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Letters to the Editor

A pilot study of autonomous artificial intelligence-based diabetic retinopathy screening in Poland

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Editor,

To date, there have been a number of diabetic retinopathy (DR) screening initiatives introduced all over the world (Lim et al. 2008; Pieczynski & Grzybowski 2015), including a few organized at a national level (most notably in the UK and Singapore) (Abràmoff et al. 2000; Lim et al. 2008). However, more often than not, these projects have been more localized mostly as a result of the associated cost, both in financial and human resources terms.

With the recent advent of commercially available automatic DR screening systems, we decided to attempt a pilot programme using an autonomous artificial intelligence (AI)-based DR system (IDx Technologies Inc., Coralville, IA, USA) for screening purposes in Poland. The programme began in May 2018 on a local scale in order to assess its effectiveness and deployment method and to locate and mitigate any issues that might arise prior to attempting a larger-scale operation.

We chose to set-up our pilot programme involving the at-risk population of a local, large diabetic clinic, as patients already visit the clinic in question for both routine and non-routine appointments. Additionally, such patients may constitute a population with more advanced stages of diabetes and as a result a higher likelihood for DR. Patients who visited the clinic for their appointments were offered DR screening based on non-mydriatic retinal images (TRC-NW400; Topcon, Tokyo, Japan) on an opt-in basis. Images were captured by diabetic nurses already employed within the clinic according to a standardized imaging protocol with one disc- and one fovea-centred 45° image per eye. These images were then submitted to the AI system for automated image quality evaluation. If the AI system detected sufficient quality, its output results in the form of a ruling of either more than mild (mtm) DR not detected, mtm DR detected or vision-threatening DR detected. Based on the AI system output of negative [i.e. no DR or only mild DR and no diabetic macular oedema (DME)], mtm DR or vision-threatening retinopathy (severe non-proliferative DR, proliferative DR and/or DME), the patient was recommended to undergo another screening after 1 year or routine or urgent ophthalmology referral, respectively. Patients whose image quality was deemed insufficient by IDx-DR system after reimaging were advised to visit an ophthalmologist.

Patients known to have DR were excluded from the screening and reminded of the need for regular ophthalmology follow-up. For legal purposes, only patients above the age of 18 years were allowed to participate in the programme.

The images were later reviewed by an ophthalmologist, and if incongruity with the IDx-DR results was identified, patients were notified at their next visit (if false-positive) or by phone (if false-negative).

In reviewing the results given by the automatic system, we decided to take a pragmatic approach. The analysis software had previously received a class IIa certification in Europe as well as United States Food and Drug Administration (FDA) authorization and may be used as an autonomous screening device, meaning that the results may be relied on for a referral decision without review by a clinician. Additionally, when starting the programme, we did not have any certainty regarding its future beyond the initial year. As we could not guarantee that patients would be screened again the following year using the same system, in reviewing the images, we chose to adopt a lower threshold for referral (and therefore a positive result) than that of the IDx-DR specified cut-off of 'more than mild DR'. Furthermore, we chose to adopt the following criteria for grading the images: threshold for DR was defined as more than three microaneurysms or any of either intraretinal microvascular abnormalities, venous beading, intraretinal haemorrhage or cotton wool spots. Additionally, when retinal changes unrelated to DR but requiring a fundus examination by an ophthalmologist were marked positive, we did not discount these as false-positives for the purpose of this screening. Some examples of such include extensive macular drusen or pigmented choroidal lesions (suspected choroidal nevi).

While the screening programme is still ongoing at this time, we have gathered and preliminarily analysed the data from 450 screening episodes so far. The IDx-DR system was able to analyse 78% of screening episodes without pharmacological dilation, judging them to be of sufficient quality, in comparison with the achievement of 82% using a human grader. Out of 278 patients judged as having no DR by the IDx-DR system, only four were subsequently found to have DR, with none having more than moderate DR or DME. Separately, out of the 76 patients for whom the screening results were deemed positive by the AI, 14 were false-positives according to the clinician review. Overall, according to the single clinician reference standard, the sensitivity and specificity of the system were 94% and 95%, respectively, and the positive predictive and negative predictive values were 82% and 99%, respectively. Our IDx-DR accuracy results are higher than those previously reported in literature, particularly for specificity: for example, the IDx-DR system was found to have a specificity of 90.7% in the FDA pivotal clinical trial as compared with the true reference standard, Early treatment of diabetic retinopathy study (ETDRS) level grading based on four wide-field stereo fundus photographs and optical coherence tomography (Abràmoff et al. 2016; van der Heijden et al. 2018).

Of note, the DR screening process using the IDx-DR system for the image

analysis was easy to implement and use. Within 1 min, results were available, which were then automatically saved.

