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WIDEFIELD SWEPT-SOURCE OCT ANGIOGRAPHY METRICS ASSOCIATED WITH THE DEVELOPMENT OF DIABETIC VITREOUS HEMORRHAGE: A PROSPECTIVE STUDY.

Cui Y, Zhu Y, Lu ES, Le R, Laíns I, Katz R, Wang JC, et al.Ophthalmology. 2021 Sep;128(9):1312-1324. doi: 10.1016/j.ophtha.2021.02.020.
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ABSTRACT

Purpose: To investigate the association among widefield swept-source (SS) OCT angiography (OCTA) metrics and systemic parameters and vitreous hemorrhage (VH) occurrence in eyes with proliferative diabetic retinopathy (PDR).

Design: Prospective, observational study.

Participants: Fifty-five eyes from 45 adults with PDR, with no history of VH, followed up for at least 3 months.

Methods: All patients underwent widefield SS OCTA (Montage 15 × 15 mm and high-definition (HD)-51 line scan) imaging. Images were evaluated independently by 2 graders for quantitative and qualitative widefield SS OCTA metrics defined a priori. Systemic and ocular parameters and widefield SS OCTA metrics were screened using least absolute shrinkage and selection operator and logistic or Cox regression for variable selection. Firth's bias-reduced logistic regression models (outcome, occurrence of VH) and Cox regression models (outcome, time to occurrence of VH) were used to identify parameters associated with VH occurrence.

Main outcome measures: Occurrence of VH.

Results: Over a median follow-up of 363 days (range, 28-710 days), 13 of 55 PDR eyes (24%) demonstrated VH during the follow-up period. Presence of extensive neovascularizations (odds ratio, 8.05; 95% confidence interval [CI], 1.43-58.56;

P = 0.02), defined as neovascularizations with total area of more than 4 disc diameters, and forward neovascularizations (odds ratio, 5.42; 95% CI, 1.26-35.16; P = 0.02) that traversed the posterior hyaloid face into the vitreous were associated with the occurrence of VH. The presence of flat neovascularizations (odds ratio, 0.25; 95% CI, 0.04-1.01; P = 0.05) confined to the posterior hyaloid face was associated with a lower risk of VH with borderline significance. Similarly, presence of extensive neovascularizations (hazard ratio, 18.24; 95% CI, 3.51-119.47; P < 0.001) and forward neovascularizations (hazard ratio, 9.60; 95% CI, 2.07-68.08; P = 0.002) was associated significantly with time to development of VH.

Conclusions: Widefield SS OCTA is useful for evaluating neovascularizations and their relationship with the vitreous. The presence of forward and extensive neovascularizations was associated with the occurrence of VH in patients with PDR. Larger samples and longer follow-up are needed to verify the risk factors and imaging biomarkers for diabetic VH.

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THRESHOLD THICKNESS OF FOVEAL OUTER NUCLEAR LAYER ASSOCIATED WITH OUTCOMES OF PHOTODYNAMIC THERAPY IN CENTRAL SEROUS CHORIORETINOPATHY

Jia Yu , Xiaofeng Ye , Lei Li , Chunhui Jiang, Qing Chang , Gezhi Xu
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ABSTRACT

Objectives: To investigate the threshold thickness of the foveal outer nuclear layer (ONL) associated with favourable visual outcome after half-dose photodynamic therapy (PDT) in patients with central serous chorioretinopathy (CSC).

Methods: The CSC patients were divided into two groups according to whether their best-corrected visual acuity (BCVA) at 1 year after half-dose PDT was 20/20 or worse than 20/20. Three multivariable logistic regression models were respectively created to determine the prognostic value of the pre-PDT foveal ONL thickness, the pre- and the post-PDT foveal ONL thickness ratio, which was defined as the foveal ONL thickness in the CSC eye to that in the normal contralateral eye, for predicting the outcome of half-dose PDT. The areas under the receiver operating characteristic curves (AUCs) were compared and the best cut-off values were determined, respectively.

