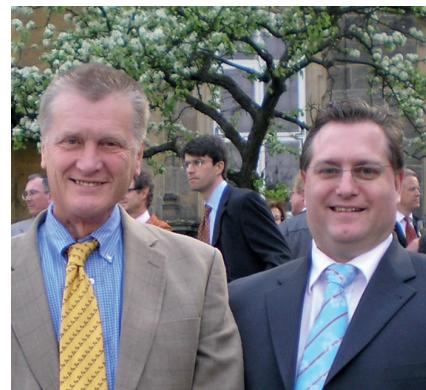


The David J Apple International Laboratory for Ocular Pathology – a legacy of pioneering IOL research

BY GERD AUFFARTH, DONALD MUNRO

The Apple Lab at the David J Apple Center for Vision Research in Heidelberg is a thriving international laboratory for research into intraocular devices. The lab continues the work of David J Apple, a world-renowned expert in ocular pathology who pioneered research into the pathology of IOL complications. In this article, **Professor Gerd Auffarth**, Director of the Centre, shares his memories of David Apple and explains how the work of the lab is changing over time.



David Apple and Gerd Auffarth.

In the early 1990s I spent two years as a research fellow at David Apple's laboratory in Charleston at the Medical University of South Carolina.

David was uniquely trained as an ophthalmic surgeon and as an ophthalmic pathologist. Around 1980, when he worked as a pathologist with Randall Olson in Utah, he started to get interested in the pathology of intraocular lenses (IOLs) and established the Center for Intraocular Lens Research. As he published more about the subject he soon became widely known as the leading authority in the area of IOL explant analysis, IOL design, IOL materials and the problems associated with IOL implantation; these included the variety of opacifications that can affect an IOL after it is implanted: posterior capsular opacification (PCO), silicone oil opacification, calcification and glistenings.

The fact that today cataract surgery with IOL implantation is such a very successful procedure is in part due to the advances since the 1940s in our use of instrumentation, operating microscopes and phacoemulsification, but it is also very much due to the work of David Apple and his Apple Corps. The research on cadaver eyes in the 1980s helped improve the overall success of IOL implantation and to improve patients' visual results.

In particular, David focused on avoiding complications by improving on IOL design, for example, the choice of haptic material.

At the beginning of the 1980s flexible materials such as nylon and polypropylene were used to make haptics, as they allowed the manipulation of a lens within the confines of the eye's anterior segment. However, the autopsy eyes with these lenses told a different story: nylon and polypropylene had poor 'memory' and the lens lost its shape in the eye and moved. The pathology results correlated well with the medical history: patients' symptoms of perceptible lens decentration, inflammation and other sequelae. It was clear that what was advantageous to the surgeon at the time of surgery (flexible haptics) was over time not good for the patient. The IOL industry listened to Apple and by the end of the 1980s most lenses were being made as single-piece poly(methyl methacrylate) (PMMA) lenses. The haptics were flexible enough to manipulate but the PMMA retained a better memory in the eye.

David and Harold

David was the greatest champion of Harold Ridley, the inventor of the IOL. It was astonishing to David that, in the 1980s and over 30 years after the first implantation, the inventor lived in obscurity while his invention was just starting to become so ubiquitously used in the treatment of cataract. David thought of this as an injustice and he wanted to correct it, so he made sure Harold Ridley received an honorary degree from the Medical

University of South Carolina in 1988.

The 1980s was a make or break period for both Ridley's reputation and indeed for the continued development of IOLs. The 1970s and early 1980s was the period when there were heads of eye departments in North America and Europe who flatly refused to allow IOLs to be implanted by surgeons in their departments. This older generation felt proud to say that they only explanted IOLs and never implanted them. The new generation had to wait for that older generation to move on before they could start to implant lenses.

The result was that the general public scarcely knew about IOLs and didn't know about Ridley. In May 1987 David wrote to Prime Minister Margaret Thatcher, seeking a



David Apple and Harold Ridley.

knighthood for Harold Ridley. It was not until 2000 that the knighthood was announced.

