Title: Long-term vision outcomes for patients with albinism and diabetic retinopathy

Running title: Albinism and diabetic retinopathy

Authors

Declan C **Murphy**[1,2,3] MBBS MRes (ORCID ID: 0000-0001-9295-7712)

Mohamed **Katta**[1] MBBS MA

Catherine A **Egan**[1,4] MBBS FRANZCO

Michel **Michaelides**[1,4] MD(Res) FRCOphth (ORCID 0000-0002-1552-7046)

Louisa **Wickham**[1] MD FRCOphth (ORCID 0000-0002-7430-2680)

Author list: **Murphy** DC, **Katta** M, **Egan** C, Michaelides M, **Wickham** L

Affiliations

1) Moorfields Eye Hospital, City Road, London EC1V 2PD, UK.
2) Institute of Genetic Medicine, Newcastle University, Tyne and Wear, United Kingdom
3) Northumbria healthcare NHS Foundation trust, Tyne and Wear, United Kingdom
4) UCL Institute of Ophthalmology, University College London, 11-43 Bath Street, London, EC1V 9EL, UK

Corresponding author:

Louisa Wickham

Email: louisa.wickham1@nhs.net

Affiliation: Moorfields Eye Hospital, City Road, London EC1V 2PD, UK.

Author contributions

Authors name	Research design	Data acquisition and or research execution	Data analysis and/or interpretation	Manuscript preparation	Approved final manuscript
Declan C Murphy	Yes	Yes	Yes	Yes	Yes
Mohamed Katta	Yes	Yes		Yes	Yes
Louisa Wickham	Yes	Yes		Yes	Yes
Michel Michaelides	Yes	Yes		Yes	Yes
Catherine Egan				Yes	Yes

Data availability

Data may be made available upon request from the corresponding author.

Acknowledgements

None

Conflicts of interest

The authors declare no competing financial interests.

Funding

This study was supported by a grant from the National Institute for Health Research Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology.

Ethical approval

Not required because this is a retrospective study using data collected as part of the patient's routine clinical care.

Consent to participate

Not required because this is a retrospective study using data collected as part of the patient's routine clinical care.

Consent for publication

Not required because this is a retrospective study using data collected as part of the patient's routine clinical care.

Declarations

No authors have any declarations to make.

Key messages

1. Albinism defines a group of genetic diseases characterised by depigmentation of the hair, skin and eyes in oculocutaneous albinism or isolated to the eyes in ocular albinism
2. Treating proliferative diabetic retinopathy in patients with ocular/oculocutaneous albinism may be more difficult due to potential challenges in identifying retinal vascular diseases and impaired efficacy of laser treatments
3. Despite extensive intervention, proliferative diabetic retinopathy is associated with poor long-term vision for patients with albinism.
4. Individuals without evidence of proliferative diabetic retinopathy appear to maintain stable vision so disease prevention is paramount

Abstract (248 words)

Purpose

Albinism defines a group of genetic diseases which result from disordered melanin biosynthesis. Proliferative diabetic retinopathy (PDR) results from poorly controlled type 1 or 2 diabetes mellitus (DM) and can lead to blindness due to progressive neovascularisation. However, the treatment of PDR in patients with ocular/oculocutaneous albinism may be more challenging. In this study we compared a group of patients with albinism and PDR, to a group with albinism and diabetes mellitus but no PDR, to examine the long-term implications.

Methods

Retrospective observational study including all patients with ocular albinism (OA) or oculocutaneous albinism (OCA) and DM who presented at a single specialist centre. Participants were allocated into either group 1 (eyes with PDR) or group 2 (all eyes without PDR). Statistical analysis was performed using SPSS V26.0. Between-group differences were investigated.

Results

Outcome data was available for 5 eyes from 3 participants in group 1 and 26 eyes from 13 participants in group 2. Despite interventions, a large and significant difference in vision at follow-up was observed between group 1 and group 2 (mean change in visual acuity: 1.11 (±1.00) versus -0.15 (±0.46) respectively; p=<0.0001).

Conclusion

PDR is associated with poor long-term prognosis despite interventions for patients with albinism. Those without PDR appear to maintain stable vision. Alternative

treatments for PDR and its complications may be required in this population. Measures to prevent the development of diabetic eye disease and progression towards PDR should be employed at an early stage.

