

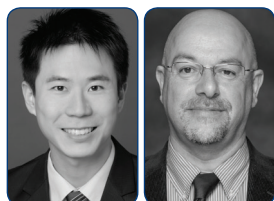
RESEARCH RESULTS



HIGHLIGHTS OF THE ARVO 2016 ANNUAL MEETING

Select research findings presented this year.

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From April 30 to May 5, 2016, downtown Seattle was teeming with participants in the Annual Meeting of the Association for Research in Vision and Ophthalmology (ARVO). After walking through the poster halls

and listening to the presentation of papers, we chose several abstracts to discuss. Of note, our selections do not necessarily represent the most important or cutting-edge research at this year's ARVO meeting, but they are findings that caught our attention.

INJECTABLE BIMATOPROST IMPLANT

Shamira Perera, FRCOphth, of the Singapore National Eye Centre shared the 12-month interim results of bimatoprost sustained-release (SR) implants (Allergan) on behalf of investigators from multiple sites in Asia, the Middle East, and the United States. This single-use biodegradable implant is placed in the anterior chamber. It typically rests in the inferior angle and releases bimatoprost over 4 months. Dr. Perera's presentation focused on the safety and efficacy of the implant.

In this prospective 24-month study, after washout, 75 patients with open-angle glaucoma received an intracameral injection of the bimatoprost SR implant with various doses of active ingredient (6, 10, 15, or 20 μ g) in the study eye. Rescue topical medication or a single repeat treatment with an SR implant was allowed for failure to attain the target IOP. The overall mean IOP reduction from baseline through week 16 (data censored at rescue/retreatment) was 7.2, 7.4, 8.1, and 9.5 mm Hg with the 6-, 10-, 15-, and 20- μ g dose strengths, respectively. A single implant controlled IOP in 91% of subjects at the 16-week time point. Conjunctival

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hyperemia was the most common adverse effect in study eyes; it usually occurred within 2 days of the injection and was transient. Eyelash growth was not noted in the injection group, but it was observed in 7% of the control eyes receiving topical bimatoprost. According to Dr. Perera, “endothelial cell counts were performed and will be presented in future reports.” He concluded, “All SR implant dose strengths were comparable with topical bimatoprost in overall IOP reduction through week 16, and ... a single dose of SR controlled IOP [for] up to 12 months in 41% of patients.” Phase 3 trials of bimatoprost SR are underway.¹

TABLET GLAUCOMA SCREENING

Frequency doubling technology (FDT) has been touted as an effective method of detecting early glaucomatous visual field changes, but glaucoma screening in the community frequently relies on IOP measurements and optic disc photography without evaluation of the visual field. Recently, applications on the iPad (Apple) have been developed in an effort to assess the visual field in a convenient manner.

Meredith Kim and colleagues compared iPad-based visual function tests to FDT. The study included 76 eyes with early manifest glaucoma and 13 age-matched controls. Each eye underwent FDT and testing with three different iPad apps. The visualFields easy app (George Kong software) displays 94 size V points sequentially. The user is asked to touch the point on the screen when he or she sees it. If at least three points are missed, the test result is considered abnormal. Developed by Louis Pasquale, MD, the blue arc entopic phenomenon test displays a red vertical band of light and asks the user if he or she perceives blue arcs in scotopic conditions. If not, the test result is considered abnormal. It should be noted that, unlike the visualFields easy test, this test is fixation independent. The quick contrast sensitivity function (QCSF) test (Adaptive Sensory Technology) displays a chart of letters at different contrast levels and is fixation independent as well. Each of the iPad app tests can be completed within 3.5 minutes.

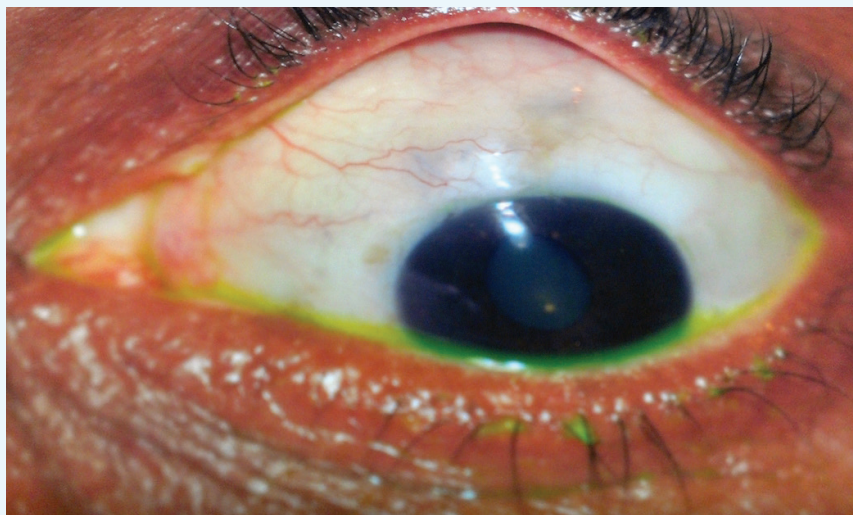


Figure. A low, thick filtering bleb from encapsulation.

