Ali E. Ghareeb

"How will the patient with ophthalmic problems be cared for in 30 years' time?"

It is tempting in answering this question to let one's imagination run wild and write of hover cars and surgical robots with integrated artificial intelligence performing vitreoretinal surgery. However, the question is rather more nuanced and so I will resist the temptation to get carried away. In making a specific projection of the state of ophthalmic clinical practice in 30 years, we need to understand the recent history of ophthalmology and its current trends. In doing so, let us recall the canon of Thomas Kuhn, that scientific progress occurs in 'revolutions' and is not a gradual accumulation of knowledge[1].

The journal *EYE* recently celebrated 30 years of the Royal College of Ophthalmologists with a series of reviews on the past 30 years of progress in our understanding and treatment of age-related macular degeneration (AMD) and glaucoma, respectively the first and second most common causes of blindness in England and Wales[2].

An article by Garg and Gazzard on the past and future perspectives of Selective Laser Trabeculoplasty (SLT) encapsulates the principles which I wish to outline in this essay[3]. The discovery by Anderson and Parish of selective photothermolysis: that a pigmented cell population could selectively absorb radiation leaving adjacent non-pigmented tissue unharmed led to the development of SLT, which is now a mainstay treatment of glaucoma[4]. Advances in basic science and technology quickly lead to the development of novel treatments and the introduction of another piece of technology to the clinic. The selective nature of SLT allows for repeat treatments, especially important in an aging population.

I propose 3 key trends which will significantly influence developments in ophthalmology.

1. Increasing integration of technology,
2. Development of novel biological therapies,
3. Aging population.

Increasing integration of technology

At the tradeshow of a large ophthalmology congress, I was amazed by the plethora of gadgets on display. Because of the optical principles which govern the eye, and because of the relative

[1] Thomas S. Kuhn and Ian Hacking, *The Structure of Scientific Revolutions*.

[2] A Quartilho and others, 'Leading Causes of Certifiable Visual Loss in England and Wales during the Year Ending 31 March 2013', *Eye*, 30/4 (2016), 602–7 <http://www.ncbi.nlm.nih.gov/pubmed/26821759> [accessed 15 October 2018].

[3] A. Garg and G. Gazzard, 'Selective Laser Trabeculoplasty: Past, Present, and Future', *Eye*, 32/5 (2018), 863–76 <http://www.nature.com/articles/eye.2017.273> [accessed 13 October 2018].

[4] Dov B Kagan, Nathan S Gorfinkel and Cindy ML Hutnik, 'Mechanisms of Selective Laser Trabeculoplasty: A Review', *Clinical & Experimental Ophthalmology*, 42/7 (2014), 675–81 <http://doi.wiley.com/10.1111/ceo.12281> [accessed 13 October 2018]; R R Anderson and J A Parrish, 'Selective Photothermolysis: Precise Microsurgery by Selective Absorption of Pulsed Radiation.', *Science (New York, N.Y.)*, 220/4596 (1983), 524–27 <http://www.ncbi.nlm.nih.gov/pubmed/6836297> [accessed 13 October 2018].

ease of access to its tissues, ophthalmology is a specialty which lends itself well to the application of new technology.

Many of the instruments I saw at the tradeshow were devises used in cataract surgery. Ophthalmology has witnessed several revolutions in cataract surgery which have benefitted both patients and surgeons. In modern cataract surgery, these revolutions have often depended on the introduction of new technology, the most important example of which is phacoemulsification. Before the introduction of phacoemulsification, patients in the UK endured an average hospital stay of 10 days. Patients spent 3-5 days completely immobilised with both eyes occluded by eye patches. Complication rates were high, and recovery required several weeks. In contrast, cataract removal by phacoemulsification is typically performed as a day-case, and patients return home with ideal or near-ideal vision[5].

