to meet every year during the eighties, once a year at each B&L ERS but it wasn't until 1992 that IACLE changed significantly with a new

Executive Board with Holden elected as the President, a position that he held until 2000.



Portrait of Brien Holden in the eighties.

The impetus for change from a 'social club' of Eurocentric educators that met once a year at the B&L ERS and exchanged information on contact lens education to a truly global organization with a mission to increase the number of educators world-wide and raise the standard of education, was a negotiation between Brien Holden and Juan Carlos Aragon who represented B&L. Aragon facilitated a

grant of 1 million dollars from B&L in 1989 over four years for IACLE to become a global enterprise of contact lens education. This magnanimous grant further incentivized Holden (with the help of some of his executive committee members) to successfully convince all of the other large international contact lens corporations (Vistakon, CibaVision, Allergan, Wesley Jessen, Alcon, CooperVision and others) to contribute to IACLE's mission.

From inception to the end of the eighties the membership only grew to 50 but by 2019 (IACLE'S 40TH anniversary) there were almost 1,000 members. IACLE was divided into four regions: Europe, Asia Pacific, Latin America and Africa/Middle East, each with its own Board. North America was not represented as a region because it had its own Association of Optometric Contact Lens Educators but some of these people were also members of IACLE. There are many reasons for the phenomenal success of the IACLE enterprise. These include the extraordinary work performed by the members who served (and still do) on the Executive and Regional boards and the employees of the organization, as well as the munificent contribution of the Industry; however Brien Holden's sagacity and inspiration just might out-rank the previous two.

INTERNATIONAL SOCIETY FOR CONTACT LENS RESEARCH (ISCLR)

Dr. Ray Myers has written about the historical events of the first 30 years of the ISCLR.⁶ He describes Past President Miguel Refojo suggesting that - as Otto Wichterle was the patron of ISCLR then - Brien should be the Godfather for his leadership and influence in ISCLR affairs. Although Myers' book details the history, it is important to elucidate the genesis of the ISCLR and for this article to show the expanse of Holden's influence on forming the Society.

Propelled by the development of the SCL there was a group of ophthalmologists and optometrists who thought that it would be useful - to form an international contact lens association of members - including the unification of the various contact lens associations that already existed might be possible in order to advance knowledge in the field. Professor Montague Ruben, Director of the Contact Lens and Prosthetics department at

Moorfields Eye Hospital, Dr. Ray Myers, Dr. Robert Koetting (an American Optometrist), Michel Guillon (a PhD student) and Brien Holden met at Moorfields during June 1978. Discussion revolved around the interprofessional obstacles as an impediment to forming such an association. It was then that Holden suggested establishing a closed research society of academic apolitical Optometrists, Ophthalmologists, practitioners interested in clinical research and scientists employed by the contact lens industry. Holden convinced the others in this steering committee of the need for an independent "think tank" later called the ISCLR Scientific Meeting that would be held biannually and funded by the contact lens industry to discuss how to advance knowledge in the field of contact lenses. Holden (and others subsequently) was chiefly responsible for convincing the contact lens industry to jointly fund the Scientific meeting.

INTERNATIONAL CENTRE FOR EYECARE EDUCATION (ICEE)

Through Brien's travels and meetings, he had become aware of the problem of "avoidable" blindness and vision impairment due to uncorrected refractive error which was supported by published evidence.^{13,14} Untreated presbyopia in developing countries, particularly in Africa and Asia was also rife. It was also obvious that the millions of people suffering from uncorrected refractive error and presbyopia was because of lack of service and training of personnel in those regions. For example, it was established at that time that in Africa there was one practitioner for 500,000 people compared to the US of one per 10,000. His quite brilliant initiative was to establish ICEE. At an informal meeting in 1998 of Holden, Nag Rao and Desmond Fonn, Brien suggested that we should use the model of IACLE to create an international centre for eyecare education. At its inception ICEE consisted of a board of the following members: Holden, Nag Rao from LV Prasad Eye Institute in India, Brian Layland, an optometrist from Australia, Deborah Sweeney and Desmond Fonn. Holden was elected as the Chief Operating Officer. Sylvie Franz (née Sulaiman), formally from the CCLRU and IACLE was appointed as the Executive Director.

