Automated Diabetic Retinopathy Image Assessment Software: Study of Diagnostic Accuracy and Cost-Effectiveness of Available Systems

- Adnan Tufail, MBBS, MD, FRCOphth
- Alicja R. Rudnicka, BSc, MSc, PhD
- Paul Taylor, PhD
- Aaron Y. Lee, MD, MSCI
- Srinivas Reddy Sadda, MD
- Christopher Owen, PhD
- Catherine Egan, FRANZCO

OBJECTIVE To determine if available (CE marked) automated diabetic retinopathy image assessment software (ARIAS) can safely be introduced into diabetic retinopathy screening pathways to replace human graders.

PURPOSE With the increasing prevalence of diabetes, annual screening for diabetic retinopathy by expert human grading of retinal images is challenging. Computer analysis of retinal images may provide an effective and cost-effective detection of retinopathy. A study, independent of software developers, to evaluate the available ARIAS for diagnostic accuracy and cost-effectiveness was therefore undertaken.

METHODS Retinal images from 20,258 consecutive patients obtained as part of their routine annual diabetic eye check underwent in addition to standard manual assessment additional grading with each of the following three ARIA systems: iGradingM, Retmarker, and EyeArt. Discrepancies in grading were sent for arbitration to a reading center. Screening performance (sensitivity, false positive rate, likelihood ratios), and diagnostic accuracy (95% confidence intervals of screening performance measures) were determined. Secondary analysis explored the influence of patients' ethnicity, age, sex and camera on screening performance. Economic analysis estimated the cost per appropriate screening outcome.

RESULTS The sensitivity point estimates (95% confidence interval) of the ARIA systems are as follows: EyeArt 94.7% (94.2-95.2) for any retinopathy, 93.8% (92.9-94.6) for referable retinopathy (human graded as either
ungradable, maculopathy, preproliferative or proliferative) 99.6% (97.0-99.9) for proliferative retinopathy; Retmarker 73.0% (72.0-74.0) for any retinopathy, 85.0% (83.6-86.2) for referable retinopathy 97.9% (94.9-99.1) for proliferative retinopathy. iGradingM classified all images as either having disease or being ungradeable. EyeArt and Retmarker are cost saving compared to manual grading both as a replacement for Level 1 human grading, or as a filter prior to primary (Level 1) human grading, although the latter approach is less cost-effective.

CONCLUSION Retmarker and EyeArt achieved acceptable sensitivity for referable retinopathy when compared with human graders and had sufficient specificity to make them cost-effective alternatives to manual grading alone. ARIA systems have the potential to reduce costs in developed world healthcare economies and to aid delivery of diabetic retinopathy screening to developing or remote healthcare settings.

TAKE HOME MESSAGE The good sensitivity and acceptable specificity of two of the tested ARIAS (Retmarker, EyeArt) makes them potential alternatives to pure human grading for deployment in Diabetic Screening Pathways.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema: Two-Year Results from a Comparative Effectiveness Randomized Clinical Trial

- John A. Wells, MD, FACS

OBJECTIVE To report the relative gains in vision, reductions in DME as measured by OCT, and relative safety at 2 years in the treatment of center-involved DME with aflibercept, bevacizumab and ranibizuamb.

PURPOSE To provide 2-year efficacy, safety and treatment frequency results comparing three anti-vascular endothelial growth factor (anti-VEGF) agents for center-involved diabetic macular edema (DME) utilizing a standardized follow-up and retreatment regimen.

METHODS A randomized clinical trial of 660 eyes with center-involved DME causing visual acuity (VA) impairment. Eyes were randomized to 2.0-mg aflibercept, 1.25-mg repackaged (compounded) bevacizumab, or 0.3-mg ranibizumab intravitreous injections performed as frequently as monthly utilizing a protocol-specific follow-up and retreatment algorithm. At 6 months focal/grid laser was applied for persistent DME not improving from the previous 2 injections; laser could be repeated as often as every 13 weeks for persistent DME. Visits occurred every 4 weeks during year 1 but could be extended up to 4 months in the second year when VA and macular thickness were stable.