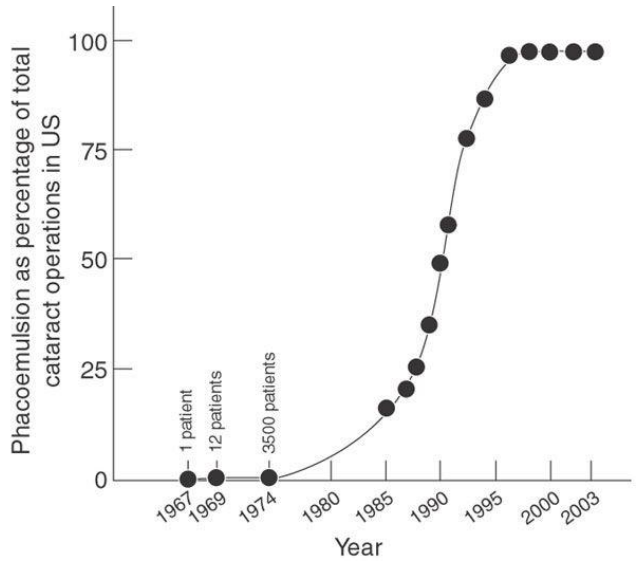

Figure 1: The Phaco-Revolution. Although his discharge of patients on the day of surgery was seen as heretical by colleagues, Kelman's phacoemulsification quickly dominated cataract surgery, moving from 16% of all surgeries in 1985 to 97% in 1996.

What is most intriguing about the invention of phacoemulsification by Charles Kelman is that it completely revolutionised the most common operation in the world (Figure 1) and yet depended on technology which his dentist had used to clean his teeth[6]. This must prompt us to ask: *what further revolutions which utilise technology we take for granted lie in wait?*

The introduction of optical coherence tomography (OCT) has over the past decade revolutionised diagnostics in retinal diseases. OCT is the medium of choice for monitoring

[5] Joseph L Goldstein, 'How a Jolt and a Bolt in a Dentist's Chair Revolutionized Cataract Surgery', *Nature Medicine*, 10/10 (2004), 1032–33 <http://www.ncbi.nlm.nih.gov/pubmed/15459696> [accessed 14 October 2018].
[6] Goldstein, 'How a Jolt and a Bolt in a Dentist's Chair Revolutionized Cataract Surgery', 1032–33.

disease progression in AMD through the measurement of central retinal thickness[7]. *In vivo* confocal microscopy is now used to monitor corneal health post-keratoplasty via, amongst other things the measurement of endothelial cell density[8].

With the development of new imaging technologies comes a need for sophisticated methods of data analysis to comprehend the vast data generated from these images. This paradigm is analogous to that of astronomy, which through advanced telescopes generated *astronomical* amounts of data requiring computational analysis. We now have *biological* quantities of data. A collaboration between DeepMind and Moorfields Eye Hospital recently published results showing that DeepMind's neural network-based artificial intelligence was able to make expert-level diagnoses on a large bank of OCT scans comprising a wide range of pathologies[9]. Artificial intelligence already has protean applications in common use such as autopilots in aviation or Google Maps.

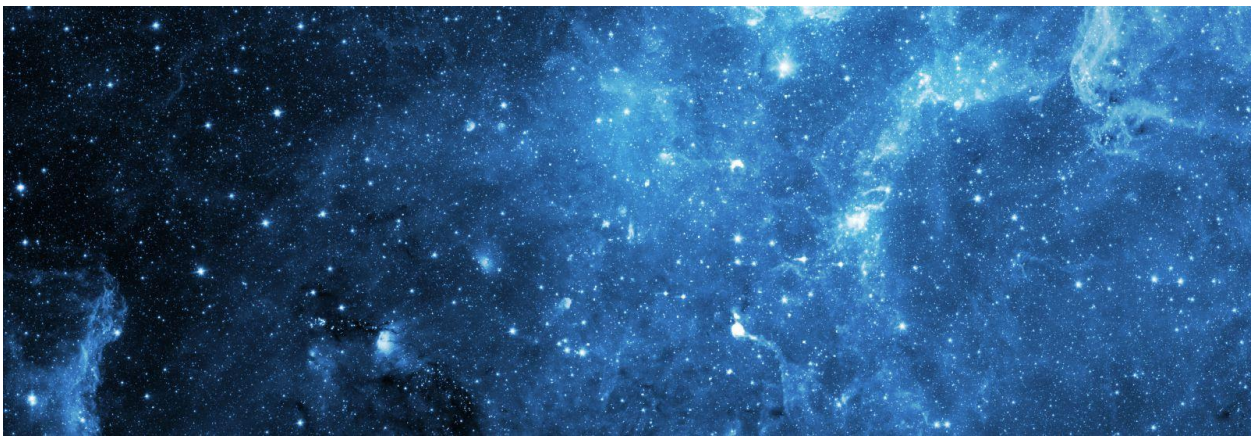

Figure 2: Patients treated with adeno-associated virus (AAV)-delivered gene therapy for choroideremia reported being able to see the stars at night[10] (image from www.nasa.gov).