The mission of ICEE was threefold: to gather teaching materials from Optometry schools; syllabi, teaching notes, slides and videos and rationalize and re-engineer them into eight modules of refractive procedures, dispensing, and prescribing spectacles. These modules would be provided to institutions with minimal resources in developing countries. A team of instructors was hired by ICEE to deliver courses and to train the personnel in those communities, that is develop the local infrastructure for education and increase the number who could provide eyecare regardless of their sophistication. The second objective was to provide low cost spectacles at minimal cost: US\$1, 3 or 5, dependent on the affordability of the community. ICEE was able to initially source 200,000 pairs of low-cost spectacles to start the program. Fortunately, Holden supported by Franz, was instrumental in securing a very large five-year grant from Essilor to support these and other efforts of ICEE.

Brien's third and most ambitious objective was for ICEE to become a task force member of Vision 2020: The Right to Sight - the Global Initiative to Eliminate Avoidable Blindness and Low Vision by the Year 2020, established by an alliance of the World Health Organization. ICEE appealed to the Task Force to include uncorrected refractive error as a cause of avoidable blindness

and vision impairment. At the time Uncorrected Refractive Error was not on the Vision 2020 radar. Nag Rao who served as Secretary General of International Agency for the Prevention of Blindness (IAPB) at the time facilitated an ICEE invitation to the WHO meeting of Vision 2020. In February 2000 ICEE was accepted as a Task Force member. Refractive error was included in the Prevention of Blindness Program and Holden became the chair of the Refractive Error working group. Starting soon after the launch of the program, he became a powerful advocate of this cause and convinced the global eye care community of its significance with research and evidence. He forged global collaborations to tackle this leading cause of vision impairment globally. Scores of programs of ICEE in many developing countries touched millions of lives. He set the direction for the elimination of this problem through models of service delivery, education and research, advocacy, planning and formulation of policy. Millions born and yet unborn will continue to benefit from the efforts of this large-hearted man.

As Africa was one of the main targets of ICEE's objectives, Holden met Dr. Kavin Naidoo, an Optometrist and lecturer at the University of Durban Westville (UDW) in South Africa, for the first time in 1997 at the World Council of Optometry Meeting in South Korea before the formation of ICEE. They clicked, and a professional relationship and friendship developed. Brien, on hearing that Kavin had returned to South Africa from studying in the US and was planning to expand public health programs by forming an NGO in Africa, informed him about his idea to start ICEE and convinced him to instead work with him in the development of ICEE. On the formation of ICEE Kavin opened and led the Africa office at UDW which drove most of the on ground public health programs of the organisation. He later assumed the role of Global Programs Director.

There were innumerable challenges facing ICEE not the least of which was to fund the operation beyond the 5-year grant from Essilor. Brien was so passionate about this project that he committed funding from IER as bridging finance but knew that additional funding would have to be obtained. In addition to philanthropists and optical companies, he felt strongly that Optometry should be a stake holder and an advocate of providing "vision for all" by establishing its own fund which Brien named as Optometry Giving Sight.

OPTOMETRY GIVING SIGHT (OGS)

Funding OGS was an example of Brien's optimism. He convinced the IAPB and the World Council of Optometry (WCO) to join the Brien Holden Vision Institute in establishing OGS. His initial thoughts were to fund the operation through donations by patients at Optometrists' offices and at Optometry School clinics. The patient would contribute a dollar and all these donations would be channelled to OGS. His proposed system was very similar to the OVRF collection system in Australia. However, it evolved into a much more elaborate and extensive funding enterprise detailed on the OGS web site¹⁵ that includes corporate donors, media partners and optometrists and their associations. The organisation founded in 2003 now consists of operational personnel in the US and Canada and a board of Directors. Holden chaired the OGS global board for 10 years and was succeeded by his dear friend Juan Carlos Aragon in 2013.