RESULTS Change in ETDRS VA letter score measured by protocol refraction, change in central subfield thickness (CST) measured by central macular OCT scans, re-treatment frequency including number of intravitreous injections and laser treatments, and ocular/systemic adverse events at 2 years will be presented. The 2 year data from Protocol T are embargoed at the time of the ASRS abstract submission deadline.

CONCLUSION One year results from this randomized clinical trial showed that in eyes with baseline vision of 20/32-20/40, the three agents were equally effective at improving vision, but in eyes with baseline vision 20/50 or worse, aflibercept was superior to the other two agents at improving vision. This report will present the two year relative efficacy, retreatment frequency and safety of the three agents.

TAKE HOME MESSAGE The Protocol T 2 year data remain under embargo at the time of the astract submission deadline so the take home message cannot be revealed.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

Automated Detection of Diabetic Retinopathy Lesions on Ultra-Widefield Pseudocolor Images

- Srinivas Reddy Sadda, MD
- Kang Wang, MD, PhD
- Chaitra Jayadev
- Muneeswar Nittala, MS
- Chaithanya Ramachandra, PhD

OBJECTIVE To develop an algorithm to automatically identify referral warranted retinopathy from ultrawidefield pseudocolor images.

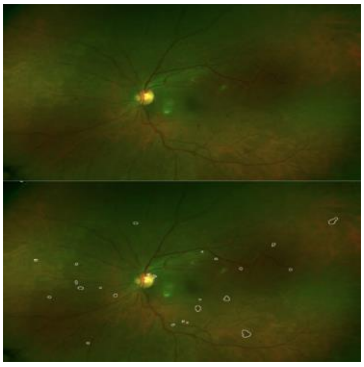
PURPOSE Peripheral lesions have been shown to be of prognostic significance in eyes with diabetic retinopathy (DR), raising interest in the use of ultrawidefield images for screening and staging DR. In this study, we sought to determine the sensitivity and specificity of an automated algorithm for detecting referral-warranted DR in Optos ultrawidefield (UWF) pseudocolor images.

METHODS A total of 383 diabetic subjects (739 eyes) were enrolled (IRB-approved) from the Narayana Nethralaya eye clincis and a total of 1661 UWF pseudocolor images (Optos Daytona) were obtained, and graded for referral warranted diabetic retinopathy (moderate NPDR or higher). Fifty percent of the images were then used to train the classifiers in the automated algorithm (a modified version of the EyeArt automated diabetic retinopathy software that has been validated for standard flash color images). The other half of the dataset was used to assess system performance. Sensitivity and specificity of the referral classification were computed at both the “patient level” and the “eye level”.

RESULTS The software automatically detected DR lesions (hemorrhages, microaneurysms, lipid exudates, cotton wool spots) using the previously trained classifiers, and classified each image in the test set as “referral warranted” or “not warranted.” The top figure shows a cropped UWF image of an eye with diabetic retinoparhy, and the bottom figure shows the intraretinal hemorrhages automatically identified by the algorithm. For detection of referral warranted retinopathy in either eye (“patient level”), the automated algorithm achieved a 90.0% sensitivity (95% CI 88.1-91.8) with a 49.1% specificity (95% CI 34.3 – 73.0), with an AUROC (Area under Receiver Operating Curve) of 0.850 (95% CI 0.783 - 0.904). For detection of referral warranted retinopathy for each eye (“eye level”), the automated algorithm achieved a 90.0% sensitivity (95% CI 88.8- 91.1) with a 35.7% specificity (95% CI 25.2 – 54.8), with an AUROC (Area under Receiver Operating Curve) of 0.803 (95% CI 0.751 - 0.853).

CONCLUSION DR lesions could be detected from Optos UWF images using a commercial automated algorithm, and referral warranted diabetic retinopathy could be identified with good sensitivity and moderate specificity, despite not having optimally tuned the algorithm for UWF pseudocolor images. Automated analysis of UWF images could prove to be of value in DR screening programs and for more accurate staging.

TAKE HOME MESSAGE Automated detection of diabetic retinopathy on ultrawidefield pseudocolor images may be useful for more optimal screening and staging of the disease.



HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board