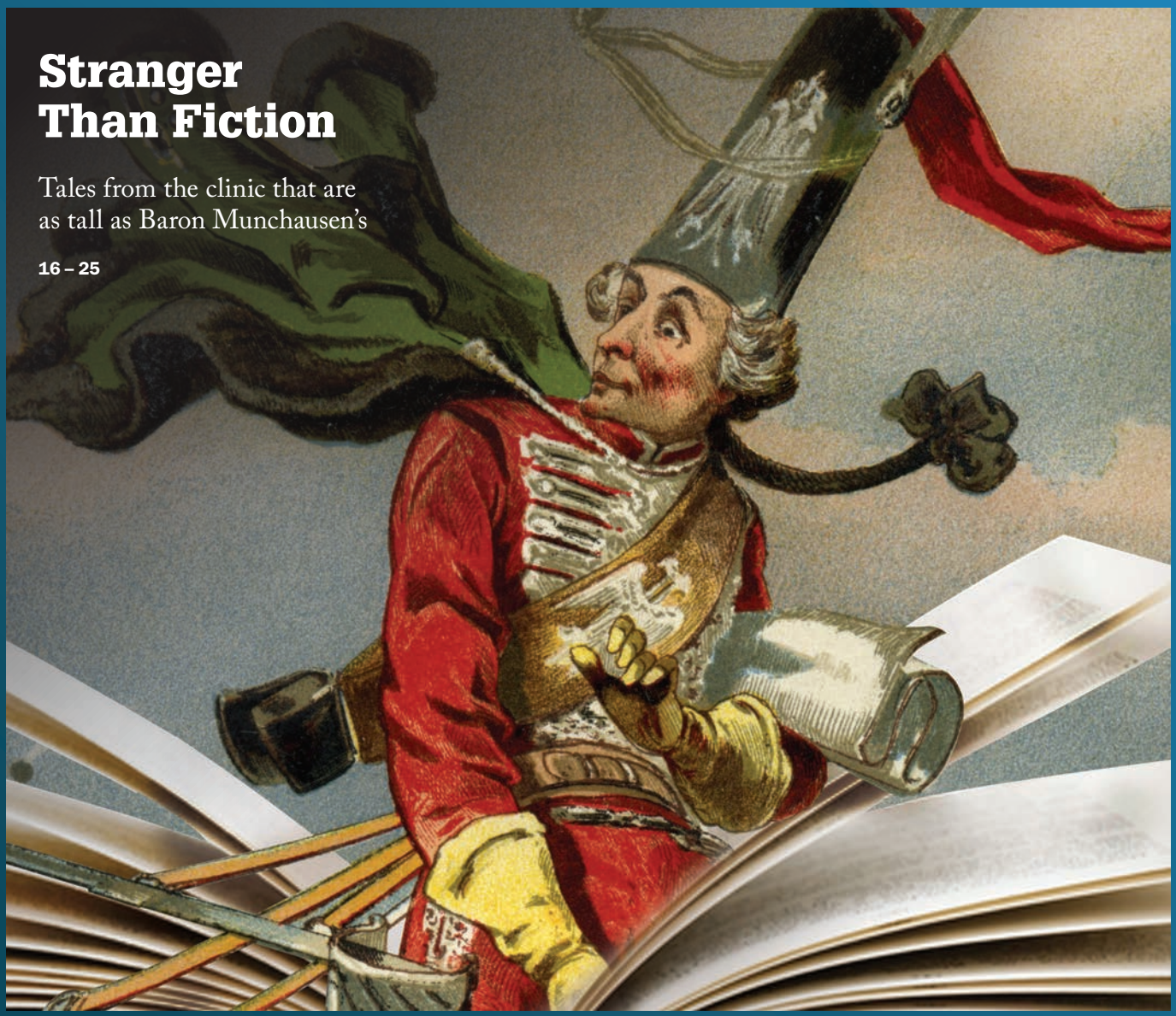
FEBRUARY 2017 # 06

the Ophthalmologist



Stranger Than Fiction

Tales from the clinic that are as tall as Baron Munchausen's

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IMPORTANT PRODUCT INFORMATION FOR THE ACRYSOF® IQ RESTOR® FAMILY OF IOLs

CAUTION: Federal (USA) law restricts this device to the sale by or on the order of a physician.

INDICATIONS: The AcrySof® IQ ReSTOR® Posterior Chamber Intraocular Lens (IOL) is intended for primary implantation for the visual correction of aphakia secondary to removal of a cataractous lens in adult patients with and without presbyopia, who desire near, intermediate and distance vision with increased spectacle independence. The lens is intended to be placed in the capsular bag.

WARNINGS/PRECAUTIONS: Careful preoperative evaluation and sound clinical judgment should be used by the surgeon to decide the risk/benefit ratio before implanting a lens in a patient with any of the conditions described in the Directions for Use labeling. Physicians should target emmetropia, and ensure that IOL centration is achieved. Care should be taken to remove viscoelastic from the eye at the close of surgery.

Some patients may experience visual disturbances and/or discomfort due to multifocality, especially under dim light conditions. As with other multifocal IOLs, visual symptoms may be significant enough that the patient will request explant of the multifocal IOL. Spectacle independence rates vary with all multifocal IOLs; as such, some patients may need glasses when reading small print or looking at small objects.

Clinical studies with the AcrySof® ReSTOR® lens indicated that posterior capsule opacification (PCO), when present, developed earlier into clinically significant PCO. Prior to surgery, physicians should provide prospective patients with a copy of the Patient Information Brochure available from Alcon for this product informing them of possible risks and benefits associated with the AcrySof® IQ ReSTOR® IOLs.

Studies have shown that color vision discrimination is not adversely affected in individuals with the AcrySof® Natural IOL and normal color vision. The effect on vision of the AcrySof® Natural IOL in subjects with hereditary color vision defects and acquired color vision defects secondary to ocular disease (e.g., glaucoma, diabetic retinopathy, chronic uveitis, and other retinal or optic nerve diseases) has not been studied. Do not resterilize; do not store over 45° C; use only sterile irrigating solutions such as BSS® or BSS PLUS® Sterile Intraocular Irrigating Solutions.

ATTENTION: Reference the Directions for Use labeling for a complete listing of indications, warnings and precautions.

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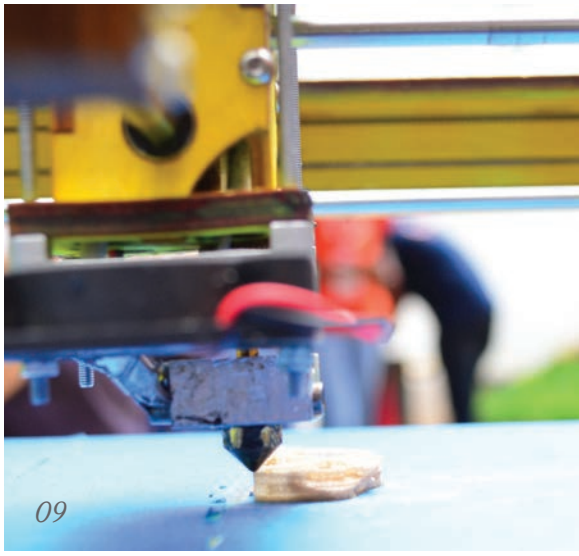
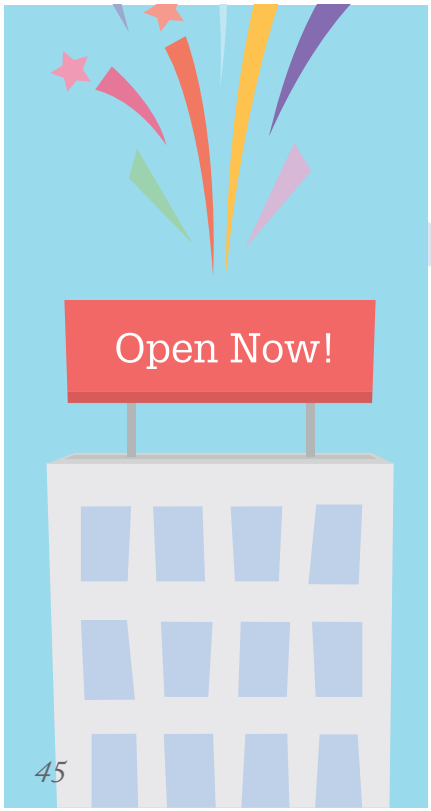


On The Cover

Baron Munchausen, an infamous teller of tall tales, climbing out of a story book.



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In Practice

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the Ophthalmologist
ISSUE 06 - FEBRUARY 2017

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Annual subscription for non-qualified recipients US$140.

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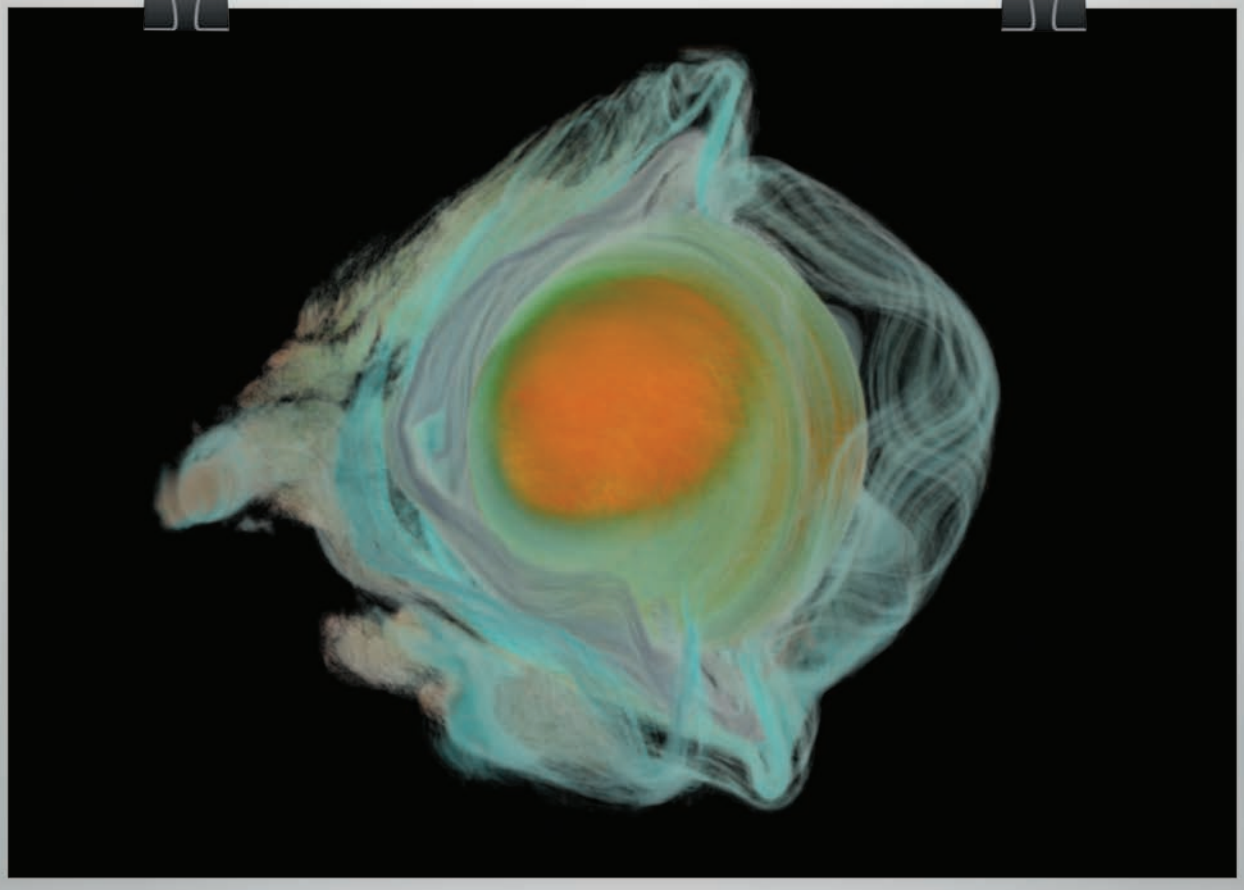
Distribution:
The Ophthalmologist (ISSN 2398-9270) is published monthly by Texere Publishing Ltd and is distributed in the USA by UKP Worldwide, 1637 Stelton Road B2, Piscataway, NJ 08854. Periodicals Postage Paid at Piscataway, NJ and additional mailing offices
POSTMASTER: Send US address changes to The Ophthalmologist, Texere Publishing Ltd, c/o 1637 Stelton Road B2, Piscataway NJ 08854

Image of the Month



GoldenEye

This image of a rat eye was created using 810 Masson-Goldner stained histological sections to produce a 3D reconstruction.

Image courtesy of microDimensions, with section preparation by Morphisto GmbH.

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OCT for all, and all for OCT

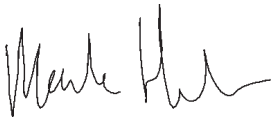
Eye exams can detect more than ocular disease. Is there a place for it in general practice?

What might the future of diagnostics in healthcare look like in 10 or 20 years' time? If you speak with general practitioners and hospital doctors, some believe that every patient will go through an MRI scanner as a matter of course. I can see how that would make sense; diagnostic algorithms are run, and a report pops up on the future physician's... future information delivery device. Add in a blood panel, and you would be able to make a large number of diagnoses in little more than the time it takes to run the tests. But MRI doesn't resolve fine details like microcapilliaries or nerve fiber bundles – in theory, you would need phenomenally powerful superconducting magnets to do that. So we return to the eye.

Eye specialists already diagnose half of all type II diabetes cases. Cardiologists can (and do) refer their patients for fundus imaging to detect pathologies such as arterial hypertension. The presence of hypertensive retinopathy strongly predicts stroke risk (1). RNFL thickness reductions have been associated with both the stage and duration of schizophrenia, as well as decreased cognitive function (2,3). In terms of both vascular and neurological disease, the eye offers a clear view (cataract notwithstanding), and highly precise measurements can be made, in the case of fundus photographs and OCT scans, in seconds – or, if techniques such as OCT angiography are used, tens of seconds. Add in artificial intelligence image analysis algorithms like those being developed by Alphabet's Google DeepMind and Verily divisions, and you've got access to rapid diagnoses and risk predictions as well.

Cost is always the barrier to widespread adoption of new technologies. But the cost of adoption will fall. My knowledge of the MRI scanner market is not even superficial, but with OCT, we're already seeing a trend towards smaller, all-in-one, simple-to-use, lower-cost OCT instruments that patients could almost operate by themselves. You can see the endgame – a simple and effective (and perhaps even portable [4]) diagnostic and screening method for multiple diseases. I can see a scenario in the future where my doctor's appointment begins with an eye scan that takes 30 seconds, giving the GP time to load my records onto a screen and glance at my history, before they ask, "And what can we do for you today?" Perhaps they'll already know the answer.

Mark Hillen
Editor



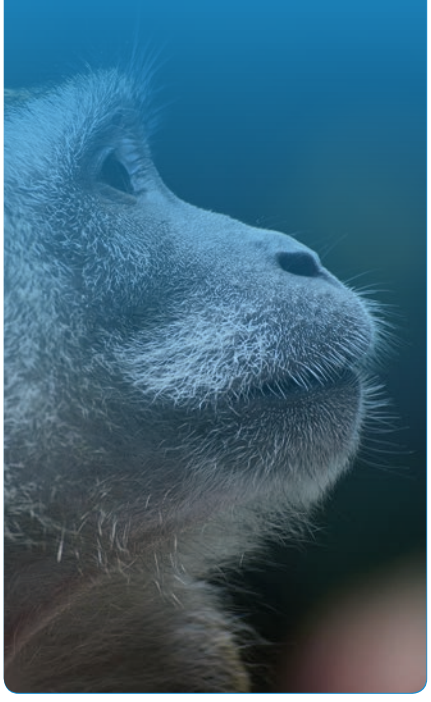
References

1. *YT Ong et al., "Hypertensive Retinopathy and Risk of Stroke," Hypertension, 62, 706–711 (2013). PMID: 23940194.*
2. *WW Lee et al., "Retinal nerve fiber layer structure abnormalities in schizophrenia and its relationship to disease state: evidence from optical coherence tomography", Invest Ophthalmol Vis Sci, 54, 7785–7792 (2013). PMID 24135757.*
3. *F Ko et al., "Retinal nerve fiber layer thinning associated with poor cognitive function among a large cohort, UK Biobank", Presented at Alzheimer's Association International Conference; 2016, Toronto, Canada. Abstract: a10202.*
4. *P Keane, A Walsh, "The OCT Exam's Quantum Leap", The Ophthalmologist, 26, 20–27 (2016). Available at: http://top.txp.to/issues/0116/301. Accessed January 19, 2016.*

Upfront

Reporting on the innovations in medicine and surgery, the research policies and personalities that shape the practice of ophthalmology.

We welcome suggestions on anything that's impactful on ophthalmology; please email edit@theophthalmologist.com



Mouse Versus Monkey

New AAV vectors promise better retinal cell type targeting… in mice. But does this hold up in non-human primates?

The era of gene therapy is coming – there's no doubt about that. And the eye is a promising candidate, as it provides easy surgical access, good visualization of the treated tissue, and has a (relatively) immune privileged status. Over a dozen gene therapies for retinal disease are currently in clinical trials, and many more are in the pipeline.

Adeno-associated virus (AAV) serotype 2 (AAV2) is the vector that, for the most part, has been used safely and successfully in the vast majority of these trials. But there's a problem. Mouse studies have shown that intravitreal injection (IVI) of AAV2 results in the transduction of the innermost retinal ganglion cells, but not the photoreceptors in the outer retina. Subretinal injection transduces both, but this approach is considerably more challenging, invasive, costlier and riskier to perform than an IVI. In an ideal world, you'd have a vector and genetic payload that can be injected by IVI, and penetrate and target the cell types of interest – even those in the outer retina.

Fortunately, other AAV serotypes have emerged since AAV2's discovery, and have the ability to target particular cell types and effectively penetrate certain tissues. We now have the capability of performing in vivo-directed evolution whereby the configuration of the virus' capsid (and therefore the cells it infects and delivers its payload to) can be altered to target a desired cell type (1). The problem is, most of the work with these vectors has been limited to mouse studies – and the anatomical and physiological differences between murine and human eyes means that what might work in mice, might not work in the clinic.

A team from the Perelman School of Medicine, Philadelphia, decided to put two eGFP-expressing AAV serotypes to the test, namely AAV7m8 and AAV8BP2, both of which had successfully been used to transfect mouse retinal cells. But instead of using mice, they used non-human primates (NHPs; cynomolgus macaques to be specific) in the hope of providing a better prediction of the outcome in the human retina (2).

They found some important interspecies differences: in mice, AAV7m8 was able to reach photoreceptor and retinal pigment epithelium cells in the outer retina after IVI, whereas in NHPs, this happened only at the highest dose of vector (which was also associated with severe inflammation and cell injury). One of the reasons AAV8BP2 attracted interest was because it transfects cone photoreceptors and bipolar cells after subretinal injection in mice, but in NHPs it only transfected cone receptors efficiently. After intravitreal delivery, both vectors achieved transduction in the anterior chamber and the optic pathway. Notably, AAV8BP2 had the better safety profile, even at higher doses.

