

## Retina Roundup

February 2020

## Quantitative optical coherence tomography angiography features for objective classification and staging of diabetic retinopathy.

Alam M, Zhang Y, Lim JI, Chan RVP, Yang M, Yao X

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PMID: 31972803

#### **ABSTRACT**

#### **PURPOSE:**

This study aims to characterize quantitative optical coherence tomography angiography (OCTA) features of nonproliferative diabetic retinopathy (NPDR) and to validate them for computer-aided NPDR staging.

#### **METHODS:**

Forty eyes of 29 patients with treatment-naïve center-involved macular edema secondary to diabetes mellitus were included (The DAVE study, NCT01552408) in this analysis. Ultrawidefield fluorescein angiography (UWF FA) images were transmitted to the Doheny Image Reading Center, where they were corrected using stereographic projection to adjust for peripheral distortion. Two independent, certified graders manually evaluated the NPR and classified the nonperfusion as being associated with leakage, or without leakage. The size of these two subtypes of NPR were computed in mm2 and assessed across the entire retina and within three concentric retinal zones. The relationship between subtype of NPR and the severity of DME was assessed.

#### **RESULTS:**

Among 6 individual OCTA features, blood vessel density shows the best classification accuracies, 93.89% and 90.89% for control versus disease and control versus mild NPDR, respectively. Combined feature classification achieved improved accuracies, 94.41% and 92.96%, respectively. Moreover, the temporal-perifoveal region was the most sensitive region for early detection of DR. For multiclass classification, support vector machine algorithm achieved 84% accuracy.

#### **CONCLUSION:**

Blood vessel density was observed as the most sensitive feature, and temporal-perifoveal region was the most sensitive region for early detection of DR. Quantitative OCTA analysis enabled computer-aided identification and staging of NPDR.

# Validation of Deep Convolutional Neural Network-based algorithm for detection of diabetic retinopathy - Artificial intelligence versus clinician for screening.

Shah P, Mishra DK, Shanmugam MP, Doshi B, Jayaraj H, Ramanjulu R

Indian J Ophthalmol. 2020 Feb;68(2):398-405. doi: 10.4103/ijo.IJO 966 19.

PMID: 31957737

#### **ABSTRACT**

#### **PURPOSE:**

Deep learning is a newer and advanced subfield in artificial intelligence (AI). The aim of our study is to validate a machine-based algorithm developed based on deep convolutional neural networks as a tool for screening to detect referable diabetic retinopathy (DR).

#### **DESIGN:**

Retrospective interventional case series and cost comparison.

#### **METHODS:**

An AI algorithm to detect DR was validated at our hospital using an internal dataset consisting of 1,533 macula-centered fundus images collected retrospectively and an external validation set using Methods to Evaluate Segmentation and Indexing Techniques in the field of Retinal Ophthalmology (MESSIDOR) dataset. Images were graded by two retina specialists as any DR, prompt referral (moderate nonproliferative diabetic retinopathy (NPDR) or above or presence of macular edema) and sight-threatening DR/STDR (severe NPDR or above) and compared with AI results. Sensitivity, specificity, and area under curve (AUC) for both internal and external validation sets for any DR detection, prompt referral, and STDR were calculated. Interobserver agreement using kappa value was calculated for both the sets and two out of three agreements for DR grading was considered as ground truth to compare with AI results.

#### MAIN OUTCOME MEASURES:

Characteristics associated with best-corrected visual acuity (BCVA) and anatomic outcomes. Cost analysis and potential cost savings comparing PR to scleral buckle and vitrectomy.

#### **RESULTS:**

In the internal validation set, the overall sensitivity and specificity was 99.7% and 98.5% for Any DR detection and 98.9% and 94.84% for Prompt referral respectively. The AUC was 0.991 and 0.969 for any DR detection and prompt referral respectively. The agreement between two

observers was 99.5% and 99.2% for any DR detection and prompt referral with a kappa value of 0.94 and 0.96, respectively. In the external validation set (MESSIDOR 1), the overall sensitivity and specificity was 90.4% and 91.0% for any DR detection and 94.7% and 97.4% for prompt referral, respectively. The AUC was. 907 and. 960 for any DR detection and prompt referral, respectively. The agreement between two observers was 98.5% and 97.8% for any DR detection and prompt referral with a kappa value of 0.971 and 0.980, respectively.