The mission of OGS was (and is) to solve the problem of avoidable blindness and vision impairment due to uncorrected refractive error by providing access to eyecare and spectacle correction. How to do that in underserved communities? The OGS solution is to provide training for local eyecare personnel (whatever the level of experience/education may be) to conduct "eye exams", to establish optometry schools and vision care centers, either stand alone or integrated in hospitals and provide low cost spectacles. OGS like so many other of his ventures is an amazing success story. To date OGS has facilitated and funded training for 14,000 eye care personnel, has provided eye care services for about 7.6 million people in 40 countries and established 133 vision centers.

COOPERATIVE RESEARCH CENTRE FOR EYE RESEARCH AND TECHNOLOGY (CRCERT) AND VISION COOPERATIVE RESEARCH CENTRE (VISION CRC)

The Australian government established the Cooperative Research Centres (CRC) program in 1990. The objective was for a collaboration between university researchers and business to solve industry-identified challenges. This was a timely opportunity for Holden as he and his team had been working with Australian and major multinationals collaboratively for many years. The CRCERT was one of a handful of CRCs that was funded in 1991. Its mission was to carry out research on contact lenses and related products, biomaterials, polymers and polymer surface chemistry, ocular physiology and microbiology. CRCERT was dedicated to developing better ways of correcting vision. As stated on their website "with almost two thirds of the world's population requiring some form of vision correction, and through its dynamic integrated research program, and communication links with international research and industry, CRCERT aimed to contribute to eyecare and the ophthalmic industry in Australia and internationally."

The result was the development of the first silicone hydrogel contact lenses, Focus Night and Day, for 30-day continuous wear. It involved a worldwide collaboration between the CRCERT, Novartis based in Switzerland, and CIBA Vision in Atlanta, Georgia. The CRCERT and CCLRU clinical and biological scientists were responsible for determining the clinical performance goals of the contact lens material, while the material scientists, polymer chemists and surface scientists from the consortium determined the material requirements. The three entities involved in research and development had joint ownership of the intellectual property and the resultant breakthrough of highly oxygen permeable silicone hydrogel contact lenses revolutionized the contact lens market. The royalties that were returned to CRCERT were re-invested in further research and humanitarian activities (notably ICEE and OGS).

The CRCERT was so successful, it received four rounds of funding from the CRC program over 25 years. CRCERT was eventually integrated into the Vision CRC which was funded as a new grant in July 2003. The Vision CRC went on to become the largest vision correction research center in the world. It employed high-class national and international researchers to conduct major programs in the areas of myopia, presbyopia, vision care delivery, business growth, and professional and academic education in collaboration with the Centre for Contact Lens Research at the

University of Waterloo, LVPEI, Bascom Palmer Eye Institute, Centre for Eye Research Australia and the University of Houston, College of Optometry.



Members of the Vision CRC, ICEE, IER and IACLE during the 90s.

LV PRASAD EYE INSTITUTE AND IER COLLABORATION

In April 1978 when I (Nag Rao) was attending a symposium on Corneal Endothelium in Zurich, Switzerland, I had just completed my corneal fellowship in Rochester, New York and was presenting my work on Polymegethism. Following my presentation, I was sitting alone in a corner during the coffee break as I didn't know anyone. Most in attendance were eminent corneal researchers from around the world. This handsome fellow who also presented a paper in the same session on endothelial bleb response in contact lens wearers walked up to me and congratulated me on my presentation and complimented our observations. I felt very elated that someone really cared to make that warm gesture to a nobody. That was none other than Brien Holden. Thus, began a long and very warm and productive friendship and collaboration that continued in strength until his untimely demise.

While I lived in Rochester until 1986, it was mostly meeting him at conferences and during his visits to Bausch & Lomb in Rochester. I also got to know his very diligent associate, Debbie Sweeney well, during this time. He invited me and my wife, Pratibha, to Sydney for the inauguration of the CCLRU he founded at the University of New South Wales. It was a very historic event with the "who's who" of contact lenses in attendance.