The upshot? The authors state in the paper: "This study shows that one cannot extrapolate directly between mice and 'men.'" *RM*

References

1. *D Dalkara et al., "In vivo-directed evolution of a new adeno-associated virus for therapeutic outer retinal gene delivery from the vitreous", Sci Transl Med, 5, 189ra76 (2013). PMID: 23761039.*
2. *PS Ramachandran et al., "Evaluation of dose and safety of AAV7m8 and AAV8BP2 in the non-human primate retina", Hum Gene Ther, [Epub ahead of print] (2016). PMID: 27750461.*

3D-Printable Prototypes

How to develop a new tool for strabismus surgery – using additive manufacturing

With the advent of 3D printing comes almost infinite possibility. Household items, artificial limbs, and even concept cars... What can't be manufactured by these marvelous machines?

But the world of 3D printing isn't only about creating increasingly impressive items. The potential to get from page to product in just a few clicks has led many inventors to embrace the technology for rapid prototyping. And eyecare is no exception. Here, Donny Suh, a pediatric surgeon and keen inventor from the University of Nebraska Medical Center (UNMC) and Children's Hospital and Medical Center, shares how he developed an improved version of a tool commonly used in pediatric strabismus surgery.

What inspired you to develop the prototype?

The traditional needle driver used in eye surgeries today (invented over 80 years ago) works very well. However, some situations require the surgeon to use their non-dominant hand in tight spaces, making it harder to place the suture with extreme precision. I have long thought about creating an instrument that could make surgery easier to perform and safer for patients. Our new instrument aims to make these challenging procedures less difficult by allowing the surgeon to place the needle with their dominant hand.

Why 3D printing?

Using this technology, the whole development process becomes more efficient. When it comes to designing a new surgical instrument, you need to physically hold it and try it in a laboratory setting. Being able to 3D print each of the prototypes allowed me to deliver immediate feedback and make as many modifications as needed. If we were to solely use titanium or stainless steel prototypes, the development would be extremely costly and time consuming.

How was the prototype tool designed?

The initial prototypes were based on digital designs that the UNMC Makers (our 3D printing club) and I created, with the support of the McGoogan Library of Medicine. Firstly, the instrument was sketched and converted into a digital format (Figure 1). With the help of the UNMC makers, I was then able to physically hold a 3D-printed prototype. After giving them feedback, they made several alterations to the plastic design.

How did you test your prototype?

I tested a plastic version of the prototype on an eye model. Once the titanium version arrives, it will undergo experimental trials to confirm its viability in a surgical setting, at which point it may undergo further alterations.

Any notable challenges?

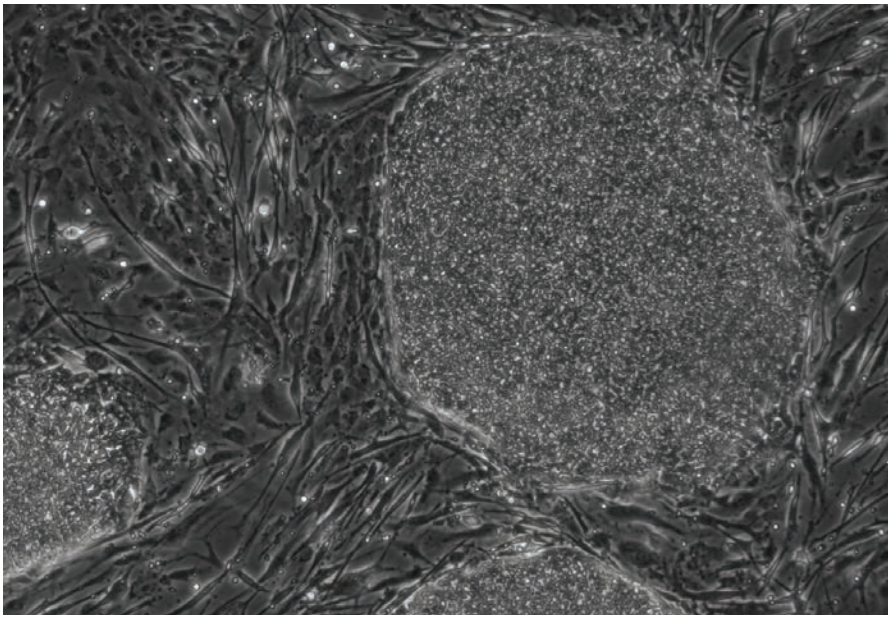
When I first came up with the idea, the manufacturers I approached felt that creating the instrument would be extremely difficult because of the curved nature of the small, delicate needle driver tip. That's when I turned to making a 3D-printed prototype; I wanted to check the feasibility of the design and to demonstrate the viability of the instrument to the manufacturer.

Credit: Donny Suh, University of Nebraska Medical Center and Children's Hospital and Medical Center.

Figure 1. Three drawings of the new tool.

Long Live the Stem Cell!

hESCs transplanted into immunocompromised murine retina exhibit increased longevity and long-term functionality

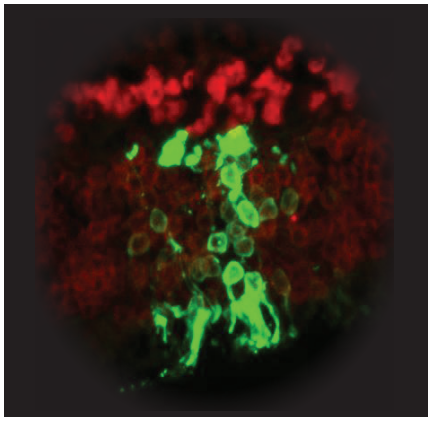


In 2014, Silicon Valley-based entrepreneur Joon Yun launched his $1 million Palo Alto Longevity Prize as an incentive to scientists to fix the "problem" of aging. In nearby Novato, Deepak Lamba's group at the Buck Institute for Research on Aging have been focusing on fixing this problem (or at least the retinal degenerative disorders associated with aging) with stem cell therapy (1).

To be efficacious as regenerative therapies, stem cells must be able to live long enough to integrate into the host tissue and "do their job." Currently, this isn't always the case; they can be rejected by the immune system shortly after transplantation or fail to thrive in degenerated or diseased tissues. Although Lamba's group had previously shown that human embryonic stem cell (hESC)-derived photoreceptors transplanted into murine retinas could integrate and function (2), it has been difficult for researchers to demonstrate long-term functionality and restoration of vision. "A major controversy in the field is whether the transplanted photoreceptors simply die off or are actively rejected by the immune system," says Lamba.

To try and settle the matter – and potentially improve stem cell longevity – the team transplanted hESCs into severely immunodeficient interleukin 2 receptor γ chain (*IL2rγ*) null mice ($IL2r\gamma^{-/-}$), which are essentially phenotypically normal, apart from the fact that they can't reject transplanted cells (1). In such mice, the team found that the number of mature hESC-derived cells that integrated into the retina increased 10-fold (3). They also showed that transplanted hESCs could restore light sensitivity in congenitally blind Crx^{tvrm65} mice, and that this restoration of visual function was significantly greater in immunodeficient $Crx^{tvrm65}/IL2r\gamma^{-/-}$ mice at three and nine months post-transplantation than $Crx^{tvrm65}/IL2r\gamma^{+/+}$ mice ($p<0.001$ and $p<0.01$, respectively) (1).

"We show that these mice can now perceive light as far out as nine months following injection of these cells – that gives us a lot of hope for patients," says Lamba. The team's findings suggest that an immune suppression approach might be an effective method of increasing the functional lifespan of stem cells used for photoreceptor replacement therapy and potentially improve clinical outcomes. Lamba notes, "We have found that we can't ignore cell rejection when trying to transplant stem cells into the eye." *RS*



Credit: Jie Zhu, Buck Institute for Research on Aging.

Transplanted GFP-expressing human stem cell-derived photoreceptors integrated in a host rodent retina stained for the photoreceptor marker, Otx2, in red.

References

1. *J Zhu et al., "Immunosuppression via loss of IL2rγ enhances long-term functional integration of hESC-derived photoreceptors in the mouse retina", Cell Stem Cell, (2016). [ePub ahead of print]. PMID: 28089909.*
2. *DA Lamba et al., "Transplantation of human embryonic stem cell-derived photoreceptors restores some visual function in Crx-deficient mice", Cell Stem Cell, 4, 73–79 (2009). PMID: 19128794.*
3. *Buck Institute for Research on Aging, "Improving the longevity of functionally integrated stem cells in regenerative vision therapy", (2017). Available at: bit.ly/BuckRelease. Accessed January 24, 2017.*

Sex, Bucks, and Bills n' Codes

How wide is the payment gap between male and female ophthalmologists?

January 21, 2017 marked two key events in history – President Trump's first full day in office and the Women's March, which saw millions across the globe raising awareness of equality issues. The field of ophthalmology is not immune. Just two days prior, a collaboration of ophthalmologists and researchers published their gender-comparing study online on JAMA Ophthalmology (1).

The group wanted to know "How do the earnings and clinical activity of men and women compare?" To answer this, they used the publicly available Centers for Medicare and Medicaid Services (CMS) database to perform a retrospective review of the payments made to ophthalmologists (reflected in reimbursements from CMS) between January 1, 2012 and December 31, 2013. What did they find? We summarize the key findings (Figure 1):

- For every dollar earned by a male ophthalmologist through the CMS in 2012 and 2013, female ophthalmologists collected an average of 58 cents ($p<0.001$).
- Women submitted an average of 1120 and 1200 fewer charges than men in 2012 and 2013, respectively (both $p<0.001$).
- Mean collections in 2012 and 2013 by female ophthalmologists were $78,473 and $77,464 less than mean collections by male ophthalmologists, respectively ($p<0.001$).
- The mean payment per charge for both men and women was $66 in 2012 and $64 in 2013.
- Remuneration was lower for women, even when men and women with similar levels of clinical activity were compared.

Although the results reveal that there were disparities between men and women in terms of CMS payments, the study was not designed to answer why. Conceding that further research might "illuminate the reasons for clinical activity and financial differences," the study authors conclude: "there is face validity to the position that women have fewer opportunities to pursue the same economic prospects as men. This finding warrants formal attention."

But what of pay gaps? Ruth Williams of Wheaton Eye Clinic, Illinois, in a corresponding commentary article (2), noted that: "There is debate about whether lower pay for women is related to personal choices or to systemic inequities. It's both. [...] Women often have a different cadence to career. At the same time, institutional barriers still exist for women, and we are increasingly aware of them and increasingly free to point them out." *RS*

References

1. *AK Reddy et al., "Differences in clinical activity and Medicare payments for female vs. male ophthalmologists", JAMA Ophthalmol, (2017). [Epub ahead of print]. PMID: 28114631.*
2. *RD Williams. "Medicare payments and physician sex in ophthalmology", JAMA Ophthalmol, (2017). [Epub ahead of print]. PMID: 28114640.*

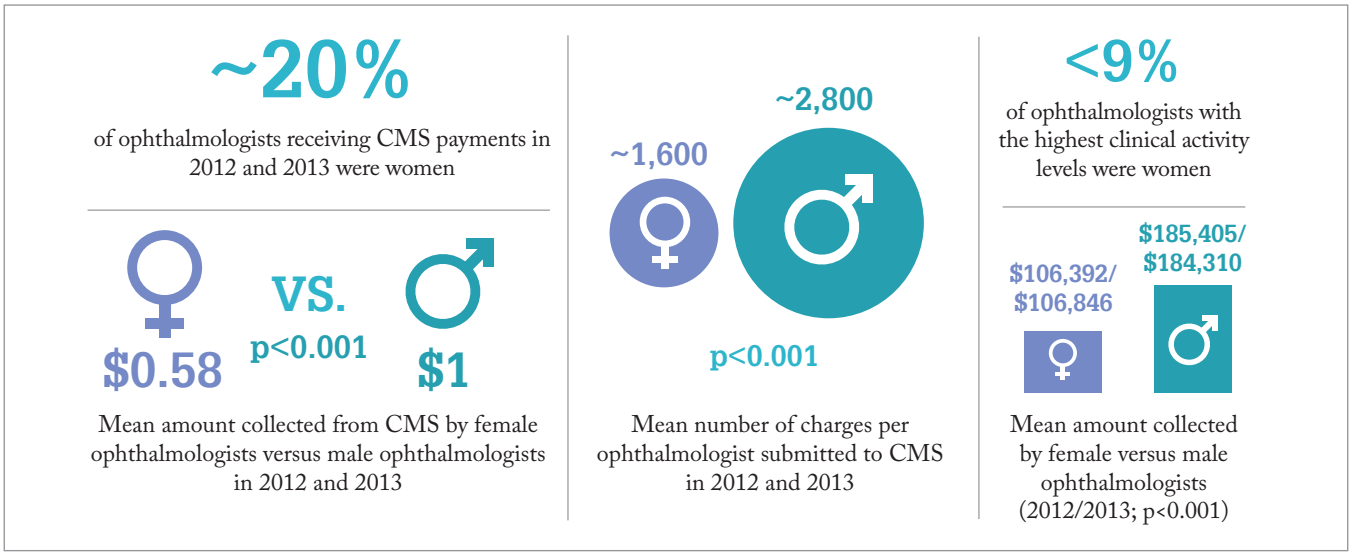


Figure 1. Summary of key results from the retrospective review comparing collections and clinical activity of female and male ophthalmologists in 2012 and 2013. Adapted from (1). CMS, Center for Medicare and Medicaid Services.

Tears of Blood

Are new oral anticoagulants more or less likely to cause intraocular bleeding than warfarin?

The problem with aging is that it doesn't just increase the risk of developing age-related ophthalmic disease – it also increases the risk of developing age-related everything else. And co-morbidities require concomitant treatment, which, in the case of vascular disease, can include anticoagulant drugs. Until about a decade ago, the options available were either intravenous, relatively short-acting, heparin-based agents (essentially for acute use only) or, quite literally, rat poison (oral warfarin). Warfarin is a tricky beast; it interacts with many foods and drugs, and its efficacy varies by the contents of a person's last meal. It's fair to say that pharmacokinetics and pharmacodynamics [PK/PD] can be... unpredictable. Plasma levels of warfarin (and its active metabolites) must be tightly controlled, which necessitates regular monitoring and dose adjustment, otherwise patients risk one of two potentially deadly extremes: bleeding or thrombosis.

The drawbacks of warfarin spurred the development of new oral anticoagulants (NOACs) that have fewer drug and dietary interactions, more predictable PK/PD, and, therefore, less requirement for monitoring or dose adjustment. Take one or two pills a day and forget about it. They've made a big impact – in 2014, the bestselling NOAC of them all, rivaroxaban (Janssen/Bayer), made US$3.7 billion. But bleeding is still their biggest complication (1) – and in the eye, that can have serious consequences that may take a long time (or even require surgery) to resolve.

It's known from epidemiological studies that NOACs do cause ocular hemorrhages – but the question for ophthalmologists is:

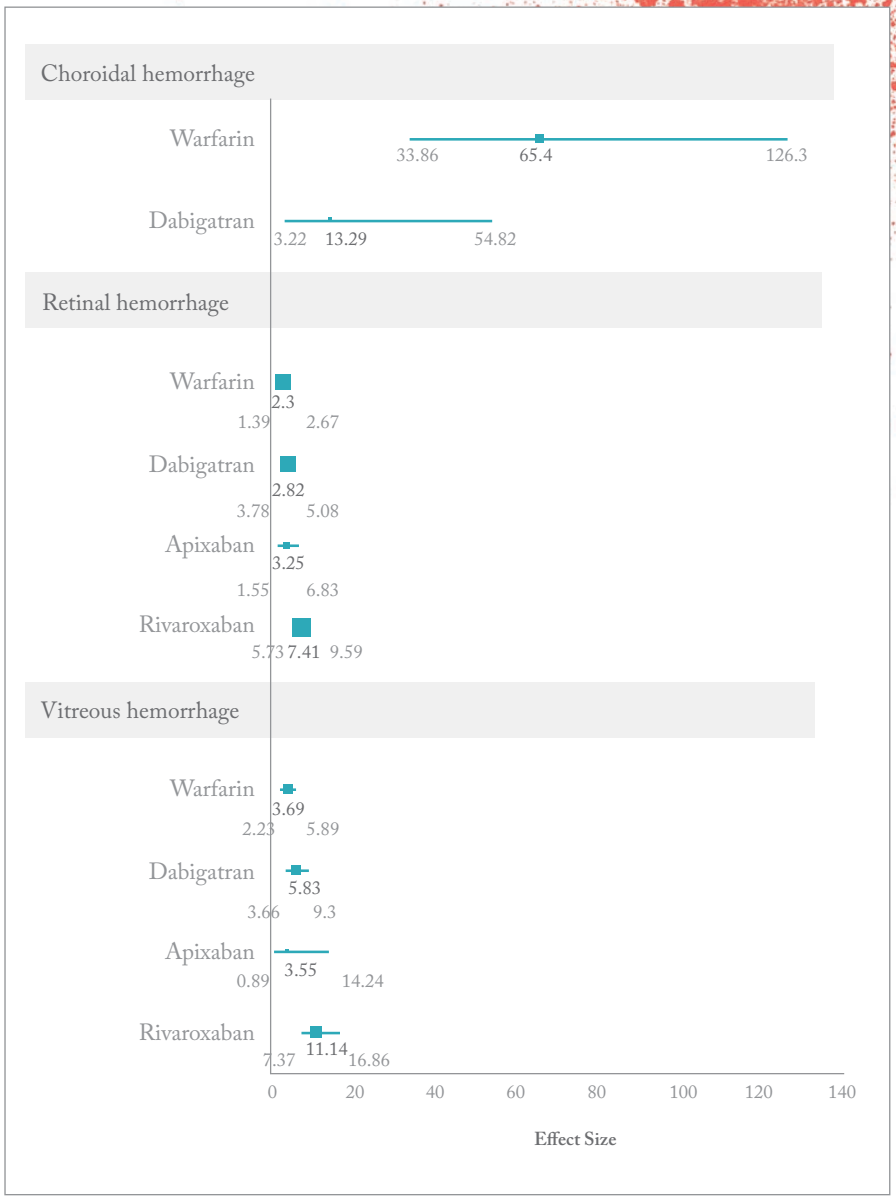


Figure 1. Reporting odds ratios for choroidal, retinal and vitreous hemorrhage with warfarin, dabigatran, apixaban and rivaroxaban (an effect size of 1 equals the average effect of all drugs in the Vigibase database on ocular bleeding). Adapted from (2).

are they more or less likely to cause bleeding than warfarin? A team from the University of British Columbia decided to find out by mining the World Health Organization's Vigibase drug adverse reaction database from the period of 1968–2015 (a total of 11,582,092 events) to find out (2). They employed a disproportionality analysis to do so, computing the reported odds ratios (RORs) of all of the ocular (choroidal, retinal or vitreous) hemorrhage events that occurred with warfarin and each of the NOACs and then compared it with all other adverse reactions reported to Vigibase.

