

# AMERICAN JOURNAL OF OPHTHALMOLOGY®

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### EDITORIAL

- 215 **A new paradigm in the treatment of advanced periocular basal cell carcinoma?** *Shelby P. Unsworth, Curtis J. Heisel, and Alon Kahana*

### ORIGINAL ARTICLES

- 1 **Posterior chamber phakic intraocular lens implantation for the correction of myopia and myopic astigmatism: a retrospective 10-year follow-up study.** *Tomoaki Nakamura, Naoki Isogai, Takashi Kojima, Yoko Yoshida, and Yasuo Sugiyama*

To assess the 10-year clinical outcomes of implantable collamer lens (ICL) implantation in 114 eyes of 61 patients with myopic refractive errors (−4.1 to −17.0 D). The mean safety and efficacy indices were 0.88 and 0.66, respectively, 10 years postsurgery. Twelve eyes developed anterior subcapsular cataract. No vision-threatening complications occurred. ICL implantation offered good outcomes in all measures of safety, efficacy, predictability, and stability for the correction of moderate-to-high myopia throughout a long-term follow-up period.

- 11 **Shortening of interpupillary distance after instillation of topical prostaglandin analog eye drops.** *Ichiya Sano, Hidenori Takahashi, Satoru Inoda, Shinichi Sakamoto, Yusuke Arai, Yuji Takahashi, Akira Ohkubo, Hidetoshi Kawashima, and Chihiro Mayama*

Changes in the interpupillary distance (IPD) after continual instillation of topical prostaglandin analogs (PGAs) in patients with glaucoma may be useful to identify PG-associated periorbitopathy (PAP). The IPD decreased significantly after topical PGA instillation within 24 months and was significantly greater with

bimatoprost than with other PGAs. The noninvasive, immediate automatic refractometry measurement may be an objective numerical indicator of PAP.

- 32 **Refractive laser-assisted cataract surgery versus conventional manual surgery: comparing efficacy and safety in 3144 eyes.** *Harrish Nithianandan, Vibeeshan Jegatheeswaran, Vishruti Dalal, Steve A. Arshinoff, Raj Maini, Fariba Nazemi, Tran Le, Eric S. Tam, and Sohel Somani*

This retrospective interventional comparative case series investigated one of the largest consecutive cohorts of phacoemulsification surgery and found a pronounced benefit of employing femtosecond laser-assisted phacoemulsification over conventional phacoemulsification surgery when treating more difficult eyes.

- 74 **Classification of regions of nonperfusion on ultra-widefield fluorescein angiography in patients with diabetic macular edema.** *Mengyuan Fang, Wenying Fan, Yue Shi, Michael S. Ip, Charles C. Wykoff, Kang Wang, Khalil Ghasemi Falavarjani, David M. Brown, Jano van Hemert, and Srinivas R. Sadda*

Severity of diabetic macular edema appears to be positively correlated with nonperfusion region with leakage but negatively correlated with nonperfusion region without leakage. These findings may have relevance to the pathophysiology of diabetic macular edema and the design of targeted therapeutic interventions.

- 82 **Risk factors associated with persistent anterior uveitis after cataract surgery.** *Amit K. Reddy, Jennifer L. Patnaik, D. Claire Miller, Anne M. Lynch, Alan G. Palestine, and Mina B. Pantcheva*

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Although persistent anterior uveitis (PAU) is uncommon following uncomplicated phacoemulsification cataract extraction, African Americans were at more than 11 times higher risk for developing PAU than whites. PAU does not appear to affect visual outcomes.

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• **87 Refractive error has minimal influence on the risk of age-related macular degeneration: a Mendelian randomization study.** *Ashley Wood and Jeremy A. Guggenheim*

This manuscript describes a Mendelian randomization analysis of publicly available genome wide association study data to test the hypothesis that refractive error causes an increased risk of age-related macular degeneration. The analysis suggested that a one diopter more hyperopic refractive error caused an 8-10% increased risk of age-related macular degeneration, assuming a linear relationship. Thus, past studies reporting large risks due to refractive error may have been subject to confounding bias.

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• **94 Comparison of endothelial keratoplasty techniques in patients with prior glaucoma surgery: a case-matched study.** *Shawn R. Lin, Pitchaya Prapaipanich, Fei Yu, Simon K. Law, Joseph Caprioli, Anthony J. Aldave, and Sophie X. Deng*

Descemet membrane endothelial keratoplasty (DMEK) resulted in faster and better visual recovery and a lower rate of secondary graft failure than Descemet's stripping endothelial keratoplasty (DSEK) in eyes that had previously had glaucoma surgery.