#### **CONCLUSION:**

With increasing diabetic population and growing demand supply gap in trained resources, AI is the future for early identification of DR and reducing blindness. This can revolutionize telescreening in ophthalmology, especially where people do not have access to specialized health care.

#### **KEYWORDS:**

Deep convolutional neural networks; diabetic retinopathy screening; machine learning; validation of artificial intelligence.

# Medios- An offline, smartphone-based artificial intelligence algorithm for the diagnosis of diabetic retinopathy.

Sosale B, Sosale AR, Murthy H, Sengupta S, Naveenam M.

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#### **ABSTRACT**

#### **PURPOSE:**

An observational study to assess the sensitivity and specificity of the Medios smartphone-based offline deep learning artificial intelligence (AI) software to detect diabetic retinopathy (DR) compared with the image diagnosis of ophthalmologists

#### **METHODS:**

Patients attending the outpatient services of a tertiary center for diabetes care underwent 3-field dilated retinal imaging using the Remidio NM FOP 10. Two fellowship-trained vitreoretinal specialists separately graded anonymized images and a patient-level diagnosis was reached based on grading of the worse eye. The images were subjected to offline grading using the Medios integrated AI-based software on the same smartphone used to acquire images. The sensitivity and specificity of the AI in detecting referable DR (moderate non-proliferative DR (NPDR) or worse disease) was compared to the gold standard diagnosis of the retina specialists.

#### **RESULTS:**

Results include analysis of images from 297 patients of which 176 (59.2%) had no DR, 35 (11.7%) had mild NPDR, 41 (13.8%) had moderate NPDR, and 33 (11.1%) had severe NPDR. In addition, 12 (4%) patients had PDR and 36 (20.4%) had macular edema. Sensitivity and specificity of the AI in detecting referable DR was 98.84% (95% confidence interval [CI], 97.62-100%) and 86.73% (95% CI, 82.87-90.59%), respectively. The area under the curve was 0.92. The sensitivity for vision-threatening DR (VTDR) was 100%.

#### **CONCLUSION:**

The AI-based software had high sensitivity and specificity in detecting referable DR. Integration with the smartphone-based fundus camera with offline image grading has the potential for widespread applications in resource-poor settings.

# The Comparison of the Surgical Outcome Of 27-Gauge Pars Plana Vitrectomy for Primary Rhegmatogenous Retinal Detachment between Air and SF6 Gas Tamponade.

Tetsumoto A, Imai H, Hayashida M, Otsuka K, Matsumiya W, Miki A, Nakamura M.

Eye (Lond). 2020 Feb;34(2):299-306. doi: 10.1038/s41433-019-0726-2. Epub 2019 Dec 20.

PMID: 31857712

#### **ABSTRACT**

#### **BACKGROUND**:

To compare the surgical results between air and 20% sulfur hexafluoride (SF6) tamponade in 27- gauge pars plana vitrectomy (27GPPV) for rhegmatogenous retinal detachment (RRD).

#### **METHODS:**

A retrospective, observational, and consecutive study. All patients underwent 27GPPV for RRD were divided into two groups. Group A comprised patients who underwent 20% SF6 gas tamponade. Group B comprised patients who underwent air tamponade. The anatomical success rate, visual outcome, and the type and frequency of complications were investigated and compared between the groups. All patients were followed-up for 12 months after surgery.

#### **RESULTS:**

Seventy eyes were enrolled (Group A: 35 eyes, Group B: 35 eyes). Seventeen eyes in Group A and 13 eyes in Group B had RRD with superior retinal breaks, while 14 eyes in Group A and 19 eyes in Group B had RRD with inferior retinal breaks. There was no statistically difference in preoperative demographic date between the groups. The initial and final anatomical success rates were 97.1% and 100% in Group A and 94.3% and 100% in Group B, respectively. The success rates between the groups were not statistically different (p=1). The best corrected visual acuity (BCVA) (logMAR) at 12 months after surgery was  $-0.02 \pm 0.14$  in Group A and  $-0.03 \pm 0.27$  in Group B. The BCVA between the groups was not statistically different (p=0.27).