They found 80 cases of intraocular

hemorrhage with warfarin, and 156 cases with the NOACs (82, 65 and 9 for rivaroxaban, dabigatran and apixaban, respectively). They also found that warfarin had the highest signal for choroidal hemorrhage, whereas rivaroxaban had the highest signal for retinal and vitreous hemorrhage (Figure 1).

Is warfarin getting a raw deal here? It's been around the longest, so the authors suggest there "may have been a heavier predisposing to report hemorrhage incidents with the drug." On the other hand, apixaban may be getting a better deal – the drug was associated with an excess of retinal hemorrhage events, but fewer ocular hemorrhagic events of any kind than the others, but this may be because it has been on the market for the shortest period of time. Perhaps more exposure will clarify the situation.

There's still work to be done. Operating on an anticoagulated patient isn't fun. In the eye alone, bloody tears, hyphema and vitreal, subconjunctival, subretinal and choroidal hemorrhages can all occur, but there are no substantial recommendations or guidelines regarding the modification of anticoagulant regimens before ocular surgery. Instead, it's entirely up to the surgeon's judgement for each patient. With patients receiving NOACs – just like those receiving warfarin – the lesson appears to be: tread very carefully! *MH*

References

1. *RL Summers, SA Sterling, "Emergent bleeding in patients receiving direct oral anticoagulants," Air Med J, 35, 148–155 (2016). PMID: 27255877.*
2. *G Talany, M Guo, M Etminan, "Risk of intraocular hemorrhage with new oral anticoagulants", Eye, [Epub ahead of print] (2016). PMID: 28009346.*

The Ophthalmologist Power List 2017

Who are the "rising stars" of ophthalmology?

Back in 2014, we featured our first Power List – a showcase of the 100 most influential people in ophthalmology. The popularity of the list led us to repeat the endeavor annually, and we've honored many pioneers and game-changers over the years. This year, we continue the celebration but with a twist: we will shine a spotlight on the next generation of influential individuals, trailblazing pioneers, and outspoken opinion shapers. In short, we're asking: who are the "rising stars" of ophthalmology?

Only you can answer this, by nominating those trainees or early-career professionals who are making a difference to the field today – and who you think will have a bright future ahead of them. Getting involved is easy: nominate those rising stars that you think are most likely to shape the future of ophthalmology by visiting top.txp.to/Powerlist2017/form.

Please include:

- Name, affiliation and career stage of the person you are nominating
- Why you are nominating them
- Your name, affiliation and email address

The process:

- You can nominate yourself or someone else who is within five years of obtaining their first faculty position or who are aged 40 years and under. Up to five people can be nominated
- The deadline for nominations is Friday March 3, 2017
- The full list of nominations will be put to an expert panel who will make the final selection
- The panel's decision is final and no correspondence regarding their deliberations or the final list will be entered into.

The Ophthalmologist Power List 2017 will be published in the April 2017 issue of The Ophthalmologist, in print and online.

In My View

In this opinion section, experts from across the world share a single strongly-held view or key idea.

Submissions are welcome. Articles should be short, focused, personal and passionate, and may deal with any aspect of ophthalmology. They can be up to 600 words in length and written in the first person.

Contact the team at edit@theophthalmologist.com

Too Soon to SMILE

Despite the emergence of alternatives, femtosecond LASIK remains at the cutting edge of vision correction.

By Julian Stevens, Consultant Ophthalmic Surgeon, Moorfields Eye Hospital, London, UK.

We now have almost 30 years of expertise with the excimer laser. We started with PRK treatment on the corneal surface and initially saw regression – but that is now conquered. We had issues with early LASIK procedures, particularly with flap creation, but continued improvements to microkeratomes and in surgical technique resolved them. But even with a microkeratome, LASIK was a huge improvement over the original surface ablations, and with the introduction of the femtosecond laser for flap creation, microkeratome use became less popular, and femtosecond LASIK came to be the preferred procedure.

Wavefront-guided LASIK was introduced in 2001, which offered more predictable and improved excimer laser beam delivery. Given that the predicted and postoperative outcomes are so close, some or much of the statistical differences between them are statistical noise, so it's clear that the procedure is becoming extremely precise. Iris registration for astigmatic improvement arrived next, improving not only astigmatic alignment, but also registration of higher order aberrations. Further, improvements in iris registration, cyclotorsion, laser calibration and stability, and very high resolution wavefront sensing have all taken place. Simply put, we are now approaching the limits of accuracy with excimer laser based corneal ablation.

However, another option has emerged. There has, for decades, been a desire to perform intrastromal corneal refractive surgery to effect corneal curvature change – a single femtosecond laser can be used for flap creation and refractive lenticule extraction (RELEX). Small lenticule extraction (SMILE) evolved from RELEX, and has become a clinically effective and widely performed procedure.

Some surgeons have started to see great benefits with this technique, but we have to judge this against the state-of-the-art LASIK benchmark. SMILE, in its current implementation, is a very interesting procedure and the subject of intense investigation. But there is a significant learning curve for new surgeons and those unfamiliar with the current VisuMax femtosecond laser. I have very experienced, highly capable colleagues at Moorfields who first used the VisuMax to perform SMILE without prior experience of creating LASIK flaps with the system. They found good outcomes difficult to master.

SMILE advocates argue that patients can return to their daily activities quickly due to the small incision nature of the procedure. But LASIK patients can return to work (or even visit the gym) the next day and have better early recovery of vision compared to SMILE patients.

When considering procedure options it's important to consider risk versus benefit. When performing LASIK or SMILE, the potential complications include ectasia, diffuse lamellar keratitis, epithelial ingrowth, and decentration – but SMILE also brings the risk of a unique, novel complication of incomplete lenticule removal.

One potential benefit of SMILE

is that it might have a biomechanical advantage over LASIK. Right now, we simply don't know, as we don't have true biomechanical measurement of corneal strength. There is an instrument in development for clinical use which will soon provide the answer, Intelon's Brillouin optical scanner system (BOSS), but until then, any possible biomechanical advantage, disadvantage, or equivalence between the different procedures is unproven.

SMILE will get better as the VisuMax system improves. Better centration, cyclotorsional tracking, improved laser delivery with a cleaner lenticule interface, improvements in the surgical technique for lenticule extraction, and even custom lenticule shaping should be on the horizon. But today, SMILE does not appear to provide better long-term visual and refractive outcomes compared to wavefront-guided LASIK and does not provide faster visual recovery. Moreover, LASIK offers better control of higher-order aberrations than SMILE in its current iteration. Wavefront-guided LASIK remains at the forefront, and that's why it has been and remains at the present time – my procedure of choice.

Know Your Worth

It's time we remembered that our success is down to our skill – not our equipment.

By Quresh Maskati, Consultant Eye Surgeon, Maskati Eye Clinic; Visiting Consultant, LokManya Tilak Memorial Medical College and SION Hospital, Mumbai, India

Once upon a time, there was a famous photographer who was invited by a prominent socialite to a party. As he entered, the socialite greeted him effusively saying, "I have been an ardent admirer of your photographs for years! You must have a superb camera."

When it was time to leave, the photographer profusely thanked the hostess saying, "Thank you for the delicious meal – you must own an excellent stove!"

I recently heard this short story and it really got me thinking. How often do we brag to our patients that we have the latest microscope or phaco machine – or that the IOL we are inserting is "the world's best"? Are we guilty of leading our patients into believing that the "camera" is responsible for their excellent postop vision, rather than the "photographer"?

As eye surgeons, we labor long and hard to hone our skills. Unfortunately, many of us also learn to extol the virtues of our equipment to attract patients. But there are twin dangers of doing this. Firstly, we come under pressure from the ophthalmic industry, buying equipment we can ill afford, and using IOLs we may not wish to use because of practices like IOL bundling. Then, before we're finished paying for one piece of equipment, we may find ourselves pressured to upgrade! Secondly, we make ourselves easy targets for insurance companies looking to continuously reduce the amount payable for surgery; after all, we're telling our patients that the surgery takes just 10 minutes and requires little human 'touch' as we're using fancy 'robotic' and laser equipment.

The attitude may be most damaging to younger ophthalmologists entering private practice. Without the means to afford the best high-tech equipment, they may struggle to compete with more senior colleagues and feel forced to turn to expensive advertisements and alternative ways of promoting themselves. Senior figures then bemoan the lack of ethics amongst the juniors...

I believe we need to stop the trend of pushing our cameras and stoves to the foreground. In short, we must restore dignity to our profession. And though there's no quick-fix solution, there are some things we can do. It's important that from our first contact with a patient, we reassure him or her that we have the skills needed to improve their vision. If we have trained under a well-known guru or at a distinguished institution, we should let our patients know. We need to remind patients and insurers that eye surgery is an art that requires years of training – it isn't the expensive equipment that restores vision, it's our expertise.

My advice to younger ophthalmologists is to consider going into group practice. Get together with like-minded colleagues and reduce your individual investments – in unity, there is a great deal of strength. If you are practicing in a smaller town, it's imperative to have a collegiate relationship with your neighbors – foster harmony and avoid backbiting and competition.

If you take a ten dollar note and fold it up, cover it in mud, or pour water over it, then take it the store, the shopkeeper will still sell you ten dollars' worth of groceries. Similarly, let no one – whether it's a patient or a colleague – reduce your self-esteem. Each of us is unique (just like diamonds) and we should always remember that our self-worth does not rely on our equipment. We must remain dignified and ethical, and convince patients that we are fully capable of helping them see better with the resources we have available to us, because it is our skill that matters, and nothing else.

Stranger Than Fiction

What motivates people to fake vision problems? And how should you deal with patients who are prone to fabricating the truth? Mark Feldman and Valerie Purvin share (some of) the answers...

By Roisin McGuigan

Physicians are familiar with encountering patients who are unwell – which is in no way surprising. Many will have also treated (and potentially counseled) patients who are overly anxious about a minor issue – or prone to exaggeration. But only occasionally do 'patients' present themselves with a complaint that, upon further inspection, exhibits entirely fabricated – or even self-induced – symptoms. Such patients will lie, may cover up sources of information that contradict them, can become hostile if questioned, and sometimes go so far as to harm themselves to maintain the fantasy they have created.

The terms, "Factitious disorder" (FD) – and perhaps the more familiar and extreme, "Munchausen syndrome" – account for those patients who invent illnesses or injuries for psychological reasons and attempt to deceive the professionals involved in their care. Although these patients are most likely to report endocrinological, cardiological or dermatological problems (1), they can be observed faking conditions across the medical spectrum, including ophthalmic disorders. In some extreme examples, patients have even feigned binocular blindness (2). Patients who are malingering, or who have conversion syndrome, may also describe symptoms they are not experiencing – but with different aims.

But how can these patients be spotted and what is the most appropriate way to proceed with their care? To find out the best ways of separating fact from fiction, we spoke with psychiatrist Marc Feldman – an expert on Munchausen syndrome and factitious disorder, and Valerie Purvin – a neuroophthalmologist with extensive experience in dealing with patients whose vision problems are only in their minds.

Reference

1. *GP Yates, MD Feldman, "Factitious disorder: a systematic review of 455 cases in the professional literature", Gen Hosp Psychiatry, 41, 20–28 (2016). PMID: 27302720.*
2. *MD Feldman, et al., "Psychiatric and behavioral correlates of factitious blindness", Compr Psychiatry, 49, 159–162 (2008). PMID: 18243888.*

Tales of the Unexpected

Factitious disorder in ophthalmology – a psychiatrist's perspective

By Marc Feldman

The term "Munchausen syndrome" originates from the storybook character created by Rudolph Erich Raspe, which was based on a real 18th century Prussian cavalry officer, Karl Friedrich Hieronymus, Freiherr (Baron) von Munchhausen. Throughout his adventures, Baron Munchausen performs incredible feats and goes on amazing journeys; he travels to the moon, rides on a cannonball, and saves himself from drowning by pulling on his own hair...

The term was coined by physician Richard Asher in 1951, who said: "Like the famous Baron von Munchausen, the persons affected have always travelled widely; and their stories, like those attributed to him, are both dramatic and untruthful. Accordingly, the syndrome is respectfully dedicated to the baron, and named after him."

Munchausen syndrome is an extreme subtype of factitious disorder (FD), which is defined by the Diagnostic Statistical Manual–5 of Mental Disorders as being characterized by the following behaviors:

- Falsification of physical or psychological signs or symptoms, or induction of injury or disease, associated with identified deception.
- The individual presents himself or herself to others as ill, impaired, or injured.
- The deceptive behavior is evident even in the absence of obvious external rewards.
- The behavior is not better explained by another mental disorder, such as delusional disorder or another psychotic disorder.

Some ophthalmologists could potentially go through their entire careers without encountering a patient with FD. But if you do, it's hugely helpful to be able to recognize them.

Fact or fiction?

Patients with FD can be hugely challenging to treat – they may exaggerate, lie, mimic medical or psychological symptoms, interfere with attempts at diagnosis, induce illness or even injure themselves.

These patients are not working towards obvious external gains, such as to obtain financial aid or to avoid work. Rather, their goal is often unclear, but may be to assume the "patient" or "victim" role to gain attention and sympathy from healthcare providers and others – or it may be because they get a "rush" from undergoing medical procedures. It could also be because they derive satisfaction from duping medical professionals (1).

Take, for example, the case of a woman who feigned deafblindness (see Case Study 1). It might sound fantastical, but these patients do exist. Some go even further – in one case, a women introduced alkaline chemicals into her eyes, causing corneal burns. She then used atropine eyedrops to dilate her pupils and then stared at the sun to produce retinal burns – resulting in self-inflicted blindness (2).

Although Munchausen syndrome, FD, malingering and conversion disorder patients may all display some of the same behaviors, there are important differences to be aware of.

Munchausen syndrome describes a triad of behaviors: recurrent hospitalizations, peregrination (in other words, the patient travels from one provider to another to seek care), and pseudologia fantastica (pathological lying). Munchausen syndrome describes the most severe and chronic individuals (around 10 percent of all such patients). Patients with FD, on the other hand, will display some of these behaviors but are more stable geographically, have some social network, will engage in FD only intermittently, and are more amenable to treatment.

Indicators of FD or malingering:

- The signs and symptoms do not improve with treatment
- The magnitude of symptoms consistently exceeds what is usual for the disease
- Some findings are determined to have been self-induced
- There are remarkable numbers of tests and consultations, to no avail
- The patient disputes test results that do not support the presence of authentic disease
- The patient "doctor/hospital shops"
- The patient emerges as an inconsistent, selective, or misleading informant
- The patient refuses to allow the treatment team access to outside information sources
- There is evidence from laboratory or other tests that disproves information supplied by the patient
- Even while pursuing medical or surgical assessment, the patient opposes psychiatric assessment and treatment.

Hysteria or duplicity?

When comparing FD with the other reasons people feign illnesses, the two key differences are whether they are conscious of what they are doing and what their motive is for doing it.

Conversion disorder (previously known as hysteria) is the loss of motor or sensory ability, and is produced unconsciously in response to a mental or emotional crisis. Malingering, on the other hand, is the deliberate fabrication and exaggeration of symptoms for clear external gain, such as avoiding work or gaining financial compensation. In FD and Munchausen syndrome cases, the symptoms are consciously produced, but the motivation is usually unconscious.

It may not necessarily be within the purview of the ophthalmologist to distinguish between these patients – but being able to spot a patient who is feigning illness could result in the patient being directed to psychiatric services for more appropriate treatment, rather than time being spent trying to treat an illness that doesn't exist. In conversion disorder, the patient's symptoms can improve with treatment, as they are likely to be susceptible to the suggestion that they are

improving. In FD and malingering cases, the patient is deliberately choosing to present as unwell, and will not be so susceptible (see Indicators of FD or malingering).

If the patient goes undetected, it can come at great expense, with multiple unnecessary tests, procedures and medications needing to be paid for. If they are later discovered, it can have an impact on the hospital team too – staff may feel cheated out of limited time and resources, or feel that they have been "duped" (3).

"Confronting patients with their dishonesty does not, in my experience, prove to be very effective."

Spotting tall tales

But if you think you have spotted one of these patients, what exactly can you do? Valerie Purvin provides some further advice on conversion disorder and malingering in her article "Truth, Lies, and Ophthalmology." When it comes to FD, there are some maneuvers that can be tried in the eye office: for example, aside from feigned blindness, factitious keratoconjunctivitis is a more common case for an ophthalmologist to encounter (see Case Study 2). In a case like this you could give the patient a pressure patch with subtle markings on it. This can tell you if they've removed and replaced the patch, and if they improve once they don't have access to the eye.

For unilateral visual impairments, you can use a phoropter to fog rather than close their eye, so that the patient thinks they are seeing out of their good eye, when in fact they're seeing out of the "bad" one. For bilateral visual impairment, you can create an obstacle course from your office to your examination room, and watch how they make their way to their chair – also have someone else watch them when they're not aware they are being observed.

Other approaches include the use of Snellen charts; isolate the lines as though you are showing them to someone with amblyopia, and provide the patient with no reference as to the size. You can then suggest that a very tiny letter is actually very large, and then go larger and larger until the patient finally admits to being able to see at 20/40, thinking it might be 20/400. These are just some practical suggestions on how to spot these patients (see Factitious visual impairment: some clues).

Once you have ruled out other causes to your satisfaction (and if not, a referral to neuroophthalmology may be appropriate, and allow for objective testing to be done) you can plant the idea in the patient's mind that they will get better. If they are suffering from conversion disorder, this suggestion could help them improve. If it's a situation where the patient is malingering or has FD, it will help them save face – confronting patients with their dishonesty does not, in my experience, prove to be very effective.

Simply being aware of the warning signs can help to identify patients whose problem is psychiatric rather than physical, lead to earlier intervention, and potentially prevent side effects from unnecessary treatments. As I have said previously, the deceptions in FD are limited only by the patient's creativity, knowledge, motivation and skill. Although the eyes may not be a common target for such patients, I believe that practitioners in every area of healthcare, including ophthalmology, need to be aware that these audacious deceptions are possible.

References

1. *A Lawlor, J Kirakowski, "When the lie is the truth: Grounded theory analysis of an online support group for factitious disorder", Psychiatry Res, 220, 1176–1177 (2014). PMID: 25169893.*
2. *MD Feldman, SJ Eisendrath, Editors, "The spectrum of factitious disorders", 69–71. American Psychiatric Press Inc: 1996.*
3. *SM Crawford et al., "A visitor with Munchausen's syndrome", Clin Med, 5, 400–401. PMID: 16138498.*
4. *MD Feldman et al., "Psychiatric and behavioral correlates of factitious blindness", Compr Psychiatry, 49, 159–162 (2008). PMID: 18243888.*

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Case Study 1: Factitious Deafblindness 1

Ms. A, a 50-year-old woman, was evaluated at a rehabilitation facility for the deaf and blind. She arrived escorted by a blindness counselor and her guide dog. She stated that she had become blind at a young age and deaf more recently, but simply refused to answer specific questions. She denied the staff access to next-of-kin and identified no close friends. Available records were notably vague. For example, an ophthalmologist had written, "[Ms. A] has asked me to write this note stating that she is deaf and blind. I cannot comment because I have not examined her." Her audiology report showed no response to sound at any level, but she would not permit testing that was any more objective than a standard audiogram.

