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Title:

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Date:

2019-07-01

Citation:

O'Day, R. & Wickremasinghe, S. S. (2019). Incrementally does it: Multicolour imaging in polypoidal choroidal vasculopathy. *Clinical and Experimental Ophthalmology*, 47 (5), pp.569-570. <https://doi.org/10.1111/ceo.13568>.

Persistent Link:

<https://hdl.handle.net/11343/286100>

Editorial

Incrementally does it: multicolour imaging in polypoidal choroidal vasculopathy

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Funding sources / Financial disclosure: None

Conflict of interest: None

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: [10.1111/ceo.13568](https://doi.org/10.1111/ceo.13568)

Advances in imaging technology over the past 20 years have driven improved understanding and treatment of retinal pathologies.

To be useful, a new imaging technique should achieve one of: 1) improve diagnostic accuracy; 2) provide accurate prognostic information; 3) monitor efficacy of treatment; or 4) advance our understanding of the pathophysiology of a disease.

There are many successful examples of these. Characteristic OCT and fundus autofluorescence (FAF) changes in macular telangiectasia type 2 allows this condition to be diagnosed earlier and more accurately (1); the recent description of disorganisation of the retinal inner layers is proving to be an accurate predictor of response to anti-vascular endothelial growth factor (anti-VEGF) inhibitor treatment for diabetic macular oedema (2); OCT is the mainstay of monitoring efficacy of treatment of all intravitreal therapies, the most common being anti-VEGF injections for neovascular age-related macular degeneration (nvAMD) (3); and OCT has been instrumental in delineating the relatively recently described clinical entity of paracentral acute middle maculopathy and establishing that it is most likely caused by ischaemia of the deep retinal capillary plexus. (4)

Polypoidal choroidal vasculopathy (PCV) is a prime example of a condition that would benefit from better imaging technology to aid its diagnosis. PCV has a higher prevalence in Asian populations but is likely underdiagnosed in Caucasians and although it shares many features with nvAMD, it is generally thought to have a more favourable prognosis. (5) Despite this, the response to vascular endothelial growth factor inhibition is less predictable in PCV than nvAMD; and large subretinal haemorrhages are more common, which can result in significant retinal atrophy or subretinal fibrosis and irreversible vision loss. (6,7) High calibre longitudinal studies of the natural history of PCV are, however, lacking. Furthermore, due to under-diagnosis, it is likely that many studies of nvAMD have included patients with PCV in

their cohorts. Consequently, an accurate understanding of the differences in natural history and treatment outcomes between PCV and nvAMD is not known.

In EVEREST II, combination therapy with photodynamic therapy (PDT) and ranibizumab was found to have better visual and anatomic outcomes as compared to ranibizumab monotherapy at 12 months. (8) Polyp closure was much higher in the combination group (70% vs 35%). (8) In the PLANET study, monotherapy with aflibercept was found to have non-inferior visual outcomes as compared to combined aflibercept and PDT in patients who did not respond to an initial course of aflibercept. (9) These studies certainly suggest a role for PDT in patients with centre-involving PCV, unlike the situation in nvAMD.

The difficulty for clinicians, especially those practicing in countries with supposedly lower prevalence of PCV, is to know when to investigate for the possible presence of PCV. The question as to timing is important. Should this be done prior to initiating anti-VEGF therapy, as is the routine case in many East Asian countries, or should further investigation be deferred until an unsatisfactory response is encountered following anti-VEGF monotherapy?

Indocyanine green angiography (ICGA) is the gold-standard for the diagnosis of PCV. (10) ICGA is an invasive, time-consuming test with potential side effects and can be difficult to interpret. In Australia, ICGA is almost exclusively offered in tertiary referral centres. This lack of availability limits the ability to accurately diagnose and manage patients with PCV. It is therefore imperative to find other less invasive and more widely available methods to do so.

Multimodal imaging techniques, consisting of colour fundus photography (CFP), OCT, fundus fluorescein angiography (FFA) and OCT angiography, have shown

encouraging results in accurately diagnosing PCV without the need for ICGA. (5,11-13) OCT is particularly useful at detecting shallow sub-RPE lesions, such as the 'double layer sign' which corresponds to branching vascular networks (BVN). The reported sensitivity and specificity ranged from 85 to 95% with ICGA as the comparator gold-standard technique in these studies. (5,11-13)

In their paper in this issue, Tan et al, examine the accuracy of using multicolour imaging at diagnosing PCV and nvAMD as compared to colour fundus photography (CFP). (14) This is the first report of this technique in PCV. Multicolour imaging is a false colour imaging technique that combines the reflectances of three scanning laser ophthalmoscopy wavelengths: infrared (815nm), green (518nm) and blue (486nm) on the Heidelberg Spectralis®. (Heidelberg Engineering GmbH, Heidelberg, Germany) The different wavelengths have variable penetrance of the retinal architecture, with the infrared being able to penetrate the retinal pigment epithelium (RPE) and be most useful in delineating the PCV lesions: polyps and branching vascular networks (BVNs). They found that the multicolour composite and infrared images had a greater sensitivity and specificity at detecting PCV lesions than CFP and that imaging was more reliable at detecting polyps than BVNs. The authors suggested that multicolour imaging could be used as an initial tool to assess patients with subretinal exudation to determine which would then need to progress to definitive assessment with ICGA. The authors did not assess how multicolour imaging correlated with OCT and OCT angiography. This would be a worthwhile future direction for research, as the strengths of these techniques at detecting PCV lesions are different. These could act synergistically and, potentially, obviate the need for ICGA to diagnose PCV. The patient population in this current study had a high proportion of patients of PCV. A degree of caution is warranted in extrapolating these results to other populations, such as Australian, with a lower prevalence of PCV.