Key words: Albinism; diabetes; diabetic retinopathy; ocular albinism

Introduction (1650 words)

Albinism defines a group of genetic diseases which result from disordered melanin biosynthesis and is characterised by depigmentation of the hair, skin and eyes in oculocutaneous albinism (OCA) or isolated to the eyes in ocular albinism (OA).[1] It can have a range of ocular manifestations including nystagmus, iris and choroidal hypopigmentation, foveal hypoplasia and impaired stereopsis. [2–4]

Proliferative diabetic retinopathy (PDR) is the commonest cause of severe vision loss in patients with diabetes mellitus (DM). It is characterised by progressive neovascularisation (NV) and associated complications such as neovascular glaucoma, vitreous haemorrhages and retinal detachment. The current gold standard treatment for patients with PDR remains panretinal photocoagulation (PRP); although more recently, studies using anti-vascular endothelial growth factor (anti-VEGF) agents to manage PDR have also been published.[5] 15.9% of untreated PDR is associated with blindness after two-years, compared with 6.4% in PRP-treated eyes.[6]

The identification and treatment of PDR may be more challenging in patients with albinism. The lack of retinal pigment limits the visualisation of the retina because imaging modalities such as fundus autofluorescence (FAF) and fundus fluorescein angiography (FFA) rely on retinal pigments to help differentiate anatomical structures. Moreover, the efficacy of PRP at managing neovascular retinal disease may be limited in albinism. Retinal pigments absorb retinal laser energy which is converted to thermal energy. This causes coagulative necrosis and impairs the

production of pro-angiogenic cytokines from. The deficiency of retinal pigment in albinism results in minimal or no laser energy absorption, so NV may persist.[7]

In this study we aimed to compare a group of patients with albinism and PDR and a group with albinism and DM but no PDR, to determine the implications on long-term vision.

.

Materials and Methods

Dataset

This retrospective observational study included all patients with OCA or OA and a diagnosis of DM who presented to Moorfields Eye Hospital, London, United Kingdom (UK) between the 1st November 2000 and 1st November 2019.

This study adhered to the tenets of the Declaration of Helsinki. All data and imaging were collected as part of routine care and fully anonymised, and therefore under UK guidelines this study was categorized as a service evaluation and did not require ethical approval.

This article conforms to the STROBE checklist.[8]

Inclusion and exclusion criteria

All patients with albinism and a diagnosis of DM (type 1 or type 2) were eligible for inclusion. All eyes which showed evidence of other retinal pathologies were excluded to limit potential confounding of results (n=3). Patients with less than 6 months follow up were excluded from statistical analyses relating to visual acuity outcomes (n=1).

Variables

Baseline characteristics, diabetic retinopathy grade (according to Diabetic screening programme in England and Wales[9]), interventions and best correct visual acuity (BCVA) at baseline and their most recent follow-up appointment were recorded in an electronic database.

Groups

Patients were divided into one of two categories. Group 1 included all eyes which showed evidence of PDR. Group 2 included all eyes which showed no evidence of PDR.

Statistical analysis

The patient was considered the unit of analysis when reporting baseline characteristics. The individual eye was considered the unit of analysis when reporting interventions and BCVA because the study aimed to examine vision per each eye.

SPSS V26.0 was used to perform all statistical analyses. Shapiro-wilk test was used to determine normality for continuous data. Normally distributed continuous variables are presented as means (± standard deviation (SD)). Categorical data is described as frequencies. All visual acuities were defined using Snellen acuities which were then converted to logarithm of the minimum angle of resolution (logMAR) units for statistical analysis; we defined counting fingers as logMAR 2.0, hand movements (HM) as 2.4, perception of light (PL) as 2.7 and no perception of light as 3.0.[10] Between-group differences were compared with independent samples T-tests for continuous variables. p=≤0.05 defined statistical significance.

Results

Study cohort

There were no significant between group differences at baseline. **(Table 2)**

Interventions for PDR

Interventions received by each patient are outlined in **table 3.** One patient received PRP and cryotherapy and bilateral pars plana vitrectomy (PPV) with membrane delamination and silicone oil tamponade to both eyes. One eye from one patient received intravitreal anti-VEGF (bevacizumab) on five occasions, PRP on two occasions to the right eye and PPV and membrane delamination with silicone oil tamponade. Finally, one patient received PRP and bevacizumab once to the left eye and underwent intravitreal bevacizumab on three occasions to the right eye.

