

Technology driving advances in ophthalmology

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OVER THE PAST 10 YEARS significant improvements in technology underlying ophthalmic diagnosis and treatment have led to marked improvements in visual outcomes for patients.

Optical coherence tomographic (OCT) scanning is a new technology that uses interferometry of infrared light, similar to ultrasonography, and can produce detailed retinal images of near-histological quality in vivo within a very short testing time. As shown by Rowland and Lee,¹ OCT scanning allows non-invasive diagnosis of common conditions such as neovascular 'wet' age-related macular degeneration (nAMD) and diabetic macular oedema, and has assisted understanding of new conditions such as vitreomacular interface disorders (aberrant adhesion between the vitreous body and the retina). Portable OCT scanners are now in development and are a new tool to guide vitreoretinal surgeons intraoperatively.

Artificial intelligence (AI) with deep learning neural networks is being used to assist screening for common conditions including diabetes and AMD, a previously big logistical challenge. AI screening of retinal images has already equalled, and in some cases surpassed, the best human graders in diabetic retinopathy. Clinical oversight is necessary to ensure ophthalmologists examine outlier images rather than the AI discarding or misinterpreting the information. Regulatory oversight is also needed.

Vascular endothelial growth factor (VEGF) is now known to be the underlying molecular pathology behind many common retinal-vascular conditions.

The development of anti-VEGF antibodies, delivered by intravitreal injection, has led to effective treatments for common blindness-causing conditions such as diabetic macular oedema and proliferative retinopathy, nAMD, retinal vein occlusions and rare retinal conditions. The anti-VEGF era has resulted in a marked reduction in blindness due to diabetes in adults of working age,² and nAMD in older patients. Anti-VEGF treatment is expensive because of the cost of medications and the need for frequent treatments to achieve good results; however, economic analysis demonstrates the value of treatment through lowered rates of blindness and its associated morbidity, mortality and cost of care. Hence anti-VEGF therapy has been granted Pharmaceutical Benefits Scheme and Medicare Benefits Schedule subsidies in Australia.

In the anti-VEGF era, the most common cause of blindness in adults of working age is now retinal degeneration,² and gene therapy is emerging as appropriate treatment. Preparations are underway for Australian patients to trial voretigene neparovec, the first ophthalmic gene therapy for treatment of Leber congenital amaurosis, a congenital form of retinitis pigmentosa caused by loss-of-function bi-allelic mutations in *RPE65*, a gene involved in vitamin A recycling in the retina. Internationally, trials of gene therapy have commenced for other retinal degenerative conditions (choroideraemia, achromatopsia and X-linked retinoschisis, among others) and Leber congenital optic neuropathy. *CRISPR/Cas9* gene repair, possibly coupled with stem cell transplants, is likely to be the next stage of gene therapy.

Early stage trials are also underway or in planning in Australia for previously

untreatable conditions: atrophic 'dry' AMD using complement factor B inhibition, Usher syndrome (genetic blindness and deafness) using N-acetylcysteine as an antioxidant, and Stargardt macular dystrophy (blindness in children) using agents to block vitamin A recycling.

Stem cells show promise as a treatment for ocular diseases, possibly coupled with gene repair; however, caution is necessary. One report of three patients treated for AMD with intravitreal injections of autologous adipose tissue-derived 'stem cells' showed very poor outcomes with visual acuity at one year ranging from 6/60 to no light perception caused by vitreous and retinal scarring.³ Further work is needed in this area, with effective regulation to minimise 'rogue' clinics.

Advances in technology have led to transformative change in diagnosis and management of ophthalmology patients, with appreciable reductions in blindness for adults of working age and older. Further developments will require close clinical and regulatory supervision to ensure further improvement in patient outcomes.

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