Tan et al's article (14) is the first report of multicolour imaging technology in PCV. It is certainly promising that a single image had a sensitivity and specificity of approximately 90% in diagnosing PCV lesions. Much work, however, remains to be done. Better detection rates of PCV, particularly in countries with low prevalence of the disease, will be crucial so that we can better understand the natural history and differences in treatment outcomes between patients with PCV and nvAMD.

REFERENCES

1. Sallo FB, Leung I, Clemons TE, Peto T, Bird AC, Pauleikhoff D. Multimodal imaging in type 2 idiopathic macular telangiectasia. *Retina Phila Pa.* 2015; 35(4): 742-9.
2. Radwan SH, Soliman AZ, Tokarev J, Zhang L, van Kuijk FJ, Koozekanani DD. Association of Disorganization of Retinal Inner Layers With Vision After Resolution of Center-Involved Diabetic Macular Edema. *JAMA Ophthalmol.* 2015; 133(7): 820-5.
3. Keane PA, Patel PJ, Liakopoulos S, Heussen FM, Sadda SR, Tufail A. Evaluation of age-related macular degeneration with optical coherence tomography. *Surv Ophthalmol.* 2012; 57(5): 389-414.
4. Rahimy E, Kuehlewein L, Sadda SR, Sarraf D. Paracentral Acute Middle Maculopathy: What We Knew Then and What We Know Now. *Retina Phila Pa.* 2015; 35(10): 1921-30.
5. Liu R, Li J, Li Z, et al. DISTINGUISHING POLYPOIDAL CHOROIDAL VASCULOPATHY FROM TYPICAL NEOVASCULAR AGE-RELATED MACULAR DEGENERATION BASED ON SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY. *Retina Phila Pa.* 2016; 36(4): 778-86.
6. Uyama M, Wada M, Nagai Y, et al. Polypoidal choroidal vasculopathy: natural history. *Am J Ophthalmol.* 2002; 133(5): 639-48.
7. Wong CW, Yanagi Y, Lee W-K, et al. Age-related macular degeneration and polypoidal choroidal vasculopathy in Asians. *Prog Retin Eye Res.* 2016; 53: 107-39.
8. Koh A, Lai TYY, Takahashi K, et al. Efficacy and Safety of Ranibizumab With or Without Verteporfin Photodynamic Therapy for Polypoidal Choroidal Vasculopathy: A Randomized Clinical Trial. *JAMA Ophthalmol.* 2017; 135(11): 1206-13.

9. Lee WK, Iida T, Ogura Y, et al. Efficacy and Safety of Intravitreal Aflibercept for Polypoidal Choroidal Vasculopathy in the PLANET Study: A Randomized Clinical Trial. *JAMA Ophthalmol.* 2018; 136(7): 786-93.
10. Spaide RF, Yannuzzi LA, Slakter JS, Sorenson J, Orlich DA. Indocyanine green videoangiography of idiopathic polypoidal choroidal vasculopathy. *Retina Phila Pa.* 1995; 15(2): 100-10.
11. Chaikitmongkol V, Kong J, Khunsongkiet P, et al. Sensitivity and Specificity of Potential Diagnostic Features Detected Using Fundus Photography, Optical Coherence Tomography, and Fluorescein Angiography for Polypoidal Choroidal Vasculopathy. *JAMA Ophthalmol.* April 2019.
doi:10.1001/jamaophthalmol.2019.0565
12. De Salvo G, Vaz-Pereira S, Keane PA, Tufail A, Liew G. Sensitivity and specificity of spectral-domain optical coherence tomography in detecting idiopathic polypoidal choroidal vasculopathy. *Am J Ophthalmol.* 2014; 158(6): 1228-38.e1.
13. Cheung CMG, Yanagi Y, Akiba M, et al. IMPROVED DETECTION AND DIAGNOSIS OF POLYPOIDAL CHOROIDAL VASCULOPATHY USING A COMBINATION OF OPTICAL COHERENCE TOMOGRAPHY AND OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY. *Retina Phila Pa.* June 2018.
doi:10.1097/IAE.0000000000002228
14. Tan CS, Ting DS, Lim LW. Multicolour imaging for the detection of polypoidal choroidal vasculopathy and age-related macular degeneration. *Clin Experiment Ophthalmol* 2019; 47: pp-pp (to be inserted by publishers).