"The patient's lack of concern about becoming deaf after already being blind was considered perplexing and unconvincing."

Ms. A reported having graduated from college with a double degree in accounting and journalism, but would not provide the dates of university attendance. Other unconfirmed claims included her working in the pit on racing cars and on portable jet propulsion devices. She stated that one of her current career goals was to become a lighting technician at a television station. When told that this goal was obviously impractical, she stated, "You only see my disabilities, not my abilities." She continually emphasized the "special needs" of her dog, such as strictly organic food. It was observed that, in fact, the animal was no longer functioning as a guide.

The patient's lack of concern about becoming deaf after already being blind was considered perplexing and unconvincing. The eventual consensus was that Ms. A was neither deaf nor blind. The patient precipitously withdrew from rehabilitation services because pain she attributed to a car accident made it impossible for her to participate. She was not confronted about the dubious information she provided or her refusal to allow confirmatory testing. Just before discharge however, when Ms. A was unaware of being observed during a meal, she neatly arranged her food on the plate and speared her peas with great accuracy. She was lost to follow-up.

Factitious visual impairment (VI): some clues

Does the patient:

- Describe the cause of their VI extravagantly, inconsistently, or inaccurately?
- Behave in a way inconsistent with VI, such as navigating well in unfamiliar areas?
- Have a home environment inconsistent with VI? For example, large print books are present, but they are claiming they have no useful vision
- Make ludicrous claims of their own nonvisual sensory abilities? For example, claiming they are able to hear whispers in an adjacent building
- Make excessive claims regarding the abilities of their assistance dog, if present? For example, claiming the dog is able to "read" TV guides
- Request veterinary care for their assistance dog to an unusual extent?
- Engage mobility trainers, but is also observed traveling unaided, without their cane or assistance dog? (4)

Case Study 2 – Factitious Keratoconjunctivitis 2

- A case involving a 17-year-old female "fish processor"
- Intense conjunctivitis was observed in the left eye; then later, in the right eye
- Swabs taken were negative for bacteria, viruses, and chlamydia
- The patient showed no response to steroids and antibiotics, either preserved or unpreserved
- Eventually she went through a conjunctival biopsy, which showed only nonspecific chronic inflammation
- When finally admitted, tissue paper was found in her fornix

References

1. *ID Miner, MD Feldman, "Factitious deafblindness: an imperceptible variant of factitious disorder", Gen Hosp Psychiatry, 20, 48–51 (1998). PMID: 9506254.*
2. *FR Imrie, WH Church, "Factitious keratoconjunctivitis (not another case of ocular Munchausen's syndrome)" Eye (Long), 17, 256–258 (2003). PMID: 12640421.*

Truth, Lies, and Ophthalmology

Tips for the ophthalmologist confronted with functional vision loss

By Valerie Purvin

When dealing with functional vision loss, knowing the correct terminology is the first step. We use the terms "functional," "non-organic" or "non-physiological" vision loss to describe patients who appear to be describing problems that don't appear to have a physical basis. But bedded within this larger term are subgroups – patients who have had a conversion reaction, in which visual loss is unconscious or involuntary, versus those who may be malingering or have FD (meaning there is deliberate, feigned visual loss, which may have various motives). But we don't use these terms – just larger blanket terms, such as "non-organic." Why?

The first and perhaps most important reason is that to make a distinction is to speak to the state of mind of the patient. And should you end up on the witness stand or in deposition with a lawyer, you don't want to find yourself being quizzed on your psychiatric credentials. It's not our area of expertise. We don't want to assume we know why our patient is behaving in this way. The second reason is that such behavior exists on a spectrum, so the reasons for the patient's behavior may not be so black and white; for example, a patient may have genuinely experienced a small amount of VI, but then exaggerated their symptoms because they want to make sure their doctor doesn't miss it. In any case, understanding the distinction is valuable for the management of these patients.

Look for indifference or hostility

Conversion reaction patients lie within a wide age range and sometimes exhibit "la belle indifference," which means an inappropriate response – almost an indifference – to their symptoms. They aren't feigning illness because of an underlying agenda to meet their own goals, and so they tend to be pleasant and cooperative. They are also notoriously suggestible, which is how they became convinced of their illness in the first place. As I discuss below, this can be helpful during management and testing.

In contrast, patients who are malingering are often young adults. They're likely to be under pressure at work or with their finances, often have a history of recent trivial trauma, and are frequently hostile to the person examining them. The hostility can take different forms. In my experience, these are usually the patients who arrive late, announce that they have to leave early, and take issue with your methods, making comments, such as "You're just doing the same test as the other doctor," or "You're not going to use those lights, are you? The other doctor did that, and I had a headache for three days!"

The recent trivial trauma they've experienced is often job-related. A common scenario is a patient who had a splash of some sort into their eye. The eye was irrigated and patched, but when the patch came off two days later – bam! – it was blind, and has remained blind ever since.

Control your frustration – but also listen to it

Patients who arrive in our office already displaying aggressive or hostile behavior can be upsetting for us as physicians, but it's also a very helpful diagnostic clue; it can be an indication to at least suspect that a patient has a hidden agenda. Most of your patients are visiting you because they want to get better, and have no reason to create friction with a doctor who is on their side and looking out for their best interests.

But anger from a patient isn't the only clue – if you feel yourself becoming upset or frustrated, that's another one. Don't fall prey to this, reacting with a comment, such as "Well, do those other doctors know what you had? I guess not, because that's why I'm examining you!" Instead, take a step back from the situation, assess what's happening and consider your own frustration, because it's a helpful piece of data.

Another diagnostic clue is the sunglass sign. These patients come in wearing dark glasses (sometimes more than one pair) and a hat with a brim, and have their collar popped. You have to peel each layer off to examine them and as you do so, they appear to be in agony: "Oh my God, no! Don't do that!" They act almost like a vampire being unmasked...

There are a number of examination techniques that we can use to diagnose non-organic visual loss, which generally fall into three categories – we demonstrate things like inconsistencies in vision, or non-physiologic responses like tunnel vision and, on a good day, we manage to document that the vision is good – ideally we manage to somehow get 20/20 vision out of the "bad" eye or demonstrate a full field of vision.

Using the power of suggestion

You've performed your tests and you're confident that you have a case of non-organic vision loss – what can you do about it? In many cases, the power of suggestion can be key to treatment. You already know that patients with conversion reaction are suggestible, and so may be equally suggestible to the idea that their condition is improving.

Malingering patients may maintain that their vision is poor, but they often don't know the right answer to give to your questions. Instead, they look for any clues that will help them to convince you of their feigned illness. So if you say, "I'm going to double the size of this letter; it's now twice as large," it might get a response of "Oh, okay, I can see that now." And telling them, "This lens should clear the problem right up," might prompt them to agree that, "Yes, it does."

Every doctor likely has their own way of dealing with these patients; some physicians have quite broad philosophical differences on the topic, while others only differ in the terms they use. There are physicians who use "magic eyedrops" and tell patients that they will clear up vision problems. I'm personally not so comfortable with that approach, as it does feel somewhat dishonest. And I don't tell patients that I've found something and that I'm going to fix it. Instead, I take a three-step approach – and though the following isn't based on research data, I have found it to be effective.

Step 1: the introduction

The first step is to introduce the topic. Explain, in a non-judgmental way, that you believe the problem is not physiological. Use phrases like:

"Your vision is better than you think it is."
"Your eyes are playing tricks on you."
"Your brain is capable of seeing better."
"Your brain isn't letting in the good vision."

"Should you end up on the witness stand, you don't want to find yourself being quizzed on your psychiatric credentials."

Step 2: the explanation

Next comes the explanation, which is key to the process. I start with something like this:

"Obviously, your vision was very poor when this started. You were legally blind in that eye after what happened (the splash, or the hit on the head). How scary that must have been for you! If I were you, I would have been thinking, 'Oh my gosh, what if it doesn't get better? What if I can't work and support my family? What if it just never goes away?' Those thoughts were so scary, that your brain went into a spasm. Meanwhile, your vision has improved, and the problem has gone away. But now, your brain is not letting the vision in."

My residents used to call this the "brain spasm speech." I know it perhaps sounds a little foolish to tell the patient it's not them, but their brain – and you may expect that some patients would be incredulous. But I've found that it works. You can use your own terms and explain it in your own way;

the crucial aspect is that it must be non-judgmental. You're telling the patient that there is an explanation for their problem and that if they can just relax, they will see an improvement.

Step 3: the prediction

Finally, you offer the patient a prediction on how their vision will improve. For example, I might tell them that their vision will improve every day, clearing from the outside to the center. And I'll likely offer a timeframe over which they will see total recovery: "You'll see some improvement tomorrow, more on Friday. By Sunday you'll be almost better, and on Monday morning, your vision will be back to normal, which means you can return to normal life." I'll then hand them a note clearing them to go back to work, which I will have prepared before I even enter the room. I won't recommend any further testing (I have already completed all the testing I need to make my diagnosis at this stage) and I won't suggest a return visit. It's important not to give the patient the wrong message; we don't want them to think, "Wait. If I'm okay, why do I have to come back? Why are you ordering another test, if my vision is fine?"

The clear message you're trying to send (especially to someone who is purposefully trying to deceive you, such as a malingerer) is this: "I'm giving you the best deal you're going to get. I'm not going to unmask you in front of your spouse or your employer. I'm not asking you to give back the money you've been receiving for the last six weeks. I'm not asking you to admit that you are feigning vision problems. But this is finished. I've got to go to work on Monday and so do you. You should take this deal."

Note that this is deliberately intended to be coercive. At such appointments, I behave differently than I usually do with a patient. Normally, I make a point of trying to make it easy for them to tell me how they feel by giving them time and space and by letting them ask questions. I portray this with my body language, for example by leaning back in my chair. In contrast, when I'm managing a malingerer, I don't want to know what

the patient thinks about it; instead, I need to convey a simple message: "Here's the deal. Take it."

Be confident in your diagnosis

The technique can be applied in different ways, with different language, but the five essential elements are:

- A non-judgmental explanation of the problem
- An explanation of how vision will clear
- A timeline for when it will be back to normal
- A return to work note
- No offer of further testing, and no return visit.

For conversion disorder, this offers reassurance and a strong suggestion that the patient is okay, that they're already getting better, and that there is nothing to worry about. For the patient deliberately feigning illness, you're not judging or unmasking them, but telling them that "the play" has ended.

It is important that you are confident in your diagnosis (as always) – and that you are able to convey that confidence when speaking with the patient. But it isn't always easy in such cases. If you don't feel confident or you don't feel comfortable, consider sending the patient to a neuroophthalmologist. We may also find some of these patients challenging, but they are definitely within the scope of our field – and we are always happy to help.

Valerie Purvin has been on the faculty of the Indiana University Medical Center for over 30 years with a busy clinical practice in a large, subspecialized ophthalmology group in Indianapolis, Indiana, USA. She has published on a range of topics, generally focusing on issues that arise in caring for patients with neuro-ophthalmic disorders including ischemic optic neuropathy, inflammatory optic neuropathies, and visual complications of medications.

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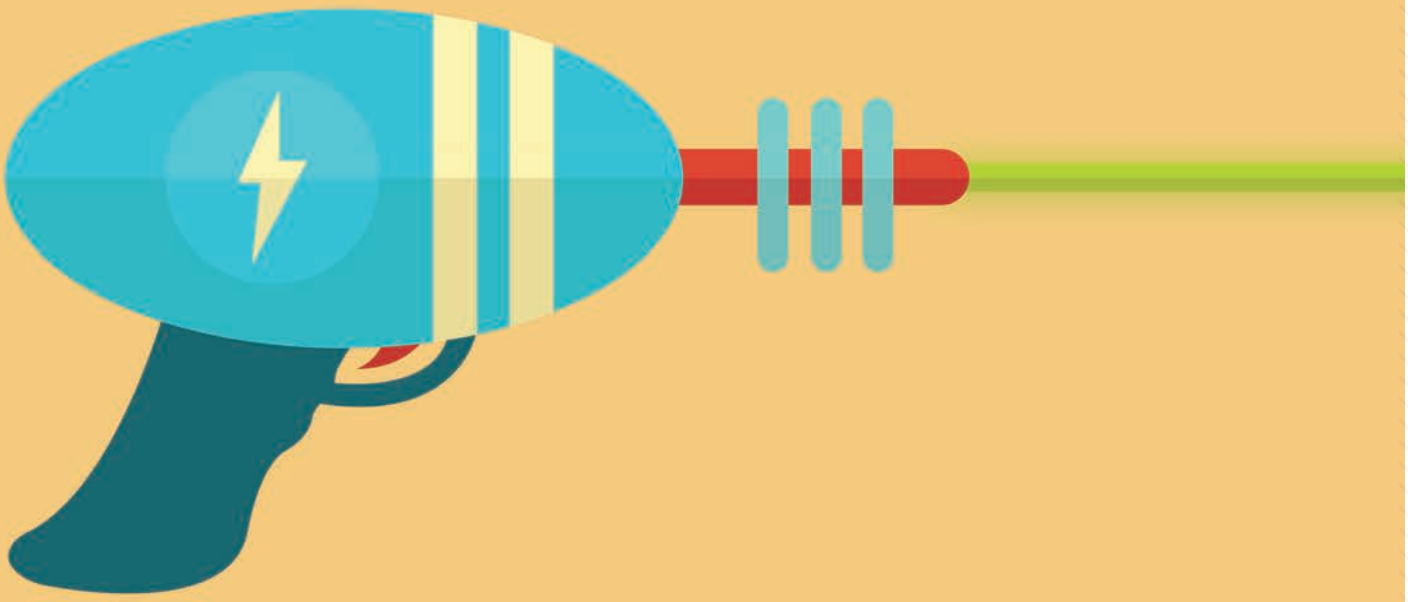
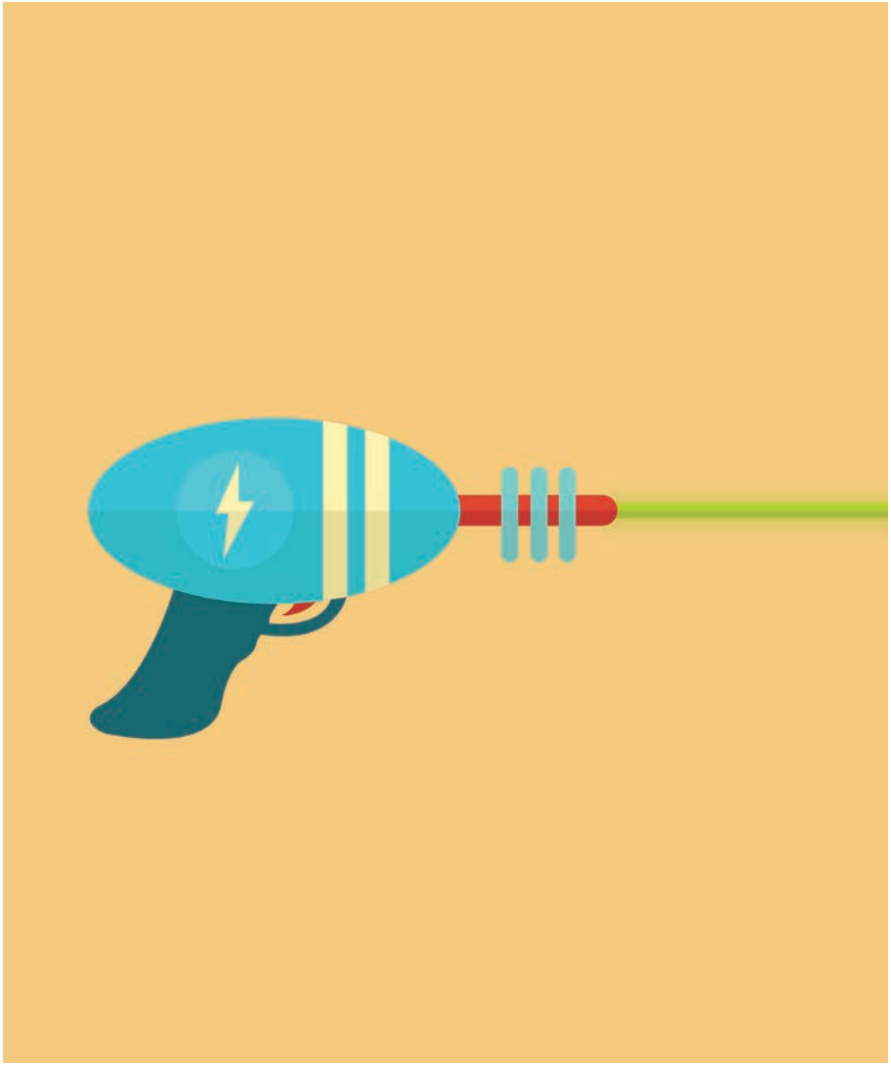


The Laser Quest for a Happy Medium

In glaucoma, medical management is plagued with noncompliance, and filtration surgery can be complex and risky. Could laser-based treatments offer a happy medium?



Few people under your care are "model patients." Almost everyone misses a dose now and then, and it's understandable. People have busy lives to lead, and some things get forgotten. The problem is, glaucoma is a progressive disease. Missed doses soon add up to progression, and unless the disease has been caught by screening measures (perhaps because of a family history), it's likely that the disease is first diagnosed at a relatively advanced stage (and age) – as that's when people start noticing vision loss. So this renders a predominantly elderly population, some of whom might be forgetful, with stiff fingers, and who need to take a considerable number of other medications to take each day (in addition to their eyedrops) just to get by – yet they are at a critical stage of their disease, where any progression equals vision loss.

Compared with only a decade ago, there are considerably more treatment options available today for glaucoma specialists to choose from. There's no longer the simple dichotomy of eyedrops and filtration surgery: there's a number of laser and micro-incisional, minimally invasive approaches that can be taken today – the challenge is to determine which approach is most suited to your patient. We asked two glaucoma surgeons to discuss the laser-based treatments that they offer, in order to understand which patients are most suitable for their procedure of choice: Dan Lindfield discusses his use of selective laser trabeculoplasty (SLT) in the clinic, and Noa Geffen reviews 5 year results of using the CO_2-based CLASS laser.

At a Glance

- *Topical glaucoma therapy is usually very effective at lowering IOP – so long as the patient follows the regimen, and self-administers the drops correctly.*
- *Even though eyedrop use can be associated with adverse events which reduce patients' quality of life, filtration surgery is still viewed by some as risky, and an "option of last resort"*
- *Is there a happy medium? An approach that lowers IOP and reduces patients' reliance on drops without requiring invasive surgery?*
- *Two glaucoma specialists review two laser-based techniques occupying the middle ground between drops and penetrating incisional techniques: SLT and CLASS*

A User's Guide to SLT

What benefits can SLT offer, and which patients are eligible?