Change in vision

The change in BCVA from baseline to the most recent follow-up appointment was compared between groups. Despite interventions, a large and significant difference was observed between group 1 and group 2 (mean change in VA: 1.11 (±1.00) versus -0.15 (±0.46) respectively; p=<0.0001). **(Figure 1)**

Patient cases with PDR

In our study, three patients showed evidence of PDR.

Case 1 (patient number 1, table 1, **figure 2**) is a thirty-one-year-old male with poorly controlled type I diabetes mellitus and Oculocutaneous albinism type 1A (OCA1A), referred for treatment of longstanding bilateral PDR. High-power laser, PRP, fluorescein-assisted diode laser photocoagulation, diode laser PRP and non-confluent cryoablation combined with intravitreal anti-VEGF were all applied to both eyes but failed to halt active proliferative disease so surgery was performed to the

right eye (PPV, delamination, PRP, cryotherapy and silicone oil tamponade). Unfortunately, one-week later the patient developed a right-sided retinal detachment requiring PPV, retinotomy and silicone oil tamponade. Two-weeks later the left-eye developed a combined tractional and rhegmatogenous retinal detachment with proliferative vitreoretinopathy requiring PPV, delamination, cryotherapy and silicone oil tamponade. BCVA did not improve beyond PL in the right-eye, and HM in the left-eye. Dense cataracts developed bilaterally; both underwent anti-VEGF one-week before phacoemulsification, capsulectomy and inferior peripheral iridectomies. Subjective vision improved in both eyes but without objective improvement.

Case 2 (patient number 2, table 1, **figure 3**) is a fifty-three-year-old male with poorly controlled type 2 diabetes mellitus, OCA1A, right-sided PDR, and a left-sided decompensated cornea and rubeotic glaucoma (Left-eye BCVA: NPL at first presentation). He presented via eye emergency with a macula-involving tractional retinal detachment, inferior diabetic vitreous haemorrhage, macular oedema and rubeosis iridis; immediate treatment with PRP was performed but AF and FFA showed no scarring post-PRP so intravitreal anti-VEGF was injected on numerous occasions but despite treatment, vision deteriorated to HM after two-months. The tractional retinal detachment progressed after two-months so managed with 23G PPV, retinal delamination, cryopexy and high-viscosity silicone oil injection; despite reattachment and regressed neovascularisation, BCVA did not improve. Three-years later rubeotic glaucoma developed in the right eye requiring a Baerveldt aqueous shunt, mitomycin C and a right scleral graft to control IOP, followed by anterior chamber paracentesis and intravitreal anti-VEGF. BCVA showed no improvement.

Case 3 (patient number 3, table 1, **figure 4**) is a twenty-eight-year-old male with OCA1A, type I diabetes and bilateral PDR, who presented with acute complete

vision loss and photopsia in the left-eye owing to a left ischaemic central retinal vein occlusion which was managed conservatively. Four-weeks later rubeotic glaucoma was identified in the right-eye which was treated using topical eye drops for three-weeks before cyclodiode laser ablation and intra-vitreal anti-VEGF were administered and IOP normalised over one-year. One-year later he presented with a left subtotal combined tractional and RRD requiring PPV, delamination, retinectomy, lensectomy and high-viscosity silicone oil tamponade. The retinectomy edge was left untreated because of laser non-uptake previously and the posterior location prohibited cryopexy. There was no improvement in vision.

Discussion

Our study suggests that for patients with albinism and DM, evidence of PDR heralds the development of severe vision loss despite interventions. Patients without PDR appear to maintain their vision for many years without significant deterioration. Treatments employed to manage PDR and its complications may be less effective in patients with albinism due to the lack of retinal pigmentation. Therefore, measures which prevent the development of PDR should be implemented at an early stage in this patient group to prevent vision loss, with patients being educated about the likely poor prognosis should they develop advanced diabetic eye disease.