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• **102 Ultra-widefield optical coherence tomographic imaging of posterior vitreous in eyes with high myopia.** *Hiroyuki Takahashi, Noriko Tanaka, Kosei Shinohara, Tae Yokoi, Takeshi Yoshida, Kengo Uramoto, and Kyoko Ohno-Matsui*

Ultra-widefield optical coherence tomographic images were obtained from 768 highly myopic eyes of patients

50-89 years of age and 54 control subjects. Widefield images of the posterior vitreous were obtained from 167 of these eyes, and they showed asymmetrical posterior vitreous detachments associated with scleral deformity. The vitreous was found to be adherent to the retinal vessels that led to myopic traction maculopathy.

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• **132 The diagnostic utility of multifocal electroretinography in detecting chloroquine and hydroxychloroquine retinal toxicity.** *Adrian C. Tsang, Sina Ahmadi, John Hamilton, Jennifer Gao, Gianni Virgili, Stuart G. Coupland, and Chloe C. Gottlieb*

This cross-sectional study examines the use of multifocal electroretinography (mfERG) for the detection of chloroquine and hydroxychloroquine retinal toxicity. mfERG was found to have a sensitivity of 1.00 and specificity of 0.78 when compared against the 2016 American Academy of Ophthalmology guidelines for toxicity. Objective measurement of parafoveal depression with mfERG may detect physiologic dysfunction before structural changes are detected by spectral domain optical coherence tomography.

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• **140 Risk of rhegmatogenous retinal detachment in acute retinal necrosis with and without prophylactic intervention.** *Sara Risseuw, Joke H. de Boer, Ninette H. ten Dam – van Loon, and Redmer van Leeuwen*

In this analysis of 63 eyes with acute retinal necrosis treated in a large tertiary referral center, 44.4% developed a rhegmatogenous retinal detachment, including 13% at presentation. No difference was observed in incidence between patients with and without prophylactic laser or vitrectomy, also when correcting for severity of disease. These results do not suggest a benefit of the commonly used practice of prophylactic laser for acute retinal necrosis.

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- **149 Utility of screening investigations for systemic sarcoidosis in undifferentiated uveitis.** *Rachael L. Niederer and Joanne L. Sims*

In undifferentiated uveitis, chest CT and chest radiograph offer the highest sensitivity and specificity for diagnosis of systemic sarcoidosis. However, no single test captured all cases, and serum ACE and lymphopenia remain clinically useful. Biopsy of skin lesions may detect patients otherwise missed by routine screening tests.

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- **154 Distribution of nonperfusion and neovascularization on ultrawide-field fluorescein angiography in proliferative diabetic retinopathy (recovery study): report 1.** *Wenyang Fan, Muneeswar Gupta Nittala, Swetha B. Velaga, Takao Hirano, Charles C. Wykoff, Michael Ip, Shaun I.R. Lampen, Jano van Hemert, Alan Fleming, Michael Verhoek, and Srinivas R. Sadda*

In eyes with early proliferative diabetic retinopathy, retinal nonperfusion appears to increase with increasing distance from the fovea. Eyes that develop neovascularization on optic disc appear to have more severe overall ischemia compared with eyes that do not. Neovascularization elsewhere appears to develop more commonly in the posterior polar retina compared to more peripheral regions, and the topographic distribution of neovascularization elsewhere appears to be influenced by factors other than ischemia alone.

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- **161 Time requirements of paper-based clinical workflows and after-hours documentation in a multispecialty academic ophthalmology practice.** *Sally L. Baxter, Helena E. Gali, Abigail E. Huang, Marlene Millen, Robert El-Kareh, Eric Nudleman, Shira L. Robbins, Christopher W.D. Heichel, Andrew S. Camp, Bobby S. Korn, Jeffrey E. Lee, Don O. Kikkawa, Christopher A. Longhurst, Michael F. Chiang, Michelle R. Hribar, and Lucila Ohno-Machado*

Electronic health records have become widespread, but baseline data regarding time requirements of paper-based workflows in ophthalmology are scarce. This is a time-and-motion study, and a structured survey of ophthalmologists aimed at better understanding these time requirements. Paper-based documentation consisted of a substantial portion of the total time spent for each patient encounter but was associated with minimal after-hours work. Understanding paper-based clinical workflows may help inform targeted strategies for improving electronic health record use in ophthalmology.

- 
- **168 Visual impairment and spectacle use in university students in central China: The Anyang University Students Eye Study.** *Shifei Wei, Yunyun Sun, Shi-Ming Li, Jianping Hu, Kai Cao, Jialing Du, Wenzai An, Xintong Liang, Jiyuan Guo, He Li, and Ningli Wang*

This is the first large-scale study to provide visual impairment and spectacle use data among university students in mainland China. This study reveals a relatively high prevalence of visual impairment and relatively low use of spectacles in Chinese university students. Given the potential impact of visual impairment, target education and accessible refraction services are highly important to solve the problem.