By Dan Lindfield

I don't believe in waiting to offer surgical intervention. It's clear that any intervention that achieves IOP control early in the disease process translates to better outcomes, so I routinely offer non-pharmacological interventions to my patients. I find that by treating early, less visual loss has occurred, and the target IOP is easier to reach – and I find that very often, this is achievable using SLT, rather than traditional filtration surgery. SLT use is not without risk (cases of transient anterior chamber inflammation, mild uveitis and cystoid macular edema have been reported), but the risks are infrequent, manageable, and are all front-loaded. This contrasts with the daily instillation of topical therapy – in fact, I think you could argue that overall, SLT has the superior risk profile.

When SLT was first introduced, there were concerns about its duration of action and its repeatability, and this stopped many glaucoma specialists from adopting the technology. But research continued, the technology advanced, and most of the issues previously identified with SLT have now been addressed. Indeed, using SLT as a primary treatment for ocular hypertension (OHT) and glaucoma was previously controversial but recent data has questioned this (1), and results from the forthcoming LiGHT (Laser in Glaucoma and Ocular Hypertension) study that's comparing SLT versus drops as first-line treatment for OHT/Glaucoma should help further clarify SLT's role in glaucoma management (2).

My patient population

I mainly use SLT to improve IOP control for patients on medication(s) to prevent them needing further medication or surgery, and I also use SLT to reduce medication dependence for patients with controlled IOP. For patients using drops who have problems with compliance, memory, side effects (ocular or systemic) or allergies, SLT is a useful option to use in order to reduce the number of medications needed for IOP control. In this setting, SLT can prove a cost-effective option, as the cost of an SLT procedure may be lower than the cost of monthly eyedrops. Indeed, patients are increasingly asking me about SLT as an alternative to using multiple eyedrops for precisely this reason.

SLT after cataract surgery?

The question of exactly how laser energy modulates trabecular function after trabeculoplasty is still debated. In my opinion, the effects of both cataract surgery and SLT can be attributed to a "trabecular meshwork modulation" process. In cataract surgery, the high volume of fluid flowing around the anterior chamber "washes out" trabecular debris, and a postoperative cytokine reaction is seen – this is similar to what happens in SLT. This means that performing SLT after cataract surgery is usually much less effective, as the outflow has already been improved. Anecdotally, three years or more post-phaco, I begin to see SLT become more effective again. I suspect that this is because, like SLT, the effect of the phaco-related trabecular modulation persists for two to three years before trabecular outflow resistance increases again. In practice, this means I usually reserve SLT for phakic patients, or those who have had cataract surgery over three years previously.

Champagne bubbles and pressure spikes

In my practice I use the OptoYag & SLT M (Optotek). Patients all receive written information about the procedure in advance. On arrival, they have their IOP checked for baseline, and pilocarpine 2% and apraclonidine 1% drops are instilled. I use a Latina gonio lens for this procedure and typically use an initial energy of 0.8 mJ, treating the inferior angle first, as it is usually the most open and the gonioscopic landmarks are clearest. I work up the power until I see what looks like fine champagne bubbles. If the bubbles are adherent or any changes on the trabecular meshwork surface persist, then I reduce the power. The power can be adjusted to the visible bubble response (in contrast to some clinicians who use a constant power throughout) – higher power is needed nasally and temporally than inferiorly and superiorly because of the changes in angle pigmentation.

I apply approximately 110 shots to each eye and usually treat the full 360 degrees. Immediately post procedure, I apply another drop of apraclonidine 1% and prescribe a topical NSAID (four times daily for five days). A spike in IOP is seen in approximately 3 percent of patients, so IOP should be checked 60 minutes after the procedure. If an IOP spike does occur, then use acetazolamide to control it. In patients with advanced field loss or heavily pigmented angles, I also use acetazolamide prophylactically 30 minutes before the procedure, to reduce the risk of a transient pressure rise. I routinely review patients after 6 weeks to assess the effect of treatment, or after 48 hours if a spike has occurred. In patients who have had the procedure with the aim of reducing topical medication, I ask them to stop using their drops one week prior to the review appointment, in order to more accurately determine the outcome of the treatment.

It is also advisable to warn patients that the average duration of SLT is two to two-and-a-half years, but the effects have been known to persist for up to five. However, since the procedure can be repeated, a customized schedule can be developed for individual patients – this usually involves retreatment every couple of years.

Getting started

I have performed over 90 cases in my first six months with an SLT laser, which I believe to be a significant demand for the procedure. In this time, I have had three non-responders and two pressure spikes, both of which settled within 90 minutes with acetazolamide and normalized by 48 hours. Indeed, in my patients, I have found that IOP reduction from SLT outperforms prostaglandin monotherapy. It is of course clear that this cohort are self-selected to be poor responders since they required SLT, as they are likely to have poor compliance or poor tolerance for topical therapy, but this biased data is a useful consideration for real life practice.

There is always some anxiety when first offering a new procedure to your patients. However, SLT is relatively easy to learn and combines two skills that glaucoma surgeons will be very familiar with – gonioscopy, and laser skills that are similar to Nd:YAG capsulotomy. Patient selection is key: always ensure that the angle is easily visible and there are no peripheral anterior synechiae. SLT requires gonio lens contact for approximately 5 minutes per eye so it is vital to select patients who will tolerate gonioscopy comfortably. Patients with tremor, or those who have difficulty with positioning make treatment more challenging, and hence are best avoided until the surgeon is very comfortable with the procedure.

These challenges aside, I have found SLT to be a useful and cost-effective alternative to medical therapy in my practice, helping me to control patient IOP, and in some cases reduce the need for eyedrops.

Dan Lindfield is a consultant ophthalmic surgeon at Optegra, and glaucoma lead at Royal Surrey County Hospital, England, UK.

References

1. *BA Francis et al., "Repeatability of selective laser trabeculoplasty for open-angle glaucoma", BMC Ophthalmol, 16, 128 (2016). PMID: 27464887.*
2. *S Tsang et al., "Developments in laser trabeculoplasty", Br J Ophthalmol., 100, 94–97 (2016). PMID: 26377417.*

A Long Term Look at CLASS

The 5-year trial results are in. How safe and effective is the CLASS procedure?

By Noa Geffen

CO_2 Laser-Assisted Sclerectomy Surgery (CLASS) is an outpatient procedure that provides significant IOP-lowering efficacy with a safety profile similar to those of manual non-penetrating deep sclerectomy. CLASS is performed through a standard, manually created superficial scleral flap, followed by repeated ablations of the scleral tissue at a depth of approximately 30 µm in a predefined pattern (see Box: The CLASS procedure). This exposes Schlemm's canal, and facilitates aqueous fluid outflow through the remaining thin trabeculodescemet membrane. Prior to unroofing Schlemm's canal, the CO_2 laser is used to create a reservoir inside the scleral flap window which is intended to reduce the final bleb size and to increase the secondary (subchoroidal) aqueous humor absorption pathway. This means that the bleb created is much less elevated than what trabeculectomy or tube shunt surgery achieves, and helps to mitigate against some of the bleb-related complications associated with trabeculectomy.

It's worth reviewing how CLASS works. It uses a CO_2 laser, which is extremely effective at ablating dry tissue. But the laser energy is also highly absorbed by water and aqueous solutions, which in effect creates a self-regulating mechanism: once the aqueous humor starts to percolate from the remaining thin membrane, it absorbs the laser energy and prevents it penetrating to deeper layers – which explains why the procedure is non-penetrating.

Looking at the long term…

A five-year clinical trial of the long-term effects of CLASS has recently been presented (1). It was a prospective, multicenter trial that involved 111 patients with primary open angle or

"At the conclusion of the study, the CLASS procedure was shown to be relatively safe with few complications."

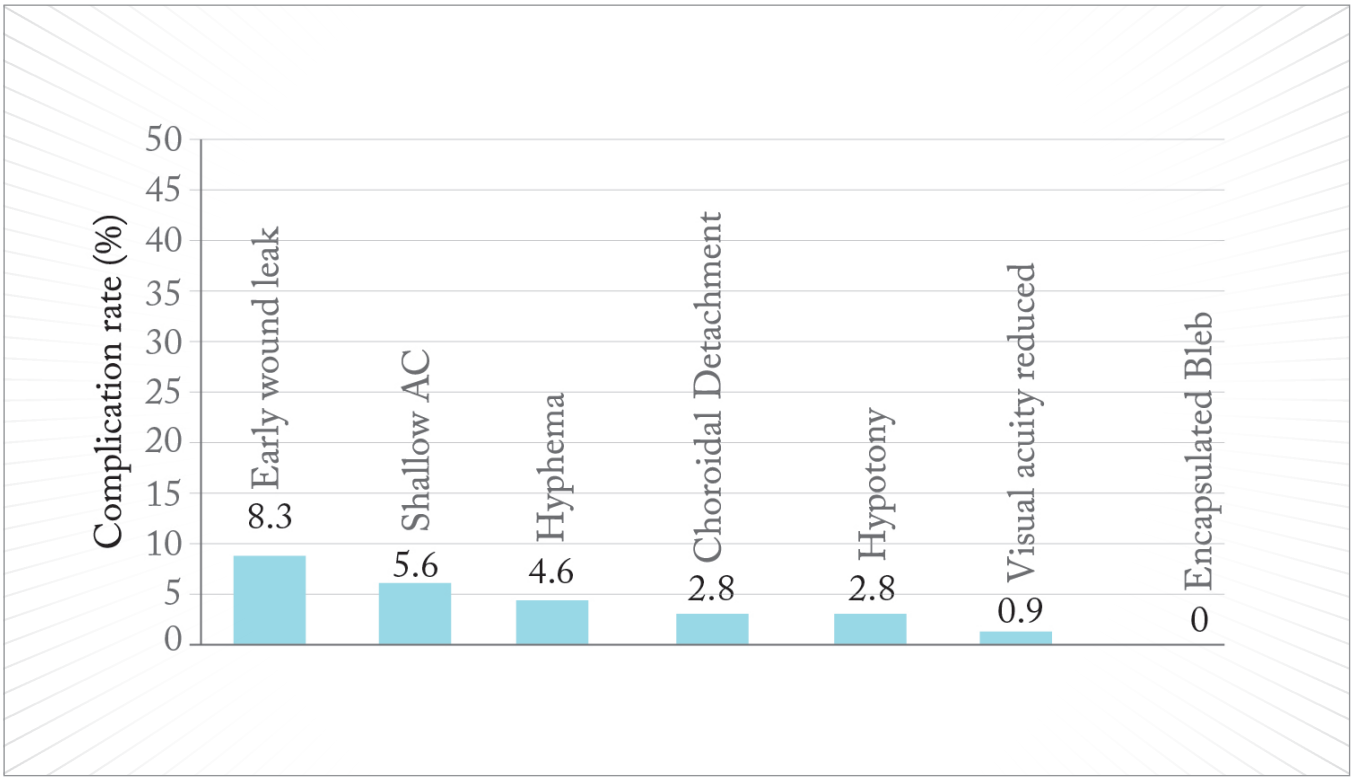


Figure 1. Complication rates in a 5-year clinical trial of CLASS. Other complications included iris incarcerations (8.3%), peripheral anterior synechiae (5.6%), transient superficial clerato keratitis (3.8%), macular edema (0.9%), and perforation by laser (4.6%). AC, anterior chamber.

pseudoexfoliative glaucoma and who had baseline IOPs of over 18 mmHg. Of the 111 patients, 11 were excluded from the efficacy analysis: five because of protocol deviations and six because the operator failed to manually create an adequate scleral flap.

At the conclusion of the study, the CLASS procedure was shown to be relatively safe with few complications (Figure 1), and was successful in lowering IOP and reducing the average number of medications in the vast majority of patients (Figures 2 and 3). There were no intraoperative safety issues noted, and postoperatively, complications were mostly mild and transitory with no sequelae. So far, there have not been any cases of endophthalmitis or blebitis. Scarring at the incision site was reported, although not unexpected;

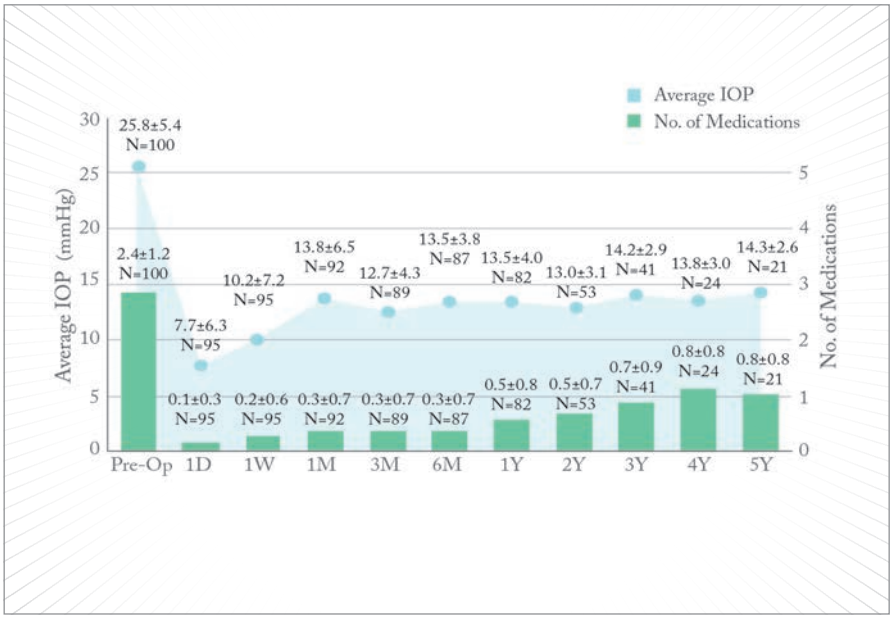
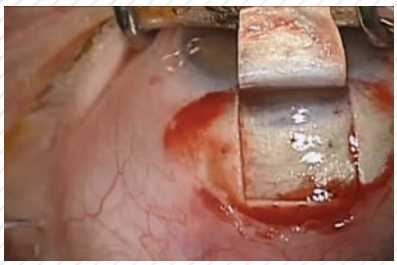
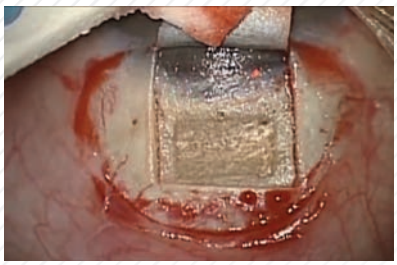


Figure 2. CLASS' efficacy over 5 years of follow-up (1). P<0.008 using Bonferroni correction for multiple comparisons.

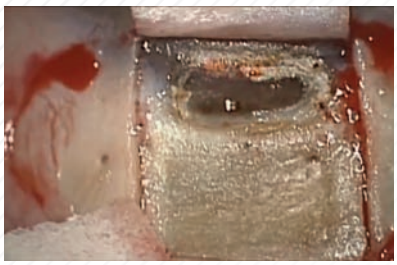
The CLASS procedure.



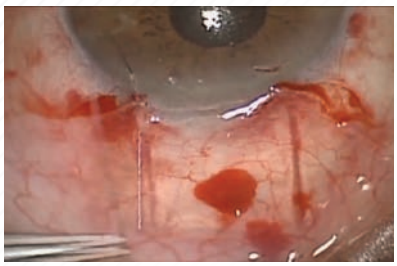
Step 1. Peritomy and superficial scleral flap dissection extending to the clear cornea.



Step 2. A 90% deep scleral reservoir is created by laser ablation at the bottom of the flap.



Step 3. Laser ablation aimed at Schlemm's canal until percolation is achieved throughout the treatment area.



Step 4. Scleral flap and conjunctiva suturing.

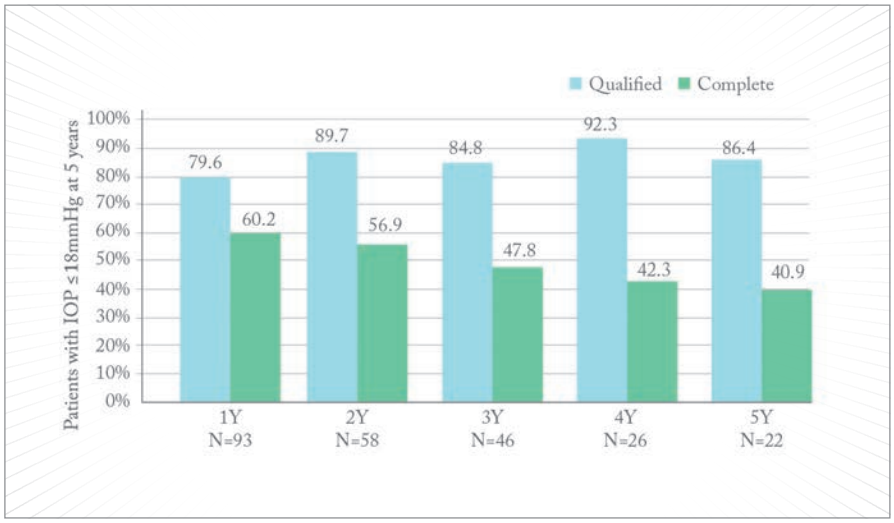


Figure 3. CLASS procedure's success rate (IOP ≤18 mmHg at 5 years) (1).

because ablation takes place below the limbus, corneal scarring near the limbus is also possible. Compared with what might be expected after the standard filtration procedures, bleb-related complications (i.e., vascular blebs and late leakage) were virtually nonexistent, and in general, blebs were diffuse with posterior location.