The sensitivities and specificities were as follows, respectively: FDT 0.84 and 0.87, QCSF acuity 0.69 and 0.85, area under the log contrast sensitivity function 0.81 and 0.69, visualFields easy 0.70 and 0.31, and blue arc entopic phenomenon testing 0.83 and 0.23. The area under the receiver operating characteristic curve was 0.82 ± 0.5 for QCSF acuity and 0.81 ± 0.6 for area under the log contrast sensitivity function. Ms. Kim concluded, "[The] QCSF test had similar sensitivity and specificity compared with FDT for the detection of early manifest glaucoma and may serve as an important teleglaucoma screening tool." The visualFields easy app and the blue arc entopic phenomenon test had lower specificities and positive predictive values, thus labeling more normal eyes as abnormal than FDT and QCSF.²



AT A GLANCE

- Twelve-month interim data on the safety and efficacy of bimatoprost sustained-release implants support further clinical development.
- A quick contrast sensitivity function iPad test has similar sensitivity and specificity as frequency doubling technology for the detection of early manifest glaucoma and may serve as an important teleglaucoma screening tool.
- The type of glaucoma medication used during the first 6 months after trabeculectomy may influence bleb morphology.
- Optical coherence tomography angiography may have a role in the detection and monitoring of patients with normal-tension or primary open-angle glaucoma.
- Research indicates that cigarette smoking is a risk factor for the development of ocular hypertension and primary open-angle glaucoma.

PROSTAGLANDIN BETTER FOR BLEB MORPHOLOGY

Bleb morphology after trabeculectomy may have to do with surgical technique and a patient's characteristics, but Yuji Yamamoto, MD, and colleagues found that the type of antiglaucoma medication used postoperatively may also be influential (Figure). The investigators extracted data on glaucoma patients who required treatment with either a topical prostaglandin analogue (PGA) or a β -blocker (BB) for less than a 6-month period after trabeculectomy in the Collaborative Bleb-Related Infection Incidence and Treatment Study, a multicenter prospective cohort study in Japan. Eyes in which no bleb formed, in which the bleb was smaller than the scleral flap, or that had undergone needling were excluded. Bleb morphology was documented every 6 months through 5 years of follow-up.

Thirty-three cases in the PGA group and 18 cases in the BB group fulfilled the criteria for analysis. The period free



of bleb failure was longer in the PGA than the BB group. When asked why the BB group did worse, Dr. Yamamoto stated, “My theory is β -blockers lower aqueous formation and flow into the bleb, causing the bleb to flatten and scar. In contrast, the prostaglandins increase uveoscleral out-flow” and have less effect on flow into the bleb.³

OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAM FOR GLAUCOMA

In addition to retinal ischemic diseases, optical coherence tomography (OCT) angiography may have a role in the detection and monitoring of patients with normal-tension glaucoma (NTG) or primary open-angle glaucoma (POAG).

Karine Bojikian, MD, PhD, of the University of Washington Seattle presented a poster on optic disc perfusion differences among 56 healthy eyes, 60 POAG eyes, and 62 NTG eyes. Using the Cirrus high-definition OCT 5000-based optical microangiography prototype system (Carl Zeiss Meditec), Dr. Bojikian and colleagues took microvascular images of the optic nerve head. In the prelaminar cribriform layer, both POAG and NTG eyes showed significantly less perfusion than healthy eyes ($P < .0001$). Dr. Bojikian added, “There was no statistical difference in perfusion between POAG and NTG eyes.” A correlation between optic disc perfusion, visual field mean deviation, visual field pattern standard deviation, and rim area in the glaucoma groups was found ($P \leq .0288$).⁴

SMOKING AS A RISK FACTOR FOR OCULAR HYPERTENSION AND GLAUCOMA

Are there modifiable risk factors other than strict adherence to prescribed medical therapy about which eye care providers can counsel glaucoma patients?

A meta-analysis of randomized controlled trials, cohort studies, and cross-sectional studies in the Medline and Embase databases revealed cigarette smoking as a risk factor for the development of ocular hypertension and

POAG. Rong and colleagues at the Chinese University of Hong Kong analyzed 41 studies involving a total of 172,314 subjects. The investigators found that current and former smokers had a higher IOP than those who had never smoked ($P < 5 \times 10^{-10}$). Current smokers had an increased risk of developing POAG compared with former smokers ($P < .05$), with an odds ratio of approximately 1.2.

If optic nerve ischemia plays a role in glaucoma, as suggested by OCT angiography, it is not surprising that smoking can affect vascular health important for optic nerve perfusion. A prospective study looking at changes in glaucomatous progression after quitting smoking is needed to support the notion that smoking affects the development of glaucoma.⁵ ■

1. Perera S, Lewis RA, Christie WC, et al. Bimatoprost sustained-release implants for glaucoma therapy: 12-month interim results from a phase 1/2 clinical trial. *Invest Ophthalmol Vis Sci*. 2016;57:e-abstract 4280.

2. Kim M, Ren A, Bex P, et al. Comparison of iPad-based visual function tests for the detection of early manifest glaucoma. *Invest Ophthalmol Vis Sci*. 2016;57:e-abstract 2277.

3. Yamamoto Y, Mori K, Yokota I, et al. Does type of postoperative anti-glaucoma drug affect morphological changes of filtering bleb after trabeculectomy? Utilizing the data from the Collaborative Bleb-Related Infection Incidence and Treatment Study. *Invest Ophthalmol Vis Sci*. 2016;57:e-abstract 2937.

4. Bojikian KD, Chen C, Wen JC, et al. Optic disc perfusion in eyes with primary open angle glaucoma and normal tension glaucoma using optical coherence tomography-based microangiography. *Invest Ophthalmol Vis Sci*. 2016;57:e-abstract 2957.

5. Rong SS, Tsui LY, Ma L, et al. Cigarette smoking increases intraocular pressure and risk of primary open-angle glaucoma: a systematic review and meta-analysis. *Invest Ophthalmol Vis Sci*. 2016;57:e-abstract 2576.

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