Possible considerations for future include a cost-effectiveness analysis, additional data acquisition regarding patients' DR risk factors and expanding the programme beyond the high-risk population of a single diabetes clinic and into a general practice-based or standalone screening programme.

Overall, we are very pleased with the results so far and look forward to expanding and improving upon the current programme at a larger scale.

References

Abràmoff MD, Staal JS, Suttorp-van Schulten MS et al. (2000): Low level screening of exudates and haemorraghes in background diabetic retinopathy. Proc. Computer Assisted Fundus Imaging Workshop.

Abràmoff MD, Lou Y, Erginay A, Clarida W, Amelon R, Folk JC & Niemeijer M (2016): Improved automated detection of diabetic retinopathy on a publicly available dataset through integration of deep learning. Invest Ophthalmol Vis Sci **57**: 5200–5206.

van der Heijden AA, Abramoff MD, Verbraak F, van Hecke MV, Liem A & Nijpels G (2018): Validation of automated screening for referable diabetic retinopathy with the IDx-DR device in the Hoorn Diabetes Care System. Acta Ophthalmol **96**: 63–68.

Lim MC1, Lee SY, Cheng BC, Wong DW, Ong SG, Ang CL & Yeo IY (2008): Diabetic retinopathy in diabetics referred to a tertiary centre from a nationwide screening programme. Ann Acad Med Singapore **37**: 753–759.

Pieczynski J & Grzybowski A (2015): Review of diabetic retinopathy screening methods and programmes adopted in different parts of the world. Review of Diabetic Retinopathy Screening Methods and Programmes Adopted in Different Parts of the World.

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First-in-human study of the safety, effectiveness and ease of use of the intra-ocular diathermy forceps during vitrectomy

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Editor,

There have been no significant advances in intra-ocular diathermy design since the 1980s (Parel et al. 1983). The design has disadvantages, which become apparent during attempted closure of hemangioblastoma feeder vessels before tumour excision, which carries considerable risk of haemorrhage (Van Overdam et al. 2017a).

Disadvantages of conventional point-shaped diathermy probe:

- Coagulation and pressure on blood vessel from one side only, requiring higher energy levels and causing more collateral damage.
- Lack of view of coagulated tissue, unless probe is removed.
- Delay between removal of instrument involved in haemorrhagic episode and introduction of diathermy probe.

Intra-ocular diathermy forceps address these weaknesses. Its advantages were demonstrated in an *ex vivo* study (Van Overdam et al. 2017b). We report the findings of a first-in-human study.

The study was granted ethics committee approval and complied with the tenets of the Declaration of Helsinki. Patients provided informed consent. We prospectively recruited five patients scheduled for vitrectomy for diabetic tractional retinal detachment at the Academic Hospital Paramaribo. All patients received intravitreal injection of 0.05 ml (1.25 mg) bevacizumab (Avastin, Roche Diagnostics GmbH, Germany) 2–8 days prior to vitrectomy.

The diathermy forceps were developed by modifying available single-use 23-gauge ILM-peeling forceps (Vitreq, the Netherlands). The emitting electrode was connected to one-half of the core and the return electrode to the other half, with one jaw of the forceps attached to each half of the core and both halves electronically isolated from each other and from the shaft that enclosed them. The diathermy forceps were connected to the vitrectomy device (Millennium, Bausch & Lomb, USA) using the standard cord of the diathermy probe. Coagulation was set to 10% of maximum (7.5 watts) output. Power was controlled linearly by foot pedal. The conventional diathermy probe was available in case haemorrhage could not be controlled with the diathermy forceps and ocular hyperpressure.

The surgeries were performed by 3 of the 4 authors (JP, DJ and SM). Use of the intra-ocular diathermy forceps can be seen in the Video. All instances of haemorrhage could be controlled with the diathermy forceps. The conventional diathermy probe did not need to be used. There was no postoperative vitreous cavity haemorrhage or vitreous haze on day 1, week 1 or month 1 after surgery. Coagulation energy applied was not measured; however, the effectiveness with which haemorrhage was stopped and the minimal coagulation reaction to collateral tissues indicate that low levels of energy were used.

Advantages of intra-ocular diathermy forceps:

- *Diathermy function*: Coagulation and closure of blood vessels by compression and diathermy between the forceps jaws. Also successful coagulation without complete jaw closure, preventing tissue sticking to the forceps and allowing better visualization between the forceps jaws and control of coagulation.
- *Peeling function*: Peeling membranes and bimanual manipulation of tissues with coagulation available instantly inside the eye to treat any occurring haemorrhage without the need to exchange instruments.