When I informed him of my decision to return to India, very few were happier than him about my decision. He promised all support. As we built our Institute in Hyderabad, he began planning to train our team in clinical research and trials with Debbie. He worked relentlessly to convince the corporations that high-quality clinical trials are possible in an Indian Institute. Thus, the chapter of intense collaboration in research started leading to multiple studies and trials over the next 25 years. We were the beneficiaries of this collaboration in a big way. Both basic and clinical research were included along with clinical trials that contributed to new contact lens materials and fundamental understanding of ocular responses to contact lens wear and other corneal responses. This also led to a strong bond between our teams that was conducive for effective collaboration. When

our institute was preparing to expand the research activity, Brien organized the funding to support the building of the laboratories. In recognition, our research center is named after him, (the Brien Holden Eye Research Centre) and it became one of the most productive eye research units in the world spanning many areas.

The next big collaboration was in education. These included programs for practitioners, educators and doctoral degrees. Through this collaboration, a number of LVPEI researchers received their doctoral qualification from the University of New South Wales, more than from any other university. The Brien Holden Institute of Optometry and Vision Sciences at our institute - established in 2017 - which canopied all the optometric activities at the LVPEI, is a tribute to his memory and will produce generations of optometrists and other technical cadres to tackle the problem of uncorrected refractive error and research

Through IACLE, our collaboration fostered the development of contact lens educators in India and helped enhance the quality of contact lens education, practice and industry significantly. This is still ongoing and very active.

Hundreds of practitioners and trainers were trained in refraction to enhance the competence in this area. This evolved into the idea of ICEE, a collaborative initiative that came out of discussions of Brien, Desmond Fonn and myself as a tripartite collaboration.

In 2011, Brien came up with the idea of the India Vision Institute to promote the quality of education in the Indian Optometry Schools through training of faculty, creation of a large group of people with doctoral qualifications and promoting industry. He also worked relentlessly to help organize the profession of optometry in India through the creation of the Optometry Council of India (ICO) and the supporting Indian Optometry Federation. These measures will help generations of optometrists in India to get better education and better systems of practice.

In his passing, the world lost a great humanitarian who worked tirelessly for education, science and service for the most-need. It is very difficult to imagine another Brien Holden in the near future.

BRIEN HOLDEN VISION INSTITUTE (BHVI)

The organizations that supported and housed the various research and humanitarian endeavors (CCLRU that morphed into IER, IACLE, CRCERT, Vision CRC, ICEE, OGS and others) had outgrown the space off-campus that was originally provided by the University for the CCLRU. Holden convinced the University to build The Rupert Myers Building which would house the School of Optometry and Vision Science and various Holden led organizations with a considerable financial commitment. The new building opened in 2000 with a fanfare of events celebrating this milestone.

Holden was of the opinion that their operations would benefit from creating an umbrella of the operational entities with a replacement of IER at the peak of the umbrella and in 2010 IER was renamed the Brien Holden Vision Institute in recognition for his contributions to research and humanitarian efforts in vision correction. There was also a consensus among the Institute Board members that creating a Brien Holden brand would have significant benefit for the long term of the Institute. ICEE was also renamed as the BHVI Foundation now known as the Brien Holden Foundation. By 2010 BHVI had a complement of approximately

300 people in research and public health of vision in offices around the world.

REVERSING THE TREND OF MYOPIA

In the latter part of his career Brien Holden became focused on one of the most significant clinical and public health challenges of our time, myopia. There were two major aspects that influenced and drove his passion for addressing myopia. The first was a WHO global collaborative study: the Refractive Error Studies in Children (RESC) at various sites across the world. ICEE Africa through Kovin Naidoo and Brien led the Africa component of this study in Durban, South Africa. The Durban and the Global studies highlighted the high prevalence of uncorrected refractive error and the significance of myopia as a major challenge particularly in places such as China.¹⁶ Brien's view was that given the prevalence of uncorrected refractive error, the increase in myopia was going to place even more burden on eye care systems. Subsequently Brien met Dr. Earl Smith, Dean of the College of Optometry, University of Houston, and Brien was impressed with the work that Earl was doing on refractive development of the eye and etiology of myopia. So began a friendship and collaboration that can be credited with elevating myopia on the global agenda.