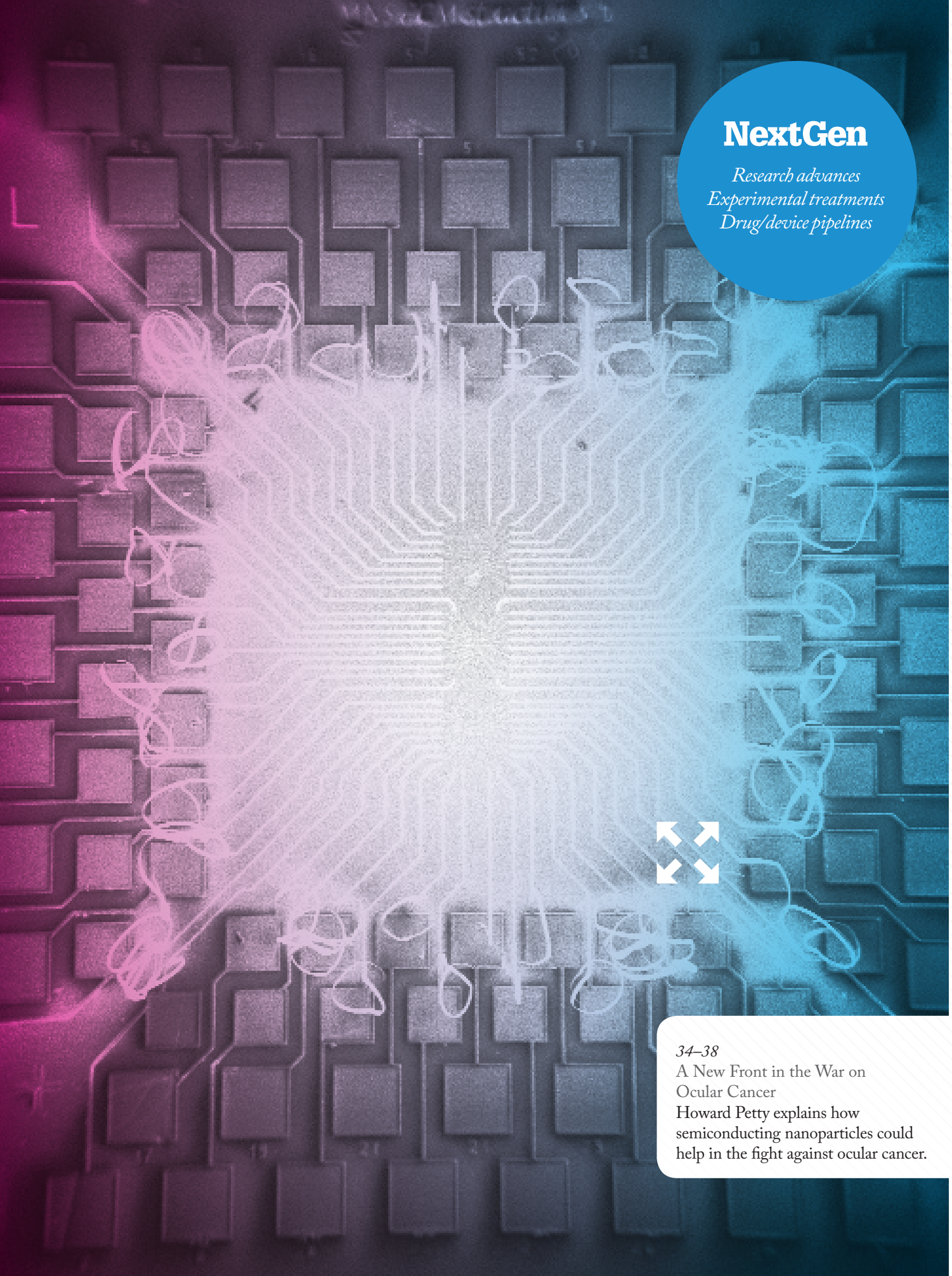
… and at the limitations

The single-arm nature of this study limited the ability to judge the outcomes in comparison to incisional procedures, but previous studies have suggested that CLASS is similar to trabeculectomy in terms of efficacy, and to manual non-penetrating deep sclerectomy in terms of safety (2). During the first year, the trial was prospective, but after the first year, treating surgeons were given latitude to use their own follow up protocols. This potentially introduced several confounding factors that might complicate analysis of the data. However, the IOP curves from each treatment center were almost identical at the end of five years, which appears to indicate a high degree of predictability and reproducibility. Although patients with treatment-naïve glaucoma (in terms of surgery) were studied in the trial, we do not believe that prior treatment should be a contraindication to performing CLASS. I believe CLASS is therefore a viable, effective and non-penetrating alternative to trabeculectomy in patients with glaucoma.

Noa Geffen is an ophthalmologist at the Department of Ophthalmology, Meir Medical Center, Kfar Saba, and the Ein-Tal Eye Center, Tel Aviv, Israel.

References

1. *M. Mimouni, E. Assia, N. Geffen. Five years follow up of CO_2 laser assisted sclerectomy surgery (CLASS) in open angle glaucoma patients – a multi-center study report. Presented at the 12th EGS Congress, Prague, Czech Republic, June 2016.*
2. *G Greifner et al., "Results of a CO_2 laser-assisted deep sclerectomy as compared with conventional deep sclerectomy", J Glaucoma, 25, e630–e638 (2016). PMID: 25383470.*



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A New Front in the War on Ocular Cancer

Could semiconducting nanoparticles improve the management of the debilitating disease?

By Howard R. Petty

Semiconductors are everywhere. The semiconductor-based microchip became a big thing in the late 1970s, and they're in everything now, from the watch on your wrist, to the TV on your wall, and even in the security tag on a packet of razor blades. Now there's a new application with huge potential – cancer therapy.

We can produce nano-sized semiconductors that, under illumination by visible light, synthesize toxins inside tumor cells. Because tissue in the eye is easily illuminated, semiconducting nanoparticles look to be an extremely promising therapeutic intervention in ocular cancer, and may spare patients from the vision loss that normally occurs with traditional anticancer treatments.

At a Glance

- *Current treatment options for ocular cancer lead to substantial, or even complete vision loss – and aren't always successful*
- *It's time to explore new approaches to improve both visual and survival outcomes for patients*
- *Nano-sized semiconductors can be used to synthesize toxins inside tumor cells, while potentially sparing vision*
- *Initial in vivo and in vitro studies show promise, but further studies of efficacy and toxicity are needed*

Preserving vision with nanometer precision

Let's establish why the unmet need exists first. Ocular cancer is usually managed by enucleation and radiation, unarguably a substantially invasive method, which inevitably leads to substantial or complete vision loss – and even then it's not always successful in managing the disease. There's a clear need for new tools that not only enable oncologists to better manage ocular cancer, but also to improve patients' vision and survival.

One of the current treatment options for certain ocular cancers is photodynamic therapy (PDT). It works – suboptimally. Today's photosensitizers are destroyed by the reactive oxygen species (ROS) produced during illumination. What my colleagues and I propose is a new generation of photosensitizers that are based on semiconducting nanoparticles: WO_3/Pt nanoparticles (1–3). The crucial difference is that these nanoparticles do not photobleach after hours of illumination, and this puts the treatment period in the hands of the physician, not the chemistry of the photosensitizer. I like to think of WO_3/Pt nanoparticles as the world's sharpest scalpels, because of their small size – and the even smaller distances that their product, hydroxyl radical, can diffuse after synthesis. In other words, this approach produces the same toxins as radiation treatment, but within a nanometer-sized region. Clearly, it could hold the promise of precise treatment, which spares healthy tissue and improves patient outcomes.

Curiouser and curiouser

As Alice discovered in Wonderland, things are not what you might expect at very small sizes – the bulk properties of a crystal do not necessarily apply to nanocrystals. This change in scale has a number of implications. Nanoparticles have a very high radius of curvature (Figure 1), and this is important as it alters bond angles and lengths between the atoms. This can cause crystal faults or vacancies on the nanoparticle surface; these tiny defects in the crystal can act as catalytic sites – and that's something we can exploit.

To give you an example, let's take the surface of a metal oxide nanoparticle. It has a vacancy on its surface thanks to a missing oxygen atom, and the pocket this makes (with its altered chemistry) could then act like the active site of a conventional enzyme and perform chemical catalysis – such as the production of hydroxyl radicals. Further, each nanoparticle has many of these catalytic sites, multiplying the overall rate of hydroxyl radical production, so even a tiny particle can produce a big amount of product.

"Semiconducting nanoparticles could be an extremely promising therapeutic intervention in ocular cancer, and may spare patients from vision loss."

A radical approach

WO_3/Pt nanoparticles contain two components: the tungsten trioxide crystal acts as a semiconducting photoanode, and the platinum acts as a nano-electrode photocathode (see Figure 2). What this

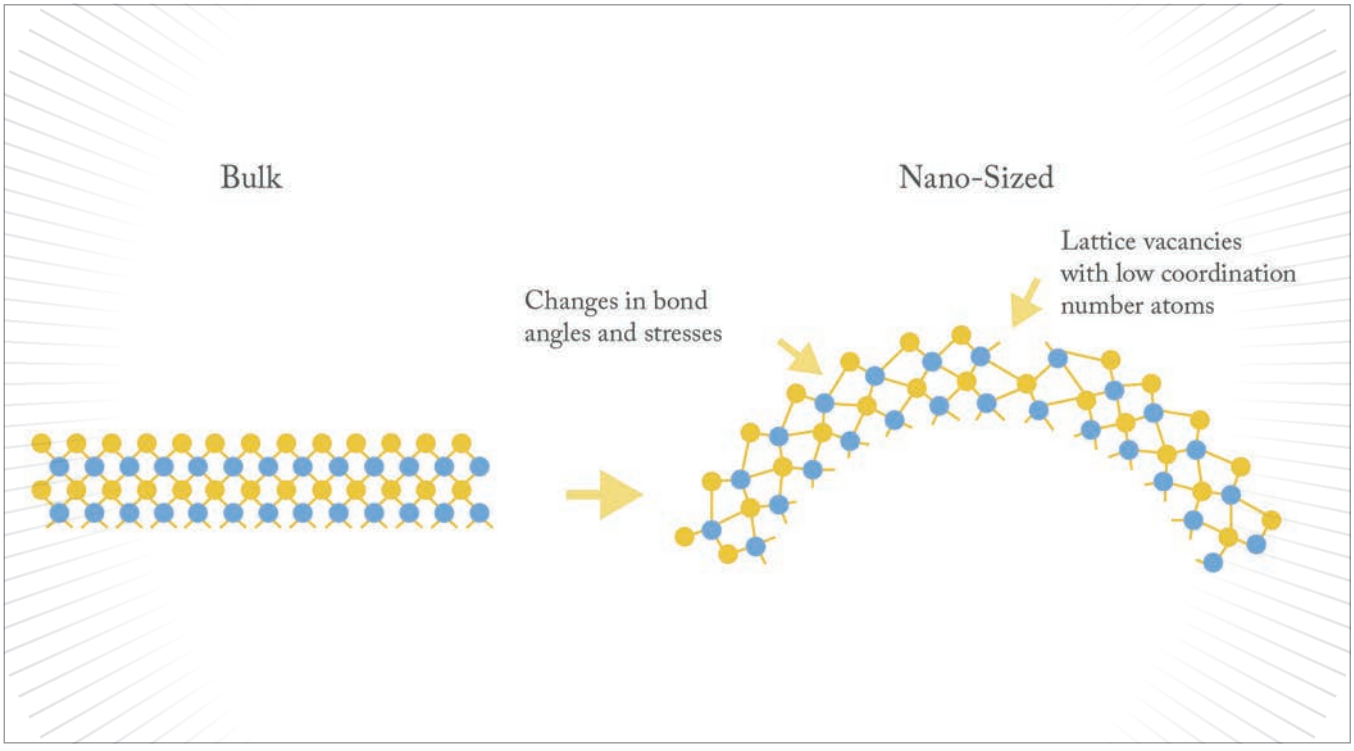

Figure 1. A schematic illustration of the effect of curvature on the relative spatial positions of atoms in bulk materials (left hand side) and nano-sized materials (right hand side).

means is that when the nanoparticles are exposed to light, current flows from the semiconductor photocathode to the platinum crystals. In doing so, the nanoparticles grab electrons from nearby organic molecules (especially electron donors such as NADPH), which then accumulate at the Pt photocathodes, and go on to reduce oxygen to hydroxyl radicals – a very highly ROS. By using NADPH to produce cytotoxic ROS, the particles mimic the NADPH oxidase of phagocytic cells. In other words, we use inorganic crystals exhibiting biological catalytic abilities to enhance or replace a normal anti-tumor response.

Creating ROS to kill cancer cells isn't a new idea – it's an approach that's common to many other anti-cancer strategies like radiotherapy and many chemotherapies. But we all know the drawbacks of these approaches: collateral damage; ROS kills normal cells too. Retinal cells are especially sensitive to ROS, and it's thought that ROS may also contribute to retinal diseases such as glaucoma, macular degeneration, and diabetic retinopathy. But the beauty of the nanoparticle approach is that it can be targeted to tumor cells with covalently-attached folate molecules, where they manufacture ROS solely within those cells, minimizing damage to neighboring cells.

Let's compare and contrast this approach with PDT. PDT dyes do bind tumor cells, but with less specificity, and you're already aware that they rapidly photobleach, limiting the period of effective treatment. With inorganic nanostructures, there's no concern over photobleaching, the substrates (oxygen and organic compounds) are readily available within cells, and they're effective over a broad range of pH values. What this all means is that these nanoparticles can generate high levels of hydroxyl radicals (roughly 10 million per nanoparticle each hour) to kill the tumor cells they're bound to.

Short-circuiting normal metabolic pathways

The process of hydroxyl radical production involves the removal of electrons from biomolecules, which has the side-effect of destroying the constituents of the tumor cell. In addition to this lysosome-like activity, nanoparticles also utilize the cell's metabolic pathways to drive tumor cell death.

Remember, an important substrate for the nanoparticle is the cellular electron carrier NADPH. When a tumor cell is exposed to ROS, it increases its

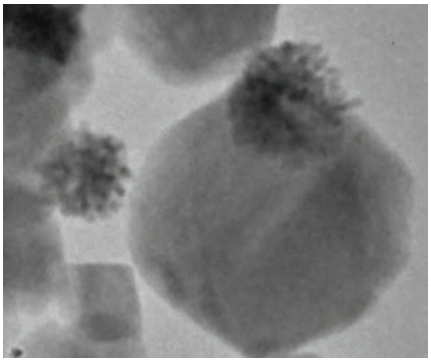

Figure 2. Appearance of a WO_3/Pt nanoparticle. Tufts of platinum crystals (the co-catalyst) are easily seen at one side of the nanoparticle.

"There's a great deal of interest in nanotechnology across all of medicine for both diagnostic imaging and therapeutic applications."

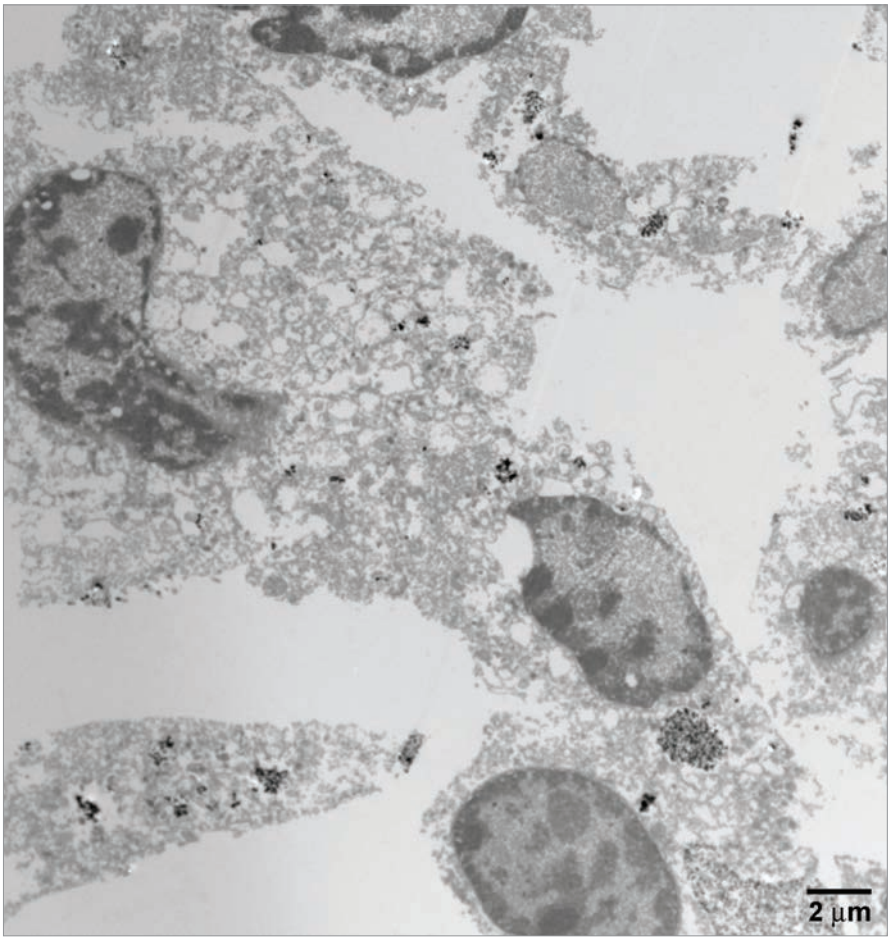

Figure 3. Transmission electron micrograph of a field of tumor cells treated with nanoparticles then exposed to light for 5 hours. Extensive cell disruption is seen. Clumps of electron-dense nanoparticles can be observed.

hexose monophosphatase activity in order to synthesize more NADPH. But this enzyme is also required to make reduced glutathione – which is used to manage toxins. Further, NADPH supplies electrons to aldehyde reductase, which also helps to deflect an oxidative attack by destroying aldehydes formed downstream from hydroxyl radicals. Finally, NADPH is used by quinone reductase in an attempt to minimize damage caused by hydroxyl radicals and lipid radicals buried within the membrane. Just one hydroxyl radical produced by the WO_3/Pt nanoparticle can lead to the formation of many lipid hydroperoxides, which are disruptive to lipid bilayers, and ultimately toxic aldehyde compounds like 4-hydroxy-nonenal, which has been shown to induce apoptosis in tumor cells.

Ultimately, the beauty of this approach is that, by short-circuiting normal metabolic pathways, the nanoparticles not only produce hydroxyl radicals, they weaken the tumor cell's ability to respond to the attack.

Efficacy and toxicity

There's a large gap between what works in theory and what works in practice. We've shown, using multiple in vitro assays, that these WO_3/Pt nanoparticles induce apoptosis in tumor cells in the presence of light (Figure 3). But what about in vivo?