- 
- **176 Aqueous humor cytokines and long-term response to anti-vascular endothelial growth factor therapy in diabetic macular edema.** *Tina Felfeli, Verena R. Juncal, Roxane J. Hillier, Michael Y.K. Mak, David T. Wong, Alan R. Berger, Radha P. Kohly, Peter J. Kertes, Kenneth T. Eng, Shelley R. Boyd, Filiberto Altomare, Louis R. Giavedoni, and Rajeev H. Muni*

Aqueous humor vascular endothelial growth factor concentration after 2 intravitreal ranibizumab injections serves as a biomarker for long-term response to anti-vascular endothelial growth factor therapy and may enable

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more effective treatment regimens in eyes with diabetic macular edema.

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- **184 The ocular phenotype in primary hyperoxaluria type 1.** Johannes Birtel, Philipp Herrmann, Sander F. Garrelfs, Simon Dulz, Yevgeniya Atiskova, Roselie M. Diederer, Martin Gliem, Florian Brinkert, Frank G. Holz, Camiel J.F. Boon, Bernd Hoppe, and Peter Charbel Issa

In a cohort of 68 patients with primary hyperoxaluria type 1 (PH1), severe ocular alterations were identified in infantile PH1. In contrast, non-infantile patients showed mild or no ocular alterations. The natural history of (sub) retinal oxalate deposits, the pathogenesis of subretinal fibrosis, and the exact factors influencing the overall severity of ocular disease manifestation remain to be determined.

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- **228 A model to predict postoperative axial length in children undergoing bilateral cataract surgery with primary intraocular lens implantation.** Rupal H. Trivedi, Eliza Barnwell, Bethany Wolf, and M. Edward Wilson

For children undergoing bilateral cataract surgery with primary IOL implantation above 2 years of age, a model was created to estimate postoperative axial length based on preoperative axial length and age.

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- **235 Postconcussion: receded near point of convergence is not diagnostic of convergence insufficiency.** Apama Raghuram, Susan A. Cotter, Sowjanya Gowrisankaran, Jameel Kanji, David R. Howell, William P. Meehan III, and Ankoor S. Shah

Near point of convergence (NPC) is a popular screening test for detecting oculomotor disorders in patients after concussion, and it is often assumed that patients with receded NPC have convergence insufficiency. In our study, although nearly all (89%) of our cohort of young patients with chronic postconcussion symptoms had receded NPCs, it was not necessarily diagnostic of convergence

insufficiency. Many other oculomotor disorders were diagnosed; disorders of accommodation were the most prevalent.

- 
- **245 Genetic correlations between diabetes and glaucoma: An analysis of continuous and dichotomous phenotypes.** Vincent Laville, Jae H. Kang, Clara C. Cousins, Adriana I. Iglesias, Réka Nagy, Jessica N. Cooke Bailey, Robert P. Igo Jr, Yeunjoon E. Song, Daniel I. Chasman, William G. Christen, Peter Kraft, Bernard A. Rosner, Frank Hu, James F. Wilson, Puya Gharahkhani, Alex W. Hewitt, David A. Mackey, Pirro G. Hysi, Christopher J. Hammond, Cornelia M. vanDuijn, Jonathan L. Haines, Veronique Vitart, John H. Fingert, Michael A. Hauser, Hugues Aschard, Janey L. Wiggs, Anthony P. Khawaja, Stuart MacGregor, and Louis R. Pasquale, and the UK Biobank, International Glaucoma Genetics Consortium, and the Neighborhood Consortium

This study explores genetic correlations between diabetes- and glaucoma-related traits. While quantitative glaucoma traits were genetically correlated with primary open-angle glaucoma, none of the diabetes-related traits exhibited genetic correlation with any glaucoma-related trait. Research should focus on non-genetic factors, such as direct effects of diabetes on the trabecular meshwork and the optic nerve, as potential sources of a link between diabetes and glaucoma.

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- **256 Telemetric intraocular pressure monitoring after boston keratoprosthesis surgery using the eyemate-IO sensor: dynamics in the first year.** Philip Enders, Jonathan Hall, Marco Bornhauser, Kaweh Mansouri, Lebriz Altay, Stefan Schrader, Thomas S. Dietlein, Bjoern O. Bachmann, Thomas Neuhann, and Claus Cursiefen

This analysis of a prospective, open-label, multicenter, single-arm clinical trial aimed to analyse the dynamics of telemetrically measured intraocular pressure (IOP) with the EYEMATE-IO sensor system during the first year after

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implantation of a Boston Keratoprosthesis Type I in a cohort of twelve patients at two clinical centers in Germany.