#### **CONCLUSION:**

The surgical results of air tamponade were not inferior to 20% SF6 tamponade in 27GPPV for RRD irrespective of retinal break locations in the present cohort.

# Age-Related Changes in Choroidal Thickness and the Volume of Vessels and Stroma Using Swept-Source OCT and Fully Automated Algorithms.

Zhou H, Dai Y, Shi Y, Russell J, Lyu C, Noorikolouri J, Feuer WJ, Chu Z, Zhang Q, de Sisternes L, Durbin MK, Gregori G, Rosenfeld PJ, Wang RK

Ophthalmology Retina , Volume 4, Issue 2, 204 – 215. DOI: https://doi.org/10.1016/j.oret.2019.09.012

PMID: 32033714

#### **ABSTRACT**

#### **PURPOSE:**

To determine age-related changes in choroidal thickness and the volume of choroidal vessels and stroma using automated algorithms based on structural swept-source OCT (SS-OCT) scans.

#### **DESIGN:**

Prospective and observational study.

#### **PARTICIPANTS:**

The study included 144 normal participants with ages ranging from 20 to 88 years.

#### **METHODS:**

A previously reported strategy was used to automatically segment the choroid using SS-OCT structural images. Attenuation correction was applied on B-scans to enhance the choroidal contrast and facilitate more accurate automatic segmentation of the 3-dimensional choroidal vessel and stroma. The parameters that we investigated included mean choroidal thickness (MCT), choroidal vessel volume (CVV), choroidal stroma volume (CSV), choroid vascularity index (CVI), and the choroidal stroma-to-vessel volume ratio (CSVR). Correlations between MCT and choroidal vessel metrics of CVV, CSV, CVI, and CSVR were studied. Regional distributions of MCT and CVI were analyzed using a grid centered on the fovea. Age-related changes in MCT, CVV, CSV, and CVI were studied in the entire scanning region, as well as in the subregions of the grids.

#### **MAIN OUTCOME MEASURES:**

Age-related changes in MCT, CVV, CSV, and CVI using 6×6-mm and 12×12-mm SS-OCT scans.

#### **RESULTS:**

The automated choroid segmentations were validated against manual segmentations, and MCT measurements were shown to be in good agreement (P < 0.0001). Choroidal vessel volume and CSV showed significant correlations with MCT (all P < 0.0001). Interestingly, CVI and CSVR were constant, with little variation among all participants regardless of age and MCT ( $61.1\pm1.8\%$  and  $0.64\pm0.05$ , respectively). Measurements on  $12\times12$ -mm and  $6\times6$ -mm scans showed excellent agreement in all scan regions (all P < 0.0001). While choroidal thickness and choroidal volume, which includes both choroidal vessels and stroma, decrease with age (all P < 0.0001), the CVI and CSVR vary little among all ages in all regions.

#### **CONCLUSIONS:**

Whereas MCT, CVV, and CSV decrease with age, the CVI and CSVR remain constant in all regions with age. Ongoing studies are using these automated algorithms on SS-OCT structural datasets to investigate the diagnostic usefulness of these choroidal parameters in a myriad of ocular and systemic diseases.

## **Complement C3 Inhibitor Pegcetacoplan for Geographic Atrophy Secondary to Age-Related Macular Degeneration**

Liao DS, Grossi FV, El Mehdi D, Gerber MR, Brown DM, Heier JS, Wykoff CC, Singerman LJ, Abraham P, Grassmann F8, Nuernberg P, Weber BHF0, Deschatelets P, Kim RY, Chung CY, Ribeiro RM, Hamdani M, Rosenfeld PJ, Boyer DS, Slakter JS, Francois CG.

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PMID: 31474439

#### **ABSTRACT**

#### **PURPOSE:**

Geographic atrophy (GA), a late stage of age-related macular degeneration (AMD), is a major cause of blindness. Even while central visual acuity remains relatively well preserved, GA often causes considerable compromise of visual function and quality of life. No treatment currently exists. We evaluated the safety and efficacy of pegcetacoplan, a complement C3 inhibitor, for treatment of GA.