Animal experiments have shown that WO_3/Pt nanoparticles significantly ($P<0.00001$) extend the lifetimes of tumor-bearing mice (2) – and that this effect required the combination of all three components: light, WO_3 and Pt to induce tumor killing, as suggested by the mechanism outlined in Figure 4. When we tested folate-modified,

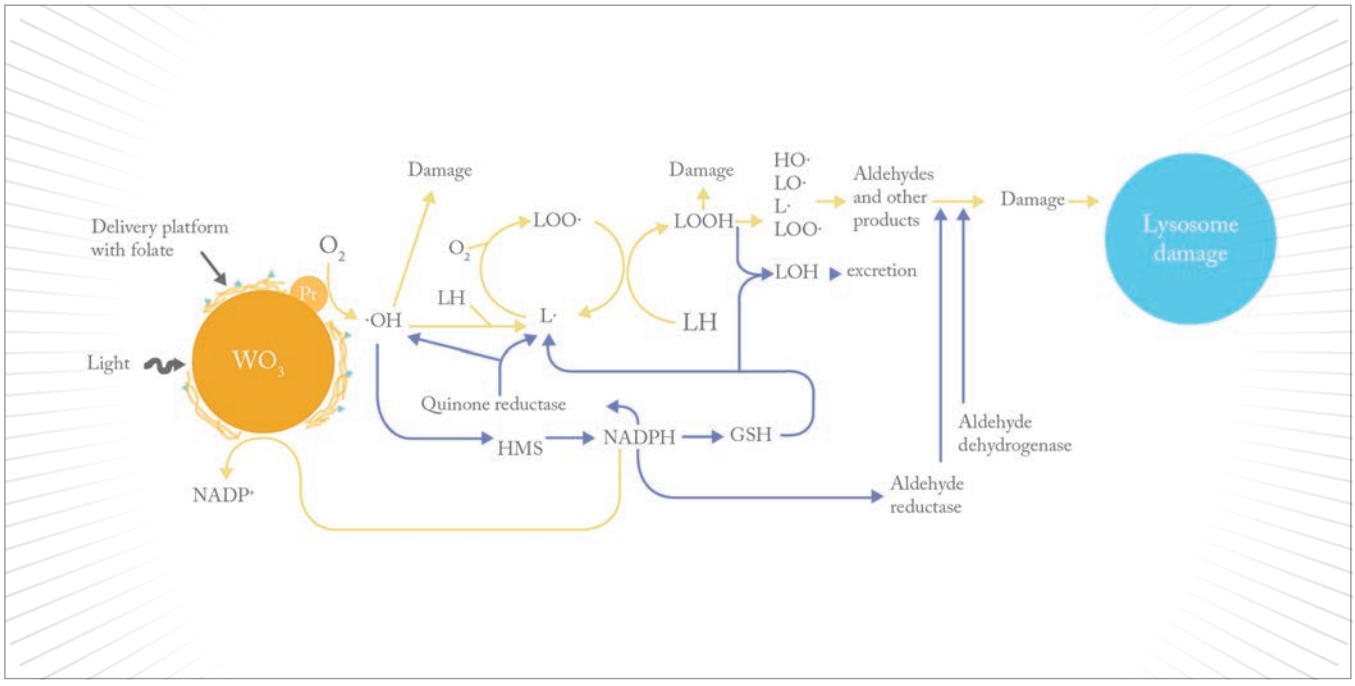

Figure 4. Biochemical pathways in nanoparticle-mediated tumor cell killing. Tumor cell killing pathways are shown in red. Pathways that deflect tumor cell killing mechanisms are shown in green (redrawn from Petty, 2016).

tumor-directed WO_3/Pt nanoparticles in a model of breast cancer metastasis to the anterior chamber, we found that not only did the nanoparticles selectively accumulate at the tumors, but that (once again) illumination resulted in ocular tumor cell apoptosis.

Knowing that the nanoparticles show efficacy in vivo is one thing, but we also need to know their potential for harm – and we do realize that further toxicology studies in animals are necessary to address this. Although monomeric WO_3 and WO_3 nanoparticles have little or no toxicity (4,5), the toxicity of WO_3/Pt nanoparticles has not been established. Our early studies at clinically relevant WO_3/Pt nanoparticle doses suggest that they have no effect on ocular structures. Moreover, the safety of these nanoparticles is also supported by the fact that the LD_{50} of monomeric WO_3 (1059 mg/kg), which can be cleared by the kidney, is higher than those of aspirin (~200 mg/kg) and caffeine (between 150–200 mg/kg).

Helpfully, some of the properties of these nano-sized semiconductor particles can be exploited in future toxicology studies: the X-ray scattering properties of metal/metal oxide nanoparticles could be used in conjunction with micro-CT scans to map the presence and movement of nanoparticles over time within animals, and it should be possible to use WO_3/Pt nanoparticles tagged with infrared probes to monitor their location within animals. These approaches would clearly complement the ongoing conventional toxicology studies of WO_3/Pt nanoparticles.

Big changes with small particles

There's a great deal of interest in nanotechnology across all of medicine for both diagnostic imaging and therapeutic applications – their use, conjugated with a cell-targeting ligand, as a drug or gene delivery vehicle is under intense investigation. Our approach of replacing ineffective biological immune

"The logical next step to try to improve anti-tumor responses would be combining this nanotherapy with conventional aldehyde dehydrogenase inhibitors."

responses with robust inorganic crystals, I believe, holds a lot of potential. But we need to tread carefully. These are very new compounds, and we need to understand the toxicology of the nanoparticles in greater detail before they might see clinical use.

There may also be room for improvement. Yes, the fact that these nanoparticles scavenge NADPH reduces the tumor's ability to deflect an oxidant attack via reduced glutathione production and quinone and aldehyde reductase activity. But aldehyde dehydrogenase, which is greatly overexpressed in cancer stem cells, is unaffected by the nanoparticles, and this may account for the ability of tumor cells to regrow in our model of breast cancer metastasis. The logical next step to try to improve anti-tumor responses would be combining this nanotherapy with conventional aldehyde dehydrogenase inhibitors. This might not be a "magic bullet," but it should hopefully make for a powerful weapon in the ocular oncologist's arsenal.

Semiconductors aren't just used to deal with bits and bytes; in my opinion, they're also one of the most promising approaches on the horizon for the treatment of ocular cancer. But in many respects, both are acting in a very binary manner: microchips deal in on/off scenarios; ones and zeros. When it comes to our nanoscale semiconductors, what's at stake is tumor cell status: dead or alive?

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References

1. *AJ Clark, HR Petty, "WO3/Pt nanoparticles promote light-induced lipid peroxidation and lysosomal instability within tumor cells", Nanotechnology, 27, 075103 (2016). PMID: 26788907.*
2. *AJ Clark et al., "WO3/Pt nanoparticles are NADPH oxidase biomimetics that mimic effector cells in vitro and in vivo", Nanotechnology, 27, 065101 (2016). PMID: 26683660.*
3. *HR Petty, "Could nanoparticles that mimic the NADPH oxidase be used to kill tumor cells?", Nanomedicine (Lond), 11, 1631–1634 (2016). PMID: 27348694.*
4. *S Lanone et al., "Comparative toxicity of 24 manufactured nanoparticles in human alveolar epithelial and macrophage cell lines", Part Fibre Toxicol, 6, 14 (2009). PMID: 19405955.*
5. *G Hasegawa et al., "Differential genotoxicity of chemical properties and particle size of rare metal and metal oxide nanoparticles", J Appl Toxicol, 32, 72–80 (2012). PMID: 22162085.*

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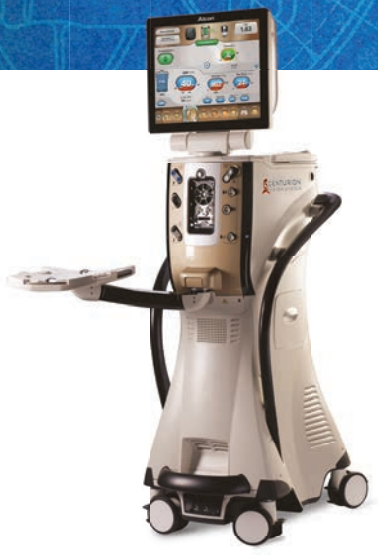

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1. Lorente R, Fanney D, Injev V, Sharif-Kashani P. Quantification of occlusion break surge in peristaltic-based phacoemulsification systems. ASCRS-ASOA Symposium and Congress; April 25-29, 2014; Boston, USA.
2. Nicoli M, Miller K, Dimalanta R, Loke D; Jules Stein Eye Institute, UCLA. IOP Stability Measurement and Comparison Between Gravity-Fed and Actively Controlled Phacoemulsification Systems. 2014.

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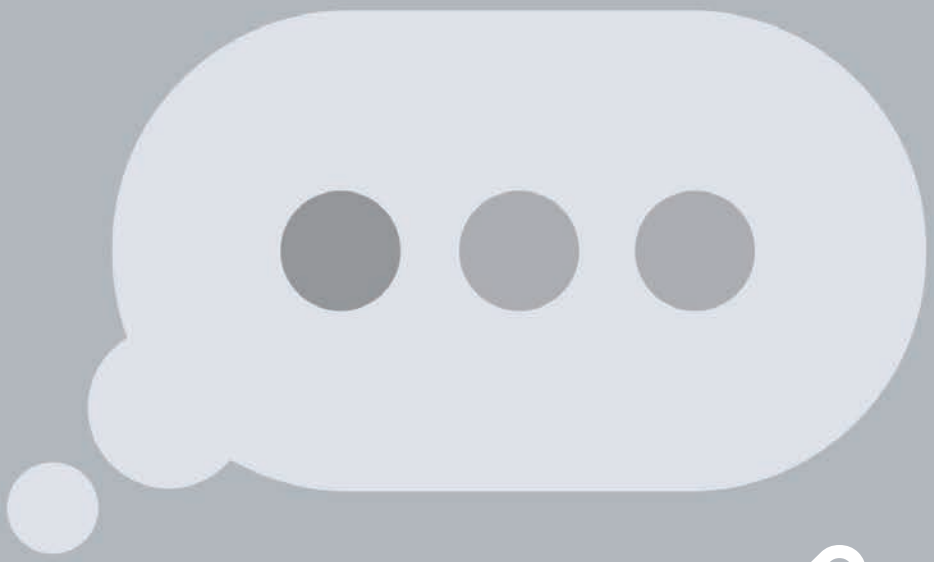


Tech Support

For the blind and visually impaired, smartphones and specialist apps offer something that's indispensable: independence

By Lee Huffman

Here's an illustration of how much smartphones have become so intimately entwined with almost all aspects of our lives. Kate gets a WhatsApp message: "We're all meeting up tonight at Tom's Diner on Main Street 6.30 pm – see you there!" She picks an outfit, checks how to get there on an app, and as she's about to leave, orders an Uber to get there. When she does, she checks out the menu – and sees her favorite burger and fries combination there, and orders it and some drinks. At the end of the evening, the partygoers split the bill (using a calculator app), and she orders an Uber home. But if I told you Kate is highly visually impaired, you'd find that the sequence of events – and smartphone usage – still holds true.

Smartphones make for fantastically useful assistive devices. Most phones have a high resolution camera and display, a flash that can work as an illumination source, internet connectivity and the ability to run apps that exploit every one of these features. Let's look at what's available.

The fundamentals

Almost every smartphone, tablet and computer operating system comes with assistive technologies built in, with the simplest and most useful being screen readers. Apple's devices that run iOS (the iPhone, iPad and iPod Touch) have VoiceOver, and devices that run Android have Google's TalkBack. Most of today's smartphones have dictation keyboards, meaning that users can give instruction to compose emails or run searches, for example. Then there's smart digital assistants: Siri, Cortana, Alexa and Google Now. "Hey Siri. Compose an e-mail to…", "OK Google. Navigate to…", "Alexa, order an Uber to take me to…" Granted, they're not perfect, but when they work, they can be very useful.

Getting ready and getting there

There are a number of apps specifically designed to increase the independence of people who are blind or visually impaired. If we go back to our example of Kate going out to a birthday gathering. What should she wear to the restaurant? Clothes that match – a blue blouse, with black jeans and a tan handbag. How can you do that? Download and run a color identifier app like Color ID, and it speaks aloud the colors that the camera sees.

Kate's now dressed for the event, but before heading out, she wants to check how much cash she has. She lives in the US, where all paper currency is the same size and shape. Is that a five or fifty-dollar bill in her purse? Unfortunately, she can't always trust bartenders, waiting staff or cab drivers, so she finds apps like LookTel Money Reader invaluable for monitoring the cash she has in her pocket.

Next, Kate need to find her way to Tom's Diner. One very popular app that would help her here is BlindSquare, which allows users to find places of interest (e.g. hospitals, restaurants, shopping malls, etc.) and gives them turn-by-turn directions. But it looks like it's a bit far to walk, so Kate asks Siri to summon an Uber.

> *"There are a number of apps specifically designed to increase the independence of people who are blind or visually impaired."*

Kate's arrived – but she's the first there. Other than munching on a breadstick, there's little else for her to do other than peruse the menu. She could open a text-to-speech app like KNFB Reader, but it turns out that BlindSquare already has the restaurant's menu available within the app (and many thousands of other restaurants too), so she decides what to order in that app, then waits for the evening's festivities to begin!

To an onlooker, this is just yet another person constantly playing with their smartphone. But to Kate, this is something completely different: independence.

At a Glance

- *Smartphones combine a lot of useful features for an assistive device: a light source, camera, display, speaker and internet connectivity*
- *Digital assistants (like Siri) plus specialist apps are helping blind and visually impaired people become even more independent*
- *From money-counting, color-coordinating your outfit, to summoning a sighted helper for a quick videoconference, it's all available with an app*
- *The apps don't stop there – they can provide patients, physicians, and families with access to invaluable networks and resources*

The Three Philosophies of Tech Development

Mainstream

Technology that's not created specifically for people with disabilities, but that's intended to be usable to the maximum possible number of people – irrespective of age, status or ability. Some people might adapt the functionality and use it in a manner that wasn't originally intended (like using the camera app as a reading aid: taking a photograph, then pinching to zoom).

Assistive

Specifically designed for people with disabilities (including vision loss) in order to make everyday life more accessible and increase their independence – optical character recognition and text-to-speech readers, a Braille display or even a videomagnifier.

Universal

The concept of designing all products and the built environment to be aesthetic and usable to the greatest extent possible by everyone, regardless of age, ability, or status in life.

housekeeping? Take a picture with the app, and it reads the text back to you.

Another fantastic app is BeMyEyes. It uses your cellphone or tablet to connect you with a sighted person, and you can show them via your camera what you need help with – for example, you're working to set the thermostat in your room, and all the buttons are the same size, shape, and color, making them hard to distinguish. The person can then assist you, saying "Okay, your temperature is set at 68°F, move your hand to the right – yes, that's the one – tap that three times and your temperature will go down."

"Being aware of the technology available for patients who are blind could help to improve their ability to navigate everyday tasks."

Objects, text and remote assistance

Apps can help with more routine and mundane tasks – like finding things in the supermarket or turning on the heating. For object identification, there's TapTapSee: if you don't know what something is, this app can tell you. If you need to know if you're picking up a bottle of shampoo or conditioner, you can take a picture with the app, and it'll process the image and tell you what it is. Kate didn't use the KNFB reader TTS app to read the restaurant's menu in the example above, but these apps are incredibly useful. Say you're staying in a hotel and find a Post-it note on your bed. Is it the breakfast menu? Information from

Working and networking

My employer, the American Foundation for the Blind, has created some apps of its own: AccessNote is a completely free productivity tool that enables the user to take notes, share documents, use a calculator, connect to their Dropbox, and more. Another is VisionConnect, which allows people in the US and Canada to share resources in their local communities, providing information on services such as computer training, Braille reading, guide dog training, and low vision services, all in a searchable directory. The information is up-to-

Task	App
Identifying colors	Color ID (free)
Identifying currency	LookTel Money Reader (this app can currently identify 21 currencies)
Navigation, wayfinding and information about surroundings	BlindSquare
Object identification	TapTapSee
Remote visual assistance	BeMyEyes
Text-to-speech	KNFB Reader App
Writing, calculating and administration	AccessNote (note-taking, sharing documents, calculations, and more)
Finding services and resources	VisionConnect (a free guide to resources for blind and visually impaired people in the US and Canada)
Employment	CareerConnect (learning about careers, job seeking, navigating interviews and employment, and mentoring)

Table 1. Smartphone apps that help to increase the independence of blind and visually impaired people.

date and pulls directly from our website (AFB.org) to quickly provide that information. This app is targeted towards physicians, professionals, and people with visual impairment. It can help provide information about eye conditions, tips on how to adapt your home for vision loss, and help to connect you to helpful services in your area.

Similarly, the AFB CareerConnect app is designed to aid people who are seeking employment, and teachers working with people with visual impairment. There are also job searching strategies and tools, answering questions like "how do I disclose my disability during the interview process?" It's a great resource for people transitioning from high school or college to the world of work, and it's also free.

Although some of the apps I've mentioned here won't be available in all countries, there are many, many more available (and in development). Resources like AccessWorld, AppleVis, and Top Tech Tidbits can all be useful sources of information for finding apps specific to your location and language – and if you aren't sure, the best way to evaluate the usefulness of an app is to simply download it, and give it a go.

"The best way to evaluate the usefulness of an app is to simply download it, and give it a go."

Assisting independence

These apps are just some of the ways in which new technologies are helping people with vision loss maintain their independence, find a job, and stay employed – and there are many more out there than I have mentioned here. Being aware of the technology available for patients who are blind or have vision loss, and introducing them, could help to improve their ability to navigate everyday tasks independently – and have a very positive impact on their quality of life.

Lee Huffman is the Editor-in-Chief of AccessWorld, the American Foundation for the Blind's monthly online magazine, which provides news and reviews of accessible technology used by blind and visually impaired people.

Hang that Shingle!

How we approached "going solo" and set up our own successful practices

Ruth Steer interviews Edwin Chen, Ravi Patel and Ajit Nemi

Conventional wisdom suggests that setting up a solo practice is a thing of the past. And it's true that "hanging a shingle" – where you could go anywhere, work hard and see things go well – doesn't really apply nowadays, because a lot more planning is required. There is also a common belief that it's too difficult unless you address an underserved area. But we would counter that starting-up in a thriving area isn't impossible. We've each succeeded in Atlanta, Jacksonville and San Diego, and we want to share and reflect on some of the lessons we've learned along the way…

Plan it

Planning is by far the most important step and should start at least 12 months from your anticipated opening day (Figure 1). The first big decision facing the budding solo practitioner is: where do you want your practice to be? Location is critical, so whether you're aiming for a big city, suburban or rural practice, it's key to look into the local demographics. MD to population ratio and the number of local optometrists are also things you can consider, but it doesn't always matter if there isn't a huge demand for eyecare: you just have to plan around it.

You do need to decide what eyecare you want to deliver: an underprivileged area may not be the best place for LASIK – and up and coming "hipster" areas aren't ideal if you want to perform lots of cataract surgery. It's also important to consider the insurance distribution of the area. Although getting the information you need can be difficult, talking to local physicians in the area can help you get the "lay of the land" in terms of patients and insurance.

"It doesn't always matter if there isn't a huge demand for eyecare: you just have to plan around it."

Once you've got the wider area mapped out, you need to pin down your site. Do you want a medical office or retail location? Each has their pros and cons: medical offices offer opportunities to build up and may be more accessible to referrals, but you may not get the foot traffic or visibility of a retail-type location. Accessibility is also a factor – if you're not familiar with the local area, it's worth talking to people to find any trouble spots that patients may avoid traveling to because of traffic or parking issues. Once you've got a location sorted, it's time to think about what you're going to need to build your practice.

Build it

What you want in your office depends on your practice vision. What kind of physician do you want to be and what you want to do? There are several aspects to consider, such as:

At a Glance

- *Many may believe that it is too difficult to set up an independent practice nowadays*
- *Whilst true that it isn't easy, we believe that it absolutely is possible to set up a solo practice in the 21st Century*
- *We should know: we've each been successful at setting up our own clinics*
- *We share our stories, provide our top tips for going solo, and reflect on the lessons we've learnt*

Ravi Patel

Co-founder of Florida Eye Specialists. Specializes in cataract, laser refractive and corneal surgery.

"Don't stress the small stuff and you can do it!"

