TITLE: Visual outcome following phacoemulsification in English Cocker Spaniels with suspected progressive retinal atrophy: A retrospective multicenter study of 54 cases (2002-2017)

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VISUAL OUTCOME FOLLOWING PHACOEMULSIFICATION IN ENGLISH COCKER SPANIELS WITH SUSPECTED PROGRESSIVE RETINAL ATROPHY: A RETROSPECTIVE MULTICENTRE STUDY OF 54 CASES (2002-2017).

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ABSTRACT

Objective: To describe the visual outcome following phacoemulsification in English Cocker Spaniels (ECS) affected by