Development of novel biological therapies

While progress in ophthalmic practice is made in leaps and bounds through technological innovation, biological advancements have been more gradual drivers of change. Stepwise chemical changes to parent molecules lead to more favourable pharmacodynamics[11]. Two areas of current biological research are promising disruptors of current practice: stem cell

[7] 'The Major Topics of the Research Work of Prof. Sobha Sivaprasad: Vision-Research.eu - The Gateway to European Vision Research' <http://www.vision-research.eu/index.php?id=1181> [accessed 15 October 2018].
[8] W Matthew Petroll and Danielle M Robertson, 'In Vivo Confocal Microscopy of the Cornea: New Developments in Image Acquisition, Reconstruction, and Analysis Using the HRT-Rostock Corneal Module.', *The Ocular Surface*, 13/3 (2015), 187–203 <http://www.ncbi.nlm.nih.gov/pubmed/25998608> [accessed 30 January 2018].
[9] Jeffrey De Fauw and others, 'Clinically Applicable Deep Learning for Diagnosis and Referral in Retinal Disease', *Nature Medicine*, 24/September (2018) <http://www.nature.com/articles/s41591-018-0107-6>.
[10] 'The Major Topics of the Research Work of Prof. Robert MacLaren: Vision-Research.eu - The Gateway to European Vision Research' <http://www.vision-research.eu/index.php?id=1027> [accessed 15 October 2018].
[11] Tony Realini and Robert D Fechtner, '56,000 Ways to Treat Glaucoma.', *Ophthalmology*, 109/11 (2002), 1955–56 <http://www.ncbi.nlm.nih.gov/pubmed/12414398> [accessed 15 October 2018].

therapeutics and gene therapy. The eye is an accepting recipient of these treatments as both the cornea and retina are relatively immune-privileged tissues[12].

Stem cell therapeutics is an area of translational research which aims to develop stem cells for transplantation to regenerate diseased tissues. This strategy is deployed in the treatment of limbal stem cell deficiency (LSCD). Limbal stem cells are the tissue stem cells of the corneal epithelium and reside in the limbus. When they are damaged, for example by a caustic or thermal insult, limbal stem cells fail to replace the corneal epithelium. This results in painful vision loss as the epithelium undergoes conjunctivalisation and neovascularisation. In unilateral LSCD, a small biopsy may be taken from the healthy eye and expanded *in vitro*. Once the graft has reached suitable size it may be transplanted to the diseased eye, thus restoring the corneal epithelium[13].

Expansion of the limbal biopsies in conducted in specialised laboratories under strict Good Manufacturing Practice conditions[14]. Such a venture requires the close collaboration of scientists and ophthalmologists, with ophthalmologists often playing a dual role. The same collaboration is seen in ongoing studies of stem cell therapy for AMD and gene therapy for choroideremia and retinitis pigmentosa (Figure 2)[15].

An ophthalmic future which involves stem cell and gene therapies will therefore involve the synergistic involvement of clinicians and scientists. Ophthalmologists will increasingly be called upon to be clinician-scientists.

Aging population

The NHS is at a crossroads. Throughout the developed world we are witnessing an important demographic shift. Aging populations have an increased demand for the most common areas of ophthalmic care: cataract, glaucoma, AMD, diabetic eye disease and emergency eye care. Cataract surgery represents 6% of all surgery in the UK. Research overseen by the Royal College projects a 25% increase in the number of cataract surgeries will be required to meet demand over the next 10 years[16].

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[12] Ru Zhou and Rachel R Caspi, 'Ocular Immune Privilege.', *F1000 Biology Reports*, 2 (2010) <http://www.ncbi.nlm.nih.gov/pubmed/20948803> [accessed 14 October 2018].