Holden and colleagues were among the first to explore the possibility of using optical means to slow myopia progression by controlling eye growth. They did so by using the patent¹⁷ of Earl Smith and colleagues in SCLs incorporating a design to create positive peripheral defocus while maintaining central clear retinal focus in order to abate the progression of myopia. Earl, and colleagues, had demonstrated in animal models that positive peripheral defocus retards axial growth of the eye which slows myopia progression.¹⁸ BHVI capitalised on their existing collaboration with CibaVision in 2008 who manufactured this novel SCL and supported a clinical trial in China, chosen because of the high prevalence of myopia in children in that region. The results of this study demonstrated that after one year, there was a 30% reduction in myopia progression in children wearing the myopia control SCL compared to a spectacle-corrected myopic control.¹⁹ BHVI continued their SCL myopia control research in the region and were also interested in the development of spectacle lenses for myopia control that was supported by Zeiss.

The major breakthrough in this area for BHVI came about when Dr. Ravi Bakaraju, formerly Brien's PhD student, described a theoretical mechanism for - and achieved evidence - that certain extended depth of focus (EDOF) contact lens optical designs had potential for controlling the development of myopia. In order to ensure that this technology became widely available to meet the huge myopia challenge as well as exploit the demonstrated potential for application in presbyopia, Brien undertook to develop and market the lens through a BHVI-owned proprietary company. It is this project that was his major focus at the time of his untimely death. While working on these contact lens and spectacle lens strategies BHVI concurrently advocated awareness of and elevated myopia on the international eye care agenda. Brien worked tirelessly to achieve two major milestones in this regard. The first was with the support of his friend and colleague Dr. Serge Resnikoff (former WHO head of the program for blindness and deafness), Brien convinced the Australian government to push for and support a WHO meeting on Myopia. The report that

subsequently emerged out of a meeting of a group of experts became a formal WHO report and helped place myopia, and more importantly myopia control, squarely on the agenda of WHO. Secondly, Brien also recognised that there were many groups working on myopia with various recommendations emerging, and at times this was creating confusion. He then suggested the establishment of the International Myopia Institute (IMI) to bring key academics and opinion leaders together to achieve consensus on epidemiological, clinical and technological aspects of myopia and myopia control. Brien was going to chair and lead this effort but unfortunately, he passed on before this could be formalised and Prof. Kovin Naidoo stepped into this role initially.



Brien Holden (seated front centre) at a meeting on Uncorrected Refractive Error organised in partnership with the WHO hosted by BHVI 2015.

CONTRIBUTIONS TO THE LITERATURE

Fueled by keen intellect, insatiable curiosity, boundless energy, tenacity, passionate commitment to the public good, early recognition of the next big challenge and uncanny knack for identifying and engaging productive collaborators, Brien and his co-authors produced a vast trove of information and insights on nearly every aspect of contact lens wear, now immortalized in the clinical and scientific literature. The output comprises 282 papers in refereed journals (a substantial proportion in our field's highest impact journals), 463 refereed abstracts, 26 book chapters and monographs, and 80 published symposium abstracts, reports and editorials.

These publications cover a wide range of topics fundamental to Brien's longstanding interests in and commitment to methods and availability of vision correction, contact lenses in particular. The latter category includes papers on designs and performance of lenses for correcting all refractive anomalies (e.g. spherical, toric and multifocal optics), all lens wearing modalities, and all lens material types. They include optical, physical and chemical metrology methods and associated lens and lens care product assessments, optical design technology, clinical performance evaluation, both objective (examiner) and subjective (e.g. patient satisfaction, comfort, quality of life). They include multiple studies on geometry, structure and physiology of the ocular tissues (cornea – all layers, conjunctiva, crystalline lens, retina) as it pertains to contact lens wear, optical correction and development of refractive status. They include many of the key early studies on corneal response to hypoxic and mechanical stress that guided the evolution of lens geometry and material properties. Heavy laboratory and clinical research emphases were placed