In patients without albinism, prompt PRP has been advised for the prevention and treatment of proliferative vascular diseases, particularly PDR[11], and for complications which arise secondary to NV.[11–16] The mechanism underpinning how PRP can treat PDR is most likely attributed to the absorption of laser energy by retinal pigment which is then converted to thermal energy. The temperature of the retina increases causing protein denaturation and coagulative necrosis, but spares

the choroid, neural retina or photoreceptors.[7] The reduced or absent retinal pigmentation in albinism likely impairs retinal absorption of laser and thereby curtails its ability to induce coagulative necrosis.[7, 17, 18] As a result, pro-angiogenic cytokines continue to be synthesized, so NV persists. Our study supports this theory because PRP failed to treat disease activity in our patients with albinism and PDR. Vision continued to deteriorate even when PRP was applied on multiple occasions by retina specialists.[12] **(Table 3)**

Treatment with intravitreal anti-VEGF therapies has been shown to provide better short-term and, either equivalent or superior long-term, clinical outcomes compared with PRP for managing PDR.[5, 19] In our study, intravitreal anti-VEGF was applied on 5 occasions to the right eye of patient 2 which resulted in less visual deterioration (0.9 logMAR units) than the other eyes with PDR. Although this approach to the treatment of PDR in patients without albinism is not currently believed to be cost effective unless diabetic macular oedema is present, in patients with albinism it is likely that an approach involving early and frequently treatment with intravitreal anti-VEGF may be more effective at preserving vision and should be considered the treatment of choice.

PDR can induce and accelerate other ophthalmological diseases such as retinal detachments, vitreous hemorrhages and neovascular glaucoma which often require surgery to restore or preserve vision.[20] In patients without albinism, surgery can successfully manage many of these NV-related complications, however, alternative approaches may be required in albinism. Firstly, peri-operative PRP is almost universally used in patients without albinism and is thought to be an essential adjunct to vitrectomy to reduce vascular proliferation. During delamination surgery creation of retinal breaks is a common peri-operative complication and without the option of

effective laser the risk of subsequent retinal detachment is high. There are some reports that long-duration laser or trans-scleral cryopexy could be a more effective alternative in albinism, however with posterior pathology and retinal traction this is not always feasible.[21–23] It is likely that several surgical interventions in combination with long-term silicone oil tamponade and/or encircling buckle will be required to treat retinal detachments associated with PDR in albinism.[12, 23],[24] Current evidence supporting the adoption of alternative surgical approaches is limited and further investigations are required.

Current methods used to image the retina such as FAF and FFA are also limited in albinism. Difficulty arises because FAF and FFA use retinal pigment to help differentiate anatomical retinal structures in the retina. Laser burns, which are usually visible within hours after PRP is applied, cannot be observed so it is difficult to determine whether PRP was unsuccessful at inducing photocoagulation or whether the laser burns could not be visualised due to limitations in the imaging modality used.[25, 26] Imaging the retina in patients with albinism using phase resolved spectral domain optical coherence tomography (SDOCT) M-mode scanning may be a more valuable alternative because it measures retinal photocoagulation independent of pigmentation by analysing changes in the local optical path of laser lesions.[27]

Limitations

Our study has several limitations. Due to the rarity of patients with concurrent albinism and DM, the sample size is very small so the study is at risk of type II errors. Patients were identified from a single centre in the UK so the generalisability of conclusions may be limited. In the future, prospective multi-centred studies are

required to determine the influence of PDR on vision outcomes when adjusted for potential confounders due to the rarity of ocular albinism. A meta-analysis using individual patient data should be performed to further understand the effectiveness of therapies at managing PDR in albinism and to derive best-practice guidance for managing patients with albinism and PDR.

Conclusions

In patients with albinism, evidence of PDR carries a poor long-term visual prognosis despite interventions. Patients without PDR appear to maintain their vision for many years without significant deterioration. Alternative treatment approaches are likely to be required in this population. Measures which prevent the development of DM and/or progression towards PDR should be employed at an early stage.