[13] Charles Osei-Bempong, Francisco C. Figueiredo and Majlinda Lako, 'The Limbal Epithelium of the Eye - A Review of Limbal Stem Cell Biology, Disease and Treatment', *BioEssays*, 35/3 (2013), 211–19 <http://doi.wiley.com/10.1002/bies.201200086> [accessed 25 February 2018].

[14] Sai Kolli and others, 'Successful Clinical Implementation of Corneal Epithelial Stem Cell Therapy for Treatment of Unilateral Limbal Stem Cell Deficiency', *STEM CELLS*, 28/3 (2009), N/A-N/A <http://doi.wiley.com/10.1002/stem.276> [accessed 11 March 2018].

[15] Kanmin Xue and others, 'Beneficial Effects on Vision in Patients Undergoing Retinal Gene Therapy for Choroideremia', *Nature Medicine*, 24/10 (2018), 1507–12.

[16] *Keeping in Touch* <www.rcophth.ac.uk/standards-publications-research/the-way-forward/> [accessed 15 October 2018].

In the NHS, spending is constrained by government spending. The Office of Budget Responsibility projects that a 4% increase NHS spending per year is required to meet increasing demands, much of which is created by an aging population[17].

A shadow hangs over NHS ophthalmic practice: the need for adequate follow-up of complex eye disease is not being met, and it has been known for over a decade that patients are experiencing irreversible vision loss due to being lost to follow-up. Currently this is around 200 patients per year across the UK[18]. The Royal College has recommended several mechanisms of change to help increase the efficiency of ophthalmic departments, however the college also admits that these are unlikely to be sufficient and more funding is needed[19].

There are two possible avenues for ophthalmic practice in the UK, moving forward. One is that the NHS may continue to struggle forward, implementing efficiency changes such as those recommended by the Royal College, but chronically unable to meet demand. The alternative is radical change to the service provision we know today. Progress in ophthalmic care will undoubtedly test current care provision as trusts are asked to fund novel treatments. On the other hand, technological advancements may increase the efficiency and effectiveness of current ophthalmic care beyond what is currently possible.

Conclusion

Ophthalmology is a multidisciplinary and rapidly evolving specialty. It has changed faster than arguably any other medical or surgical specialty over the past 30 years, as it rides a wave of mostly technological advancements. This advancement will be challenged by an aging population combined with budgetary constraints.

Thus, the British ophthalmic clinic of 2048 will meet its challenges through increased technological integration within the traditional framework of patient-centred medical practice. As imaging techniques become faster, cheaper and more readily available, they will be performed routinely. Examination will become less fruitful and greater importance will be placed on interpretation of the myriad data divulged by these scans. Perhaps this will reduce

[17] Anonymous, 'The NHS Budget and How It Has Changed', *Kings Fund*, 2017, 1 <https://www.kingsfund.org.uk/projects/nhs-in-a-nutshell/nhs-budget> [accessed 15 October 2018]; David Maguire, Phoebe Dunn and Helen McKenna, 'How Hospital Activity in the NHS in England Has Changed over Time | The King's Fund', *The King's Fund*, 2016 <https://www.kingsfund.org.uk/publications/hospital-activity-funding-changes> [accessed 15 October 2018].

[18] B Foot and C MacEwen, 'Surveillance of Sight Loss due to Delay in Ophthalmic Treatment or Review: Frequency, Cause and Outcome', *Eye*, 31/5 (2017), 771–75 <http://www.nature.com/articles/eye20171> [accessed 15 October 2018]; *Ophthalmology: Support Document for Commissioners through CCGs, STPs and Regional Reconfigurations What Are the Potential Patient Safety Risks in the Commissioning of Ophthalmology Activity and How Can They Be Alleviated?* <http://www.college-optometrists.org/en/utilities/document-> [accessed 15 October 2018].

[19] *Ophthalmology: Support Document for Commissioners through CCGs, STPs and Regional Reconfigurations What Are the Potential Patient Safety Risks in the Commissioning of Ophthalmology Activity and How Can They Be Alleviated?*

our need for nearby consultant expertise, and follow-up may be performed remotely with registrars running clinics and receiving remote consultant opinion on scans. Even more radically, perhaps we will rely on the interpretation given by artificial intelligence. However, as the history of ophthalmology has shown us, even the most heretical ideas have caused revolutions.

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