Results: Totally, 134 patients were included. The pre-PDT foveal ONL thickness, the pre-PDT and the post-PDT foveal ONL thickness ratios were all independent predictors of the outcome after half-dose PDT in their respective model (all $P < 0.05$). The AUC of the post-PDT foveal ONL thickness ratio was significantly higher than the AUCs of the other two parameters (0.940 vs 0.840 and 0.882, DeLong test: both $P < 0.05$), with the cut-off value of 0.81.

Conclusions: The threshold of the foveal ONL thickness ratio is 0.81. Active CSC eyes with a foveal ONL thickness ratio of 0.81 or more could probably retain BCVA of 20/20 after half-dose PDT. They were considered reasonable to wait for spontaneous resolution of sub-retinal fluid.

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FOUNDATIONAL CONSIDERATIONS FOR ARTIFICIAL INTELLIGENCE UTILIZING OPHTHALMIC IMAGES

Michael D Abramoff , Brad Cunningham , Bakul Patel , Malvina B Eydelman , Theodore Leng , Collaborative Community on Ophthalmic Imaging Executive Committee and Foundational Principles of Ophthalmic Imaging and Algorithmic Interpretation Working Group

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ABSTRACT

Importance: The development of Artificial Intelligence (AI) and other machine diagnostic systems, also known as Software as a Medical Device (SaMD), and its recent introduction into clinical practice, requires a deeply-rooted foundation in bioethics, for consideration by regulatory agencies and other stakeholders around the globe.

Objectives: Initiate a dialogue on the issues to consider when developing a bioethically sound foundation for AI in medicine, based on images of eye structures, for discussion with all stakeholders.

Evidence review: The scope of the issues and summaries of the discussions under consideration by the Foundational Principles of Ophthalmic Imaging and Algorithmic Interpretation Working Group, as first presented during the Collaborative Community on Ophthalmic Imaging inaugural meeting on September 7, 2020, and afterwards in the working group.

Findings: AI has the potential to fundamentally improve the access to healthcare and patient outcomes, while decreasing disparities, lowering cost, as well as enhancing the care team. Nevertheless, substantial concerns exist. Ethicists, AI algorithm experts, as well as the Food and Drug Administration (FDA) and other

regulatory agencies, industry, patient advocacy groups, clinicians and their professional societies, other provider groups, payors, and other healthcare stakeholders working together in collaborative communities to resolve such issues as non-maleficence, autonomy and equity, is essential to attain this potential, and impacts all levels of the design, validation and implementation of AI in medicine. Design, validation and implementation of AI warrant meticulous attention.

Conclusions and relevance: The development of a bioethically sound foundation may be possible if it is based in non-maleficence, autonomy and equity, for considerations for the design, validation and implementation for AI systems. Achieving such a foundation will be helpful for continuing successful introduction into medicine, before consideration by regulatory agencies around the globe. Fundamental improvements in accessibility and quality of healthcare, decrease in health disparities, and lower cost can thereby be achieved. These considerations should be discussed with all stakeholders and expanded upon as a useful initiation of this dialogue.

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STIMULATION OF α7 nAChR LEADS TO REGENERATION OF DAMAGED NEURONS IN ADULT MAMMALIAN RETINAL DISEASE MODEL

Sarah E Webster , Nathan C Sklar , Jake B Spitsbergen , Megan L Stanchfield , Mark K Webster , David M Linn , et al.