References

1. Grønskov K, Ek J, Brondum-Nielsen K (2007) Oculocutaneous albinism. Orphanet J Rare Dis 2:43. https://doi.org/10.1186/1750-1172-2-43

2. Wildsoet CF, Oswald PJ, Clark S (2000) Albinism: its implications for refractive development. Invest Ophthalmol Vis Sci 41:1–7

3. Spedick MJ, Beauchamp GR Retinal vascular and optic nerve abnormalities in albinism. J Pediatr Ophthalmol Strabismus 23:58–63

4. Khanal S, Pokharel A, Kandel H (2016) Visual deficits in Nepalese patients with oculocutaneous albinism. J Optom 9:102–9. https://doi.org/10.1016/j.optom.2015.01.002

5. Sivaprasad S, Prevost T, Vasconcelos JC, et al (2017) Clinical efficacy of intravitreal aflibercept versus panretinal photocoagulation for best corrected visual

acuity in patients with proliferative diabetic retinopathy at 52 weeks (CLARITY): a multicentre, single-blinded, randomised, controlled, phase 2b, non-inferiority trial. Lancet 389:2193–2203. https://doi.org/10.1016/S0140-6736(17)31193-5

6. The Diabetic Retinopathy Study Research Group (1978) Photocoagulation Treatment of Proliferative Diabetic Retinopathy: The Second Report of Diabetic Retinopathy Study Findings. Ophthalmology 85:82–106. https://doi.org/10.1016/S0161-6420(78)35693-1

7. Paulus YM, Blumenkranz MS (2013) Proliferative and Nonproliferative Diabetic Retinopathy. Proliferative and Nonproliferative Diabetic Retinopathy. Available at: https://www.aao.org/munnerlyn-laser-surgery-center/laser-treatment-of-proliferative-nonproliferative-. Accessed 10th October 2020.

8. Von Elm E, Egger M, Altman DG, et al (2007) Strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. Br. Med. J. 335:806–808. doi: 10.1136/bmj.39335.541782.AD

9. Harding S, Greenwood R, Aldington S, et al (2003) Grading and disease management in national screening for diabetic retinopathy in England and Wales. Diabet Med 20:965–971. https://doi.org/10.1111/j.1464-5491.2003.01077.x

10. Bach M. Visual Acuity Cheat Sheet (2017) Available at: https://michaelbach.de/sci/acuity.html. Accessed 10th October 2020.

11. Early Treatment Diabetic Retinopathy Study Research Group (1991) Early Photocoagulation for Diabetic Retinopathy: ETDRS Report Number 9. Ophthalmology 98:766–785. https://doi.org/10.1016/S0161-6420(13)38011-7

12. Mansour AM, Chhablani J, Arevalo JF, et al (2018) Retinal detachment in albinism. Clin Ophthalmol 12:651–656. https://doi.org/10.2147/OPTH.S158785

13. Kiuchi Y, Nakae K, Saito Y, et al (2006) Pars plana vitrectomy and panretinal photocoagulation combined with trabeculectomy for successful treatment of neovascular glaucoma. Graefe's Arch Clin Exp Ophthalmol 244:1627–1632. https://doi.org/10.1007/s00417-006-0321-7

14. Muqit MMK, Sanghvi C, McLauchlan R, et al (2012) Study of clinical applications and safety for Pascal® laser photocoagulation in retinal vascular disorders. Acta Ophthalmol 90:155–161. https://doi.org/10.1111/j.1755-3768.2009.01854.x

15. The Royal College of Ophthalmologists (2012) Diabetic Retinopathy Guidelines. London. Available at: www.rcophth.ac.uk. Accessed 10th October 2020.

16. Wilkinson C., Ferris FL, Klein RE, et al (2003) Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology 110:1677–1682. https://doi.org/10.1016/S0161-6420(03)00475-5

17. Evans JR, Michelessi M, Virgili G (2014) Laser photocoagulation for proliferative diabetic retinopathy. Cochrane Database Syst Rev 2014:. https://doi.org/10.1002/14651858.CD011234.pub2

18. Royle P, Mistry H, Auguste P, et al (2015) Pan-retinal photocoagulation and other forms of laser treatment and drug therapies for non-proliferative diabetic retinopathy: systematic review and economic evaluation. Health Technol Assess (Rockv) 19:1–248. https://doi.org/10.3310/hta19510

19. Gross JG, Glassman AR, Jampol LM, et al (2015) Panretinal photocoagulation vs intravitreous ranibizumab for proliferative diabetic retinopathy: A randomized clinical trial. JAMA - J Am Med Assoc 314:2137–2146. https://doi.org/10.1001/jama.2015.15217

20. Gartner S, Henkind P (1978) Neovascularization of the iris (rubeosis iridis). Surv Ophthalmol 22:291–312. https://doi.org/10.1016/0039-6257(78)90175-3