He then went on to lobby his medical colleagues and politicians to give higher recognition to Harold and honour his work. David and Harold were from such different backgrounds but they became close friends. Harold named David as his biographer and in 2006 David published his book.

To this day there is a close association between the Apple Lab and the Ridley Eye Foundation. Set up by Harold in 1967, the Ridley Eye Foundation aims to raise funds for cataract surgery in developing countries and to treat avoidable blindness, notably in the Middle East. The Foundation funds outreach projects which allow impoverished communities access to eye examinations and cataract surgery even in the most remote and poorly developed areas. Much of its activity is focused on providing cataract surgery at hospitals in Egypt, especially at Harpur Memorial Hospital in the Nile Delta.

In the 1940s Ridley had worked in Ghana (then called the Gold Coast) and he subsequently wrote a paper on River Blindness – the first comprehensive English language monograph about the disease. Tropical ophthalmology and treating blindness in Africa was also of tremendous interest to David. His laboratory was and remains an official Collaborating Center of the World Health Organisation's Prevention of Blindness Programme.

Today the Foundation is led by Nicholas Ridley, Harold's elder son and his wife Lauretta and there is good cooperation between the Lab and the Foundation. We encourage our industry sponsors of research at the laboratory to donate to the Foundation. In 2014 Lauretta and Nicholas came to Heidelberg, where Nicholas attempted cataract surgery using the laboratory's surgery simulator. Their commitment to keeping the Foundation going and bring cataract treatment to some of the world's poorest people is something that strengthens us in our laboratory work.

We still have a long way to go – there is much more that we can do together, especially in preparing a training programme in sustainable cataract surgery at Harpur Memorial Hospital. I would urge UK surgeons to support the Foundation. Increasing cataract surgery in rural, impoverished areas overseas in turn helps the overall prosperity of these communities.

The Apple Lab

At the Lab in Charleston we looked at surgical techniques that today are taken for granted (e.g. symmetric in-the-bag fixation of PCIOLs, hydro-dissection-enhanced cortical cleanup, continuous curvilinear

capsulorhexis and LASIK flap incisions). David had moved from Utah to Charleston in 1988 to take on the role of Department Chairman of the Storm Eye Institute of the Medical University of South Carolina. The IOL research centre moved too. He renamed it the Centre for Research in Ocular Therapeutics and Biodevices to acknowledge an expansion into other fields like excimer laser technology.

In the early part of the new century, the Lab was briefly moved back to Utah, but it became clear that the high altitude was inimical to David's health and convalescence, so it was moved to Sullivan's Island near Charleston, South Carolina. David knew that his age and his illness did not leave him much time and he was worried about who would continue his work. He wanted to 'get back to basics', to provide again information and advice to surgeons by reconstituting the study of autopsy eyes that he and his colleagues began years ago. I know that he was concerned that many new lenses were being implanted with virtually no oversight. To him, it seemed that these lenses came on the market without real proof of safety and efficacy. He had shown throughout the years that the careful examination of autopsy eyes can reveal a truth about how the implant works. "These findings do not lie and cannot be spun," he would say.

By the time he wrote his biography of Sir Harold, David was in very poor health. He and I would talk about what the future would hold for his laboratory and for



Photo 3: Lauretta Ridley looks on as Prof Auffarth assists Nicholas Ridley with the operation of the Surgical Simulator.

what he had started, the science of IOL research: what would be his legacy?

David was a Germanophile and learned to speak and write in German. Indeed, one of his astounding academic achievements was his translation of Professor Gottfried Naumann's textbook (now a classic) from German to English. He and I secured a visiting professorship for him at Heidelberg University with the support of The Alexander von Humboldt Foundation, a foundation established by the German government and funded by the Federal Foreign Office that allows scholars from all over the world to come to Germany, to work on a research project they have chosen themselves. But he never lived to see this happen. After a 12 year battle with cancer and the side-effects of his cancer therapy he died in August 2011. His laboratory and

"There were heads of eye departments who flatly refused to allow IOLs to be implanted by surgeons in their departments."

The newly modelled laboratory room.



papers were donated from his estate to the Heidelberg US Alumni Society in New York, who shipped them over to Heidelberg. It was a fulfilment of David's wish. So today we now have the David J Apple Center for Vision Research here in Heidelberg, which comprises my own clinical study group as well as the David J Apple International Laboratory for Ocular Pathology.