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ABSTRACT

The adult mammal lacks the ability to regenerate neurons lost to retinal damage or disease in a meaningful capacity. However, previous studies from this laboratory have demonstrated that PNU-282987, an α7 nicotinic acetylcholine receptor agonist, elicits a robust neurogenic response in the adult murine retina. With eye drop application of PNU-282987, Müller glia cells re-enter the cell cycle and produce progenitor-like cells that can differentiate into various types of retinal neurons. In this study, we analyzed the regenerative capability of PNU-282987 in two retinal disease models and identified the source of newly regenerated neurons. Wild-type mice and mice with a transgenic Müller-glia lineage tracer were manipulated to mimic loss of retinal cells associated with glaucoma or photoreceptor degeneration. Following treatment with PNU-282987, the regenerative response of retinal neurons was quantified and characterized. After onset of photoreceptor degeneration, PNU-282987 was able to successfully regenerate both rod and cone photoreceptors. Quantification of this response demonstrated significant regeneration, restoring photoreceptors to near wild-type density. In mice that had glaucoma-like conditions induced, PNU-282987 treatment led to a significant increase in retinal ganglion cells. Retrograde labeling of optic nerve axon fibers demonstrated that newly regenerated axons projected into the optic nerve.

Lineage tracing analysis demonstrated that these new neurons were derived from Müller glia. These results demonstrate that PNU-282987 can induce retinal regeneration in adult mice following onset of retinal damage. The ability of PNU-282987 to regenerate retinal neurons in a robust manner offers a new direction for developing novel and potentially transformative treatments to combat neurodegenerative disease.

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ROLE OF SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY IN THE DIAGNOSIS AND PROGNOSIS OF PAPILLEDEMA

Panyala, Rakesh; Sharma, Pradeep,; Sihota, Ramanjit; Saxena, Rohit; Prasad, Kameshwar; Phuljhele, Swati; et al.

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PMID: 34427225

ABSTRACT

Purpose: The study of papilledema with a novel noninvasive technique such as spectral domain-optical coherence tomography (SD-OCT) provides minute and detailed cross-sectional changes thus giving an insight into the application of biomechanical principles and pathophysiology of disc edema.

Methods: We measured average retinal nerve fiber layer (RNFL) thickness and the retinal pigment epithelium/Bruch's membrane (RPE/BM) angle at the temporal and nasal borders of the neural canal opening (NCO) in 30 eyes with papilledema, 30 eyes with papillitis, and 80 control eyes. The inward angulation was considered as positive and the outward as negative. Follow-up was done at 1, 2, 3, and 6 months. The main outcome measures are the average RNFL thickness and the RPE/BM angle.

Results: 29 eyes (96.6%) with papilledema had a positive RPE/BM angle (+8.11 ± 3.13). 29 eyes (96.6%) with papillitis had a negative RPE/BM angle (−1.04 ± 3.27). On follow-up at 1 month, both RNFL thickness (P = 0.01) and RPE-BM angle (P = 0.001) reduced significantly in eyes with papilledema; in eyes with papillitis, there was a significant reduction in the RNFL thickness (P = 0.02), but not in the RPE-BM angle (P > 0.05). RNFL thickness in papilledema cases

normalized at 3 months whereas RPE/BM normalized at 6 months of follow-up. To detect papilledema, OCT has a sensitivity of 96.66% and specificity of 99.09% on both nasal and temporal sides.

Conclusion: After appropriate treatment, the RPE/BM angle in papilledema decreased much later than the RNFL thickness. Hence, the RPE/BM angle in papilledema (positive) can be used to differentiate it from papillitis (negative) and also to monitor the activity of the disease.

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HEALTH- AND VISION-RELATED QUALITY OF LIFE IN A RANDOMIZED CONTROLLED TRIAL COMPARING METHOTREXATE AND MYCOPHENOLATE MOFETIL FOR UVEITIS

Kelly NK, Chattopadhyay A, Rathinam SR, Gonzales JA, Thundikandy R, Vedhanayaki R et al

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ABSTRACT

Purpose: To evaluate changes in health-related and vision-related quality of life (VRQoL) among patients with noninfectious uveitis who were treated with antimetabolites.

Design: Secondary analysis of a randomized controlled trial.

Participants: Patients with noninfectious uveitis from India, the United States, Australia, Saudi Arabia, and Mexico.