21. Huang XY, Wang Y, Wang R, et al (2012) Diagnostic and Therapeutic Challenges. Retina 32:399–402. https://doi.org/10.1097/IAE.0b013e3182252aea

22. Hiroshi MHM. (2007) A case of ocular albinism with rhegmatogenous retinal detachment. Japanese Rev Clin Ophthalmol 93:861–864

23. Yang J-W, Lee S-J, Kang S-B, Park Y-H (2008) A Case of Retinal Detachment Surgery in Albinism Patient. J Korean Ophthalmol Soc 49:840. https://doi.org/10.3341/jkos.2008.49.5.840

24. Veckeneer M, Maaijwee K, Charteris DG, van Meurs JC (2014) Deferred laser photocoagulation of relaxing retinotomies under silicone oil tamponade to reduce recurrent macular detachment in severe proliferative vitreoretinopathy. Graefe's Arch Clin Exp Ophthalmol 252:1539–1544. https://doi.org/10.1007/s00417-014-2605-7

25. Rodanant N, Bartsch D-UG, Bessho K, Freeman WR (2003) Autofluorescence image in ocular albinism. Retina 23:265–6

26. Muqit MMK, Gray JCB, Marcellino GR, et al (2009) Fundus autofluorescence and Fourier-domain optical coherence tomography imaging of 10 and 20 millisecond Pascal retinal photocoagulation treatment. Br J Ophthalmol 93:518–525. https://doi.org/10.1136/bjo.2008.148833

27. Makita S, Yasuno Y (2017) Detection of local tissue alteration during retinal laser photocoagulation of ex vivo porcine eyes using phase-resolved optical coherence tomography. Biomed Opt Express 8:3067–3080. https://doi.org/10.1364/BOE.8.003067

Figure legends

Figure 1:

A comparison of the mean change in best correct visual acuity from baseline and the most recent follow-up appointment between group 1 and group 2. Statistical analysis was based on 5 eyes from 3 patients (group 1) and 26 eyes from 13 patients (group 2). There is a significant difference observed between group 1 and group 2 (mean change in VA: 1.11 (±1.00) versus -0.15 (±0.46) respectively; p=<0.0001).

Figure 2

Patient number 1, a male with type I diabetes, oculocutaneous albinism and R3a proliferative diabetic retinopathy. Fundus image of the right eye shows proliferative retinopathy and a vitreous haemorrhage (A) and a high-magnification fundus image of the left eye (B) shows characteristic ocular albinism features such as clear choroidal vasculature, a pale retina, and indistinct optic disc margin. Fundal autofluorescence of the left eye shows a hyperfluorescent retina (C) and fundal fluorescein angiography suggests minimal uptake 6-months after panretinal photocoagulation (D). Spectral domain ocular coherence tomography (SDOCT) of the left eye shows gross macular oedema (E). A photograph of the left eye demonstrates rubeosis iridis and an inferior iridectomy (F).

Figure 3

Patient number 2, a male with type 2 diabetes, oculocutaneous albinism and R3a proliferative diabetic retinopathy. Fundus image of the right eye (A) shows proliferative vitreoretinopathy and a vitreous haemorrhage. Fundus fluorescein angiography of the right eye (B) 12-months after panretinal photocoagulation (PRP) application suggests minimal laser uptake. Fundal autofluorescence of the right eye 12-months following PRP (C). There is retinal hypofluorescence and minimal laser update.

Figure 4

Patient number 3, a male with type I diabetes mellitus, oculocutaneous albinism and bilateral R3a proliferative diabetic retinopathy. The discrepancy in the appearance of scars of photocoagulation between a fundus photo and FAF results from the differential absorption of the laser energy in patients with albinism due to the lack of pigment. High magnification (A) fundus images of the right (A) and left (B) eye which show new blood vessel formation at the optic disc, macula and peripheral retina. (C) Fundus image of the right eye 18-months after anti-vascular endothelial growth factor intravitreal injections showing evidence of blood vessel regression. (D) Right eye 9-months following panretinal photocoagulation application with active disease present, likely due to poor laser uptake. Autofluorescence images of the (E) Right and (F) left eye following panretinal photocoagulation, suggesting poor laser uptake.