My practice has grown hugely since starting out. Originally, I started out in 2009 as a solo practitioner with 2,500 square foot of office space and six staff members, but this has since meta-morphed into a group practice with multiple locations and a large number of staff. In the beginning, the challenge of managing HR was quite a surprise – and this continues to be a challenge today. I was also surprised by the costs of equipment and instruments.

It's been so rewarding to grow the practice and see it develop a good reputation amongst the community and with patients. I've really enjoyed caring for my patients and being able to provide the best patient experience possible – it's been so great to hear positive comments and receive heart-felt cards.

Ajit Nemi

Solo practitioner specializing in cataract and refractive surgery, and comprehensive eye care.

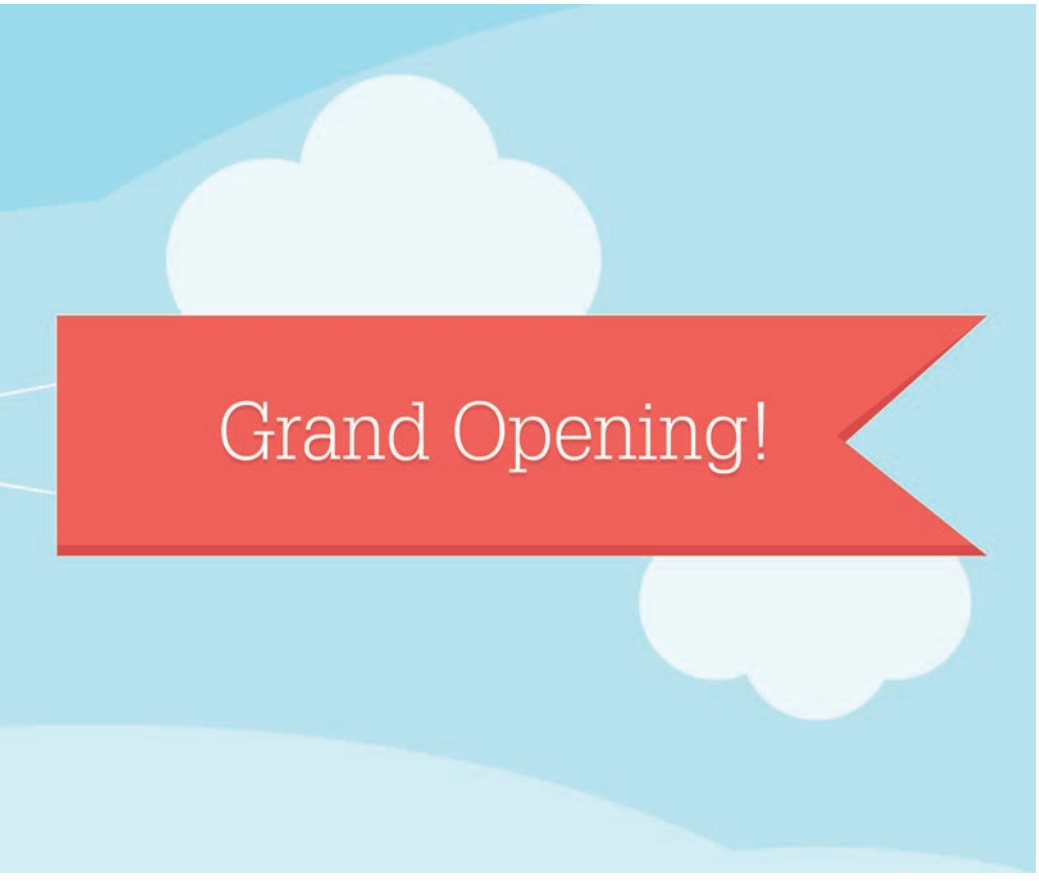
"It was a leap of faith, but I'm glad I took it."

I'd previously been working in a group practice but, realizing that it wasn't a good fit for me, I was inspired to set up my own clinic. In 2008, right at the beginning of the USA's most recent recession and as the stock and housing market were crashing, I started my practice. It then took a whole year to obtain any reimbursement from Medicare because it turned out that the electronic billing system was entering zip codes in a different format to what the Center for Medicaid and Medicare Services (CMS) accepted! Although this was a bad surprise that took a year of back and forth over the telephone to sort out, I've encountered many good surprises along the road. Word of mouth from our patients has had an exponential effect on our practice, and there've been many rewards, some of the biggest ones being the ability to execute my vision for practicing medicine, having autonomy over the practice culture, as well as the personal satisfaction of growing a business from "scratch." In the years to come, I hope to continue to grow and mature my practice.

- How many exams rooms do you need? Make sure you're going to make each square foot of what you take useful. A lot of people forget about circulation space (areas where patients walk, ends of halls, and so on) but these are still important aspects of your office, and can account for 25–30 percent of your square footage.
- What equipment do you really need? Many of us may have trained on elite equipment, but do you really need it? As equipment usually turns out to be more expensive than expected, pick and choose where you may be happier to go for the cheaper option; looking at reimbursement rates may assist these decisions as you can calculate how long it may take you to pay off equipment purchases.
- Do you want ancillary testing on-site, and if so, how much? Not only is ancillary testing "dead" square footage when you're not actually using it, but the machines can be very expensive. It's worth investigating opportunities for ancillary testing in your local area, for instance at ambulatory surgery centers (ASCs).
- Some square footage is optional. Do you really need your own office? If there's a public bathroom in your building, do you really need your own (and the additional costs of maintenance)?

Finance it

Moolah, dough, bucks – whatever you call it, none of this would be possible without it. A question we're always asked is "How much will it cost me to open my own practice?" Talking specific numbers is not always helpful – insurance contracts and office expenses vary so wildly by geography



that it is important for each physician to crunch their own numbers.

It goes without saying that you'll need some cash behind you to get a loan so the banks see you have 'skin in the game.'" But as you skip up to the bank with your deposit in tow, be aware that some lenders may want two years' experience of running a practice before they'll consider loaning money, which can be a tough bill to fit if you're striking out on your own for the first time. There are alternatives, such as small business loans guaranteed by the government, but bear in mind that these may come with associated fees and regulations. When securing the money you need, you'll also need to consider living expenses: a loan is unlikely to cover these so make sure you can put food on the table whilst setting up!

You'll also need to think about cash flow once your practice is open – what are your overheads going to be, what additional costs are there and how are you going to get paid? As a standard rule of thumb, typical overheads for an ophthalmology office lie between 55–65 percent of gross income. However, if your patients pay by credit card, the associated processing changes might cost you a further three percent from the 35 percent that you're trying to take home.

Be aware of other 'unexpected' costs associated with running a practice, and note that there are ways to reduce such expenses. For instance, a virtual phone number that re-directs callers to a number of your choosing might be a cheaper option than an on-call service.

All in all, once you're open, watch the flow of money – but don't obsess over it; there will be plenty of other things to worry about – which brings us neatly to opening your practice…

Edwin Chen

Solo practitioner practicing in cornea and anterior segment.

"In 10 years, I plan to be exactly where I am now – caring for patients the way I think they should be cared for."

I started my practice, Ocean Eye, in 2010 because I wanted to provide my patients with what I felt was the best care possible. Owning a practice was one way for me to achieve this, because I'd be able to obtain and use the diagnostics and equipment of my own choosing – and what I felt would be best for my patients. To date, the biggest reward of opening my own practice has been seeing how happy patients are, and hearing how they see our vision as a practice come through in their care. But the vision and design of setting up your practice is the easy part! It wasn't all plain sailing, and some of the greatest challenges I faced in the beginning were managing HR and other business aspects that I had little-to-no experience in. When starting out, there's a tendency to obsess over every little thing, so if I could travel back in time, I'd tell myself to focus on the things I can change and learn to adapt to the things I can't. In the end, if you're taking good care of patients and are mindful of the realities of practice, you'll do great!

Open it

It's time to consider the day-to-day practicalities. Firstly, you're going to need several key contracts. From


12 months
Research and choose general area
Consider equipment and real estate needs
Research costs
Look at hospital affiliation and apply for state medical license
6 months
Determine neighbourhood location
Business plans and financing
Meet with business attorney
Establish business entity
Apply for hospital privileges
4-5 months
Credentialing with insurance companies
Finalize financing and explore locations for office space
Research infrastructure
Begin designing website
3-4 months
Research equipment and furniture
Interview for office manage
Create business and personnel policies
Secure necessary insurances
1-2 months
Follow-up on credentialing
Sign office lease
Start training on systems (EHRs etc.)
Order equipment and furniture
Prepare office forms, fee schedule and superbill
Visit referral sources and begin advertising
Open Now!

Figure 1

merchant services to medical disposal needs, you're going to need to set up relationships to assist with running your practice. You're not going to be able to do everything yourself, but it is important to consider what to outsource versus what to keep "in house" by weighing up the out of pocket cost against your time.

"Once you're open, watch the flow of money but don't obsess over it."

The kind of things you may consider outsourcing include billing, Health Insurance Portability and Accountability Act (HIPAA) compliance, and Occupational Safety and Health Administration (OSHA) training. For many of us, human resources (HR) is the most challenging part of owning our own practices because "hiring and firing" is an acquired taste – and skill. You also need to consider payroll, federal postings and HR law, but these are other aspects that can be outsourced to ensure compliance. Additionally, when it comes to insurances, malpractice insurance is only the beginning... Be prepared to also consider worker's compensation, business liability, employment practices liability, and business overhead insurances.

Grow it

Congratulations – you're running your own practice! But there is still plenty of hard work to be done to grow your practice. Building relationships with emergency departments, referring doctors, and urgent care services is key – and you may need to "pound the pavement" to do this. Be aware that when first meeting a referral source, they may already have somebody that they're happy referring to, so why should they switch to you? You may be more convenient geographically, or you may end up as a backup when their first referral choice says "no," but whatever the reason you end up being referred to, doing a good job with that patient and communicating well with the referring physician will help forge a strong relationship. We've found that it really pays to be considerate of patients and referring physicians, and it's also highly beneficial to keep the relationship strong: go back to visit your referral source, especially if you're in a busy area; they will remember you as the physician who helped their patient.

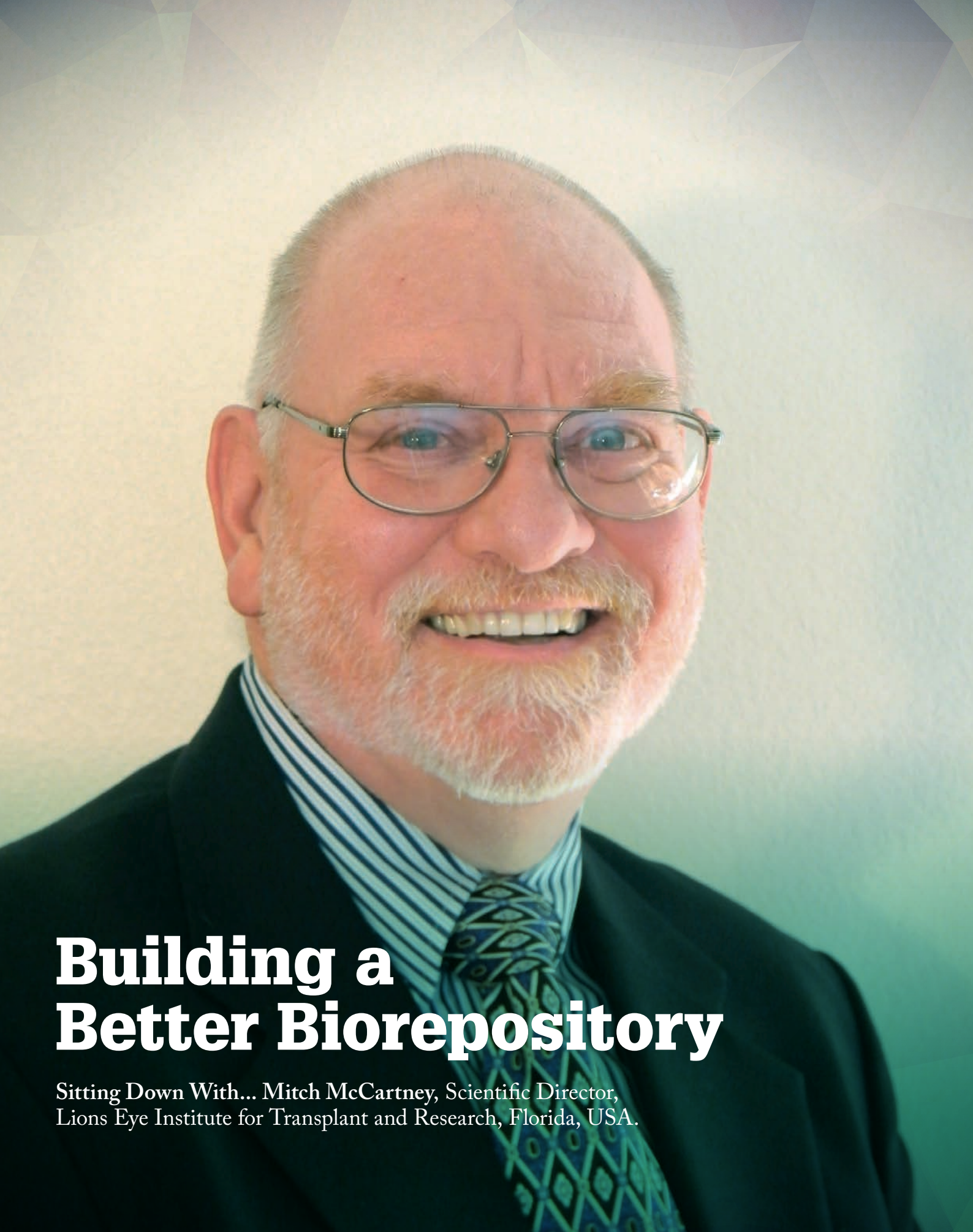
Events are also important in growing your practice. Continuing medical education, meetings with other doctors, and residency lectures are all valuable, if you have the aptitude. It's really worth holding an open house event when you first open, as it can be great way to meet people and referral sources. It's also important to bear in mind that sometimes you have to spend a little money to make some. Follow-ups with referring physicians may be uncompensated, but will go a long way in maintaining key relationships. Finally, it's always worth investing in office morale through lunches, holiday gifts, and so on, because if you keep your staff happy, they will keep your patients happy – and that will ultimately keep you happy (and in business).

Do it!

Over the past year or so, we've been offering a course on opening a solo practice, and the reason we run this is because we want people to know that it is indeed possible to start-up a solo practice in the 21st Century. It's not all smooth sailing, and there are many things to learn along the way (see Box: Things We Wish We'd Known), but we've done it and we are happy to be sharing our experiences.

Things We Wish We'd Known

- In some areas, insurance companies may not be looking for more providers, so certain patients may be off limits to you.
- Individual practices need to negotiate reimbursement rates with insurance companies. In saturated areas, some insurance companies may not accept new providers.
- Equipment is a lot more expensive than you think – and warranties are generally short. If you want extended warranties on your equipment, don't forget to budget for this.
- Before you even start using your practice, you will be paying for the room(s), so make sure you also plan this into your budget.
- Plan to run behind schedule in practice setup: there are things you can't control, and these can then control other things that you can't control...
- Don't spread yourself too thin. Just because you don't have patients to see initially does not mean you won't be working all day long.



Building a Better Biorepository

Sitting Down With... Mitch McCartney, Scientific Director, Lions Eye Institute for Transplant and Research, Florida, USA.

How did you end up studying the eye?

You're taking me quite a long way back – I've got a ribbon on my ARVO badge representing over 30 years of membership! I started out in Canada as an undergraduate studying biological sciences, and then I moved on to a Master's degree in human anatomy, and then a PhD in human anatomy and cell biology – my research was on the retina, specifically photoreceptors. Next, I took a position as a postdoc; when I got there, they'd just received a new grant for studying the cornea (back when institutions got more speculative grants than they do now). They asked if I'd be interested, so I read the grant and realized that there was a lot of clinical knowledge of the cornea (and specifically the endothelium) but there was a need for basic science information. It was a great opportunity, so I stayed for around two and a half years and then helped my boss move her lab up to the University of Louisville's Kentucky Lions Eye Institution, which is where Alcon recruited me.

Originally, I was working to set up their electron microscopy unit, but over the years I worked in many areas including cornea, glaucoma, and retina. Alcon was of course purchased by Novartis, and in 2013 the decision was made to move the research component up to its research facility in, Cambridge, MA. By this time, I was old enough, so I "retired."

But then you joined Lions Eye Institute as scientific director…

Right. Over the years, one of my duties at Alcon had been to liaise with Lions Eye Institute to secure human ocular tissue for various research models, so it worked out perfectly; I was familiar with them, and they were looking for a scientific director to help work towards their research goals.

What research is The Eye Bank focusing on?

One problem we're working on is death-to-preservation time. Ten or fifteen years ago, the type of research being done on human tissue allowed researchers to receive tissue 24–36 hours after it was harvested, without any problems. Now, with all the new molecular techniques being used, death-to-preservation time is becoming increasingly important – we want as small a window as possible. Today, we can get tissue into our lab 6–8 hours postmortem, perform a preliminary dissection, and then take the required tissues and freeze or fix them. The process essentially stops the degradation, so it doesn't matter if the researchers don't receive the tissue for 48 hours or so.

One of our longer-term plans is a biorepository. We've created a prospective model, and we have clients who want specific tissue that we dissect, freeze, and store for them. The problem is that it's an expensive process when you consider screening, recovery coordinators, lab space, and so on. And the reality is that grant-funded academics often aren't able to fully reimburse us. To address the issue, we've approached various agencies to see if we can get some basal funding. Then, if grantees want tissue, they can contact us and our basic costs are already covered. At the moment, people want rapid preservation and high-quality tissue, but for a variety of reasons they're only able to pay about a third of what it really costs us to do that... As a nonprofit, we're not trying to make money, but we do need to cover our processing costs.

What's most exciting about your work?

These days, an increasing number of surgeons are using new techniques in corneal transplantation, with endothelium and a small amount of stroma (as opposed to full penetrating techniques) – and they are improving vision amazingly. Even just a few decades ago, patients appreciated much smaller improvements. But now, they want excellent vision – and we're a part of making that happen. Instead of the surgeon sitting in the OR preparing the tissue with the patient waiting, an eye bank can provide the tissue so that it's sitting there ready to go. It also brings economic benefits, as it decreases time spent in the OR. Around 45–50 thousand transplants occur in the US every year, and as our techniques become more sophisticated, we're able to do more and more to help. And we're also able to contribute specifically to different types of research that could lead to life changing treatments for many eye diseases. It now feels like we're being considered more as partners than simply as 'the tissue providers.'

"Eventually, we want to be able to provide tissue to anybody with a National Eye Institute grant."

What do you hope to do next?

We don't want to limit our work – I've been speaking with research chairs from the Association of University Professors of Ophthalmology and they were very supportive of our plans to try and start a biorepository program. Eventually, we want to be able to provide tissue to anybody with a National Eye Institute grant. Of course, every eye bank starts small and builds up – so we'll start locally with Florida, but our eventual vision is that our tissue will be available across the country, and then around the world.

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