Methods: From 2013 through 2017, 216 participants were randomized to receive 25 mg weekly oral methotrexate or 1.5 g twice daily oral mycophenolate mofetil. Median changes in quality of life (QoL) were measured using Wilcoxon signed-rank tests, and differences between treatment groups were measured using linear mixed models, adjusting for baseline QoL score, age, gender, and site. Among Indian patients, VRQoL scores from a general scale (the National Eye Institute Visual Function Questionnaire [NEI-VFQ]) and a culturally specific scale (the Indian Visual Function Questionnaire [IND-VFQ]) were compared using Pearson correlation tests.

Main outcome measures: Vision-related QoL (NEI-VFQ and IND-VFQ) and health-related QoL (HRQoL; physical component score [PCS] and mental component score [MCS] of the Medical Outcomes Study 36-Item Short Form

Survey [SF-36v2]) were measured at baseline, the primary end point (6 months or treatment failure before 6 months), and the secondary end point (12 months or treatment failure between 6 and 12 months).

Results: Among 193 participants who reached the primary end point, VRQoL increased from baseline by a median of 12.0 points (interquartile range [IQR], 1.0-26.1, NEI-VFQ scale), physical HRQoL increased by a median of 3.6 points (IQR, -1.4 to 14.9, PCS SF-36v2), and mental HRQoL increased by a median of 3.0 points (IQR, -3.7 to 11.9, MCS SF-36v2). These improvements in NEI-VFQ, SF-36v2 PCS, and SF-36v2 MCS scores all were significant ($P < 0.01$). The linear mixed models showed that QoL did not differ between treatment groups for each QoL assessment (NEI-VFQ, IND-VFQ, PCS SF-36v2, and MCS SF-36v2; $P > 0.05$ for all). The NEI-VFQ and IND-VFQ scores for Indian participants were correlated highly at baseline and the primary and secondary end points (correlation coefficients, 0.87, 0.80, and 0.90, respectively).

Conclusions: Among patients treated with methotrexate or mycophenolate mofetil for uveitis, VRQoL and HRQoL improved significantly over the course of 1 year and did not differ by treatment allocation. These findings suggest that antimetabolites could improve overall patient well-being and daily functioning.

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MULTIFOCAL ELECTRORETINOGRAPHY-ASSISTED ANATOMICAL AND FUNCTIONAL EVALUATION OF SUBTHRESHOLD GREEN LASER IN ACUTE CENTRAL SEROUS CHORIORETINOPATHY

Goel, Neha; Mehta, Aanchal; Gupta, A K

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ABSTRACT

Purpose: To compare observation versus subthreshold green laser (STL) in acute central serous chorioretinopathy (CSC) in terms of anatomical and functional outcomes.

Methods: Prospective randomized interventional study. 30 eyes with the first episode of acute CSC underwent complete ophthalmologic examination, measurement of best-corrected Snellen visual acuity (BCVA), contrast sensitivity (CS), fundus fluorescein angiography (FFA), spectral-domain optical coherence tomography (SD-OCT), and multifocal electroretinography (mfERG) at baseline. Patients were randomized equally to group A (observation) or group B (STL using 532 nm wavelength applied to the leakage point). Outcome measures included BCVA, CS, central foveal thickness (CFT), and mean macular thickness (MMT) on SD-OCT and P1 amplitude and implicit time (IT) on mfERG. Patients were followed up for 6 months.

Results: Mean BCVA was comparable between the two groups on follow up; however, mean CS was significantly higher in group B at 6 months (P = 0.032). CFT was significantly lower in group B at 1 month (P = 0.001) and 3 months (P = 0.049); however, this difference was not maintained at 6 months (P = 0.265). P1 amplitude and IT in all 5 rings were comparable between the two groups at

baseline. On follow up, P1 amplitude of ring 1 became significantly higher in group B at 3 months (*P* = 0.036) and 6 months (*P* = 0.022).

Conclusion: Immediate treatment of acute CSC with STL, as compared to conservative management, leads to more rapid resolution on SD-OCT and superior functional outcomes as evidenced by CS and mfERG.

Compiled by Dr.Aditya Maitray, Aravind Eye Hospital, Chennai