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- **264 Retinal and choroidal optical coherence tomography findings of carotid cavernous fistula.** *Onur Inam, Yonca Ozkan Arat, Guliz Fatma Yavas, and Anil Arat*

In this first study investigating choroidal vascularity (CVI) and tortuosity indices (TIs) in carotid cavernous fistulas (CCFs), we demonstrated increased subfoveal choroidal thickness, CVI, and TI in CCFs with anterior drainage by spectral domain enhanced-depth imaging optical coherence tomography (SD-EDI-OCT). These parameters are candidates to be both evaluative and diagnostic tools for the patients with CCFs and may also provide guidance during follow-up.

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### AOS THESIS ARTICLES

- **17 Use of high-resolution optical coherence tomography in the surgical management of ocular surface squamous neoplasia: a pilot study.** *Carol L. Karp, Carolina Mercado, Nandini Venkateswaran, Marco Ruggeri, Anat Galor, Armando Garcia, Kavitha R. Sivaraman, Maria Paula Fernandez, Antonio Bermudez, and Sander R. Dubovy*

This pilot study demonstrated that a commercially available high-resolution optical coherence tomography (HR-OCT) device could successfully identify tumor margins as confirmed by histopathology in cases of ocular surface squamous neoplasia (OSSN). Optical identification of tumor borders could potentially decrease the incidence of residual positive margins and minimize healthy tissue removal. Advances in HR-OCT technology and integration into an intraoperative microscope for “real-time” imaging

could further improve this technique for the surgical excision of OSSN.

- 
- **40 An association between large optic nerve cupping and cognitive function.** *Thasarat Sutabutr Vajaranant, Joelle Hallak, Mark A. Espeland, Louis R. Pasquale, Barbara E. Klein, Stacy M. Meuer, Stephen R. Rapp, Mary N. Haan, and Pauline M. Maki*

This secondary data analysis of the Women’s Health Initiative (WHI), a randomized hormone trial, examined the relationship between large cup-to-disc ratio, defined as greater than 0.6 in either eye based on stereoscopic optic nerve photographs and global cognitive function assessed by Modified Mini-Mental State Examination (3MSE). Based on analyses including 1636 predominately white women, postmenopausal women who had large cup-to-disc ratio without glaucoma or ocular hypertension exhibited lower global cognitive function. Further investigation is warranted.

- 
- **48 Patterns and risk factor profiles of visual loss in a multiethnic Asian population: the Singapore Epidemiology of Eye Diseases study.** *Tien Y. Wong, Yih-Chung Tham, Charumathi Sabanayagam, and Ching-Yu Cheng*

In this urban multi-ethnic Asian population-based study of 10,020 participants in Singapore, we identified common traits associated with visual loss across Malays, Indians and Chinese. These data may be useful for the planning and designing of eye health services and strategies for Asia’s growing population who are increasingly living in rapidly developing urban communities.

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- **113 The role of FGF9 in the production of neural retina and RPE in a pluripotent stem cell model of early human retinal development.** *David M. Gamm, Eric Clark, Elizabeth E. Capowski, and Ruchira Singh*

FGFs play important roles in early neural development. Herein we examined expression patterns of FGFs during

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early human retinal differentiation using iPS cells derived from a normal individual and a sibling harboring a gene mutation that shifts production of neural retina to RPE. We found that exogenous FGF9 could partially reverse this phenotype, which in turn offers insight into the complex interplay among multiple factors in the establishment of the neural retina and RPE domains.

- 
- **192 Twelve-year incidence and baseline risk factors for pseudoexfoliation: the Thessaloniki Eye Study (An American Ophthalmological Society Thesis).** Fotis Topouzis, Panayiota Founti, Fei Yu, M. Roy Wilson, and Anne L. Coleman

The Thessaloniki Eye Study is one of the very few longitudinal population-based studies worldwide on the incidence of pseudoexfoliation (PEX). This study investigates: (1) the 12-year incidence of PEX and its characteristics,

(2) baseline factors associated with the development of PEX, (3) whether baseline PEX increases the risk of major cardiovascular diseases, and (4) baseline factors associated with the development of pseudoexfoliative glaucoma among those with PEX, in a well-defined elderly white population.

- 
- **217 Improved macular capillary flow on optical coherence tomography angiography after panretinal photocoagulation for proliferative diabetic retinopathy.** Amani A. Fawzi, Alaa E. Fayed, Robert A. Linsenmeier, Jing Gao, and Fei Yu

Using OCT angiography, this study shows that macular blood flow improves following pan-retinal photocoagulation in eyes with high risk proliferative diabetic retinopathy, a result that is confirmed by mathematical modeling.

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### EDITORIAL OFFICE

SARAH L. DUNCAN POWERS, *Managing Editor*

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