on understanding the ocular microbiota, the incidence and risk factors for microbial infections and/or inflammatory responses associated with contact lens wear. These studies identified lens and lens care (e.g. solutions, lens cases) contamination, hypoxia, tear stagnation and other challenges introduced by a lens draped over the cornea and limbus, all exacerbated by extended periods of eye closure. Multiple studies were published on the tear film, its composition, its flow dynamics and how both are affected by the contact lens and/or closed eye. Many of these studies were replicated with the development and commercial availability of silicone hydrogels. Brien and collaborators reported improvements in some, but not all, clinical performance variables with these more oxygen permeable lenses but increases in certain adverse responses (e.g., those apparently related to mechanical stress). Frequent replacement of lenses was consistently found to improve clinical performance and reduce incidence of adverse responses with contact lens wear.

Although Brien and his team continued unabated to produce important papers on contact lens safety and performance, his research and development interests gradually shifted toward the epidemiology of uncorrected refractive errors, especially the alarming global escalation in the incidence and progression rate of myopia. He co-authored papers estimating the economic and societal burden of uncorrected RE and the projected cost of eliminating the problem. Pursuant to having demonstrated a retinal defocus mechanism contributing to myopic progression, several papers were published on the development of methods for reliably measuring peripheral refractive error and thereafter reports comparing measurements taken from myopic and non-myopic eyes. Several clinical trials involving spectacle lenses and SCLs designed to create peripheral myopia (shift the retinal image in a myopic direction) were conducted and published as described above (see Reversing the Trend of Myopia section above).

Authors' note: To conserve journal space, we have neither cited nor listed (in References) the several hundred publications alluded to in this section.

IN MEMORY...

Brien was intent on working until 2020 but most who knew him predicted that he would never retire. He loved what he did and what he was able to accomplish, was nothing short of astounding. When asked what his recipe for success was, he replied "Surround yourself with great people". That he did! Things, that he saw as achievable, most others thought of them as impossible. He had two sayings: "Every challenge is an opportunity" and "Are we having fun yet?" He was known for his unwavering and continuous "living large" habits disregarding personal health and a slower pace as there was always "so much more to do".

He was the recipient of seven honorary Doctoral degrees, and at last count, 46 awards. He was especially proud of the following awards: Order of Australia Medal in recognition of his outstanding contributions to eye care research and education, the James Cook Medal for his outstanding contribution to science and humanity from the New South Wales chapter of the Australian Royal Society, the Prentice Medal which is the highest honour from the American Academy of Optometry awarded to a distinguished scientist in recognition of a career-long record of advancement of

knowledge in vision science and the Schwab Social Entrepreneur award for Africa 2010 at the regional World Economic Forum and one that he would have been proud of, the ISCLR established the Brien A Holden Memorial Lecture in recognition of his contributions to the Society, posthumously.



Brien receiving the Prentice Medal from President Bernard Dolan at the American Academy of Optometry meeting 2013.

There aren't sufficient superlatives to describe this unique individual. A generous, principled, sensitive, brutally honest, caring, lovely, humanitarian with unparalleled integrity whose ultimate goal was to commercialize the research endeavors of the Institute and pour those profits into vision care for the millions of underprivileged people. Earl Smith, described Holden as "the most influential optometrist of our generation". Kovin Naidoo said "he was a man of extraordinary vision who devoted himself to the service of mankind. He demanded that the research be indivisible from the service to society. He was truly an intellectual giant." This paper illustrates why he is so worthy of those accolades. There are many hundreds of people that were part of Brien's life and work that have not been acknowledged by name, and we apologise for that omission.

Brien was proud of his accomplishments but most of all of his family, his wife Yvonne, children Anthony, Karen and Daniel, their partners Kathryn, Doug and Courtenay and four grandchildren.

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