At present we have more than 25,000 autopsy and explanted IOL records and the number is growing rapidly. It is chiefly in the laboratory that we carry on David's work on IOL research and we have extended it into new research areas. David would recognise some of the work we do today since we continue to receive IOL explants from around the world and we analyse them using methods which David pioneered, such as the Miyake-Apple technique. In addition, we test new lenses, ophthalmic viscosurgical devices (OVDs), lens injectors – performing mechanical tests, optical tests, chemical analyses, videographic analysis of the implantation procedure. What is very new is our collaboration with Heidelberg University's Department of Applied Mathematics – this is a new field where we make mathematical models to predict how IOLs will behave over time in the eye. David would have loved this new approach, I'm sure.

The latest developments and the future of IOLs

It took some months to unpack the shipment that came from the USA and to sort out David's papers, equipment, his files and records. We were very fortunate to get financial support from Industry and from some notable foundations here in Germany, especially the Klaus Tschira Foundation. This kind of support allowed us to reach out to the Department of Applied Mathematics here at Heidelberg University and start a research programme devoted to predictive modelling in ophthalmology. Within a year we were able to hire a laboratory manager who has since moved on but is still our consultant for biotechnology. In 2015 we remodelled our Lab rooms and established a stipend for an optics specialist. In July 2016 we took on a new laboratory manager and cell biologist. Add to that the visiting research-fellows (we have two from China this year and we had a Korean in 2015) and we have developed a good team – the latest generation of Apple Korps!

IOL design is always advancing – just in the past three years we have seen new IOL materials, new pre-loaded injectors, new OVDs, new optical designs, and I'm very pleased that some of the products

"To him, it seemed that these lenses came on the market without real proof of safety and efficacy."

that companies bring here are really very good. When you consider the new aspects of our Lab work – mathematical modelling, predictive analyses and new measurement techniques – then I have to say this is still an exciting area of medical science. But with all this new work we've still not lost track of our core expertise – analysing autopsy and explant IOLs. Any surgeon reading this who has an explant requiring analysis should write to us through the contact page of our website www.djapplelab.com

I have big hopes for this marriage of mathematics with ophthalmology – not only in cataract surgery but in the diagnostic area too. Through time, as our database of explants grows, we may reach the stage where we are able to look at issues of lens failure – such as glistening and opacification – from an epidemiological standpoint. Ultimately I want the Lab's databases to be more accessible. It will take time – as all of David's records are on paper – but I look forward to the day that a research

ophthalmologist on the other side of the world can access online the Apple Lab database.

There is also more development likely to come in terms of lens delivery systems and new polymer biomaterial to make IOLs. I recognise what an immense effort and financial burden it is for the polymer companies and IOL manufacturers to make and register new materials but yet it is so encouraging to see them take up that challenge. I think changes in material will provide the key to answering the question of restoring accommodation. What will prevail, will it be multifocal, extended depth of field (EDOF) lenses, electro-mechanical accommodating lenses, fluid-filled lenses or refinements in optics that will restore vision or something else to which I cannot put a name? Let's wait and see but I expect we will see all of this at different stages. Whatever we get we must test, if only to avoid the mistakes made in the past. I'm excited too that at some stage new modalities might appear that will eventually mean a decline in surgery and IOL usage. I'm thinking of new developments in pharmaceutical, protein chemistry, stem-cell regenerative, tissue-regenerative and organ-regenerative medicine. It is an exciting thought. I doubt that it will happen overnight but it is fascinating to see the speed of these developments. I think our laboratory – with its independence, our competencies in so many areas of science and mathematics, our database records, our link to polymer research institutions and polymer manufacturers – is uniquely placed to serve the whole ophthalmic community.

This is just how David Apple would want it to be.



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Photographs courtesy of The David J Apple International Laboratory for Ocular Pathology.

For further information

The David J Apple Center for Vision Research: <http://djapplelab.com>
The Ridley Eye Foundation: www.ridleyeyefoundation.org