#### **DESIGN**:

Prospective, multicenter, randomized, sham-controlled phase 2 study.

#### **PARTICIPANTS:**

Two hundred forty-six patients with GA.

#### **METHODS:**

Patients with GA were assigned randomly in a 2:2:1:1 ratio to receive intravitreal injections of 15 mg pegcetacoplan monthly or every other month (EOM) or sham intravitreal injections monthly or EOM for 12 months with follow-up at months 15 and 18. Area and growth of GA were measured using fundus autofluorescence imaging.

#### MAIN OUTCOMES AND MEASURES:

The primary efficacy end point was mean change in square root GA lesion area from baseline to month 12. Secondary outcome measures included mean change from baseline in GA lesion area without the square root transformation, distance of GA lesion from the fovea, best-corrected visual acuity (BCVA), low-luminance BCVA, and low-luminance visual acuity deficit. The primary safety end point was the number and severity of treatment-emergent adverse events.

#### **RESULTS:**

In patients receiving pegcetacoplan monthly or EOM, the GA growth rate was reduced by 29% (95% confidence interval [CI], 9–49; P = 0.008) and 20% (95% CI, 0–40; P = 0.067) compared with the sham treatment group. Post hoc analysis showed that the effect was greater in the second 6 months of treatment, with observed reductions of 45% (P = 0.0004) and 33% (P = 0.009) for pegcetacoplan monthly and EOM, respectively. Two cases of culture-positive endophthalmitis and 1 case of culture-negative endophthalmitis occurred in the pegcetacoplan monthly group. New-onset investigator-determined exudative AMD was reported more frequently in pegcetacoplan-treated eyes (18/86 eyes [20.9%] and 7/79 eyes [8.9%] in monthly and EOM groups, respectively) than in sham-treated eyes (1/81 eyes [1.2%]).

#### **CONCLUSION:**

Local C3 inhibition with pegcetacoplan resulted in statistically significant reductions in the growth of GA compared with sham treatment. Phase 3 studies will define the efficacy and safety profile further.

### **Etiologies, Characteristics, and Management of Pediatric Macular Hole.**

Liu J, Peng J, Zhang Q, Ma M, Zhang H, Zhao P.

American Journal of Ophthalmology, Volume 210, 174 – 183.DOI: https://doi.org/10.1016/j.ajo.2019.09.014

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#### **ABSTRACT**

#### **PURPOSE:**

To report on the etiologies and prognosis of macular hole (MH) in children and to explore the indicators of spontaneous hole closure and poor final visual outcome (vision worse than 20/200).

#### **DESIGN:**

Consecutive, retrospective case series.

#### **METHODS:**

A consecutive series of patients aged less than 16 years with a full-thickness macular hole treated from 2013 to 2019 in a singer tertiary center was retrospectively reviewed. Data collected from charts included age, sex, best-corrected visual acuity (BCVA), etiology of MH, size of MH, clinical findings, operations, and anatomic and functional outcomes. Logistic regression models were built to establish the predisposing factors.

#### **RESULTS:**

Forty eyes of 40 patients were included. Patients were predominantly male with a mean age of 8.3 years. Among the etiologies, trauma prevailed in 29 (72.5%) eyes. Twenty-nine patients underwent surgery, and 18 (62.1%) had traumatic MH. All had achieved hole closure. BCVA improved at the final visit. Spontaneous closure was found in 10 (25%) eyes after an average 2 months after trauma. Regression analysis showed that a relatively smaller macular hole (P = .006) was likely to experience spontaneous closure. Presence of macular lesions (P = .001) was identified as risk factor for poor final vision.

#### **CONCLUSION:**

Most pediatric MH was caused by blunt trauma. BCVA improved after MH closed, regardless of surgery or spontaneous closure. Smaller MH secondary to trauma was more likely to experience spontaneous closure with an average time of 2 months. Presence of macular lesions was a risk factor for final poor vision.

February Segment Compiled by: Dr. Indu Govindaraj, Aravind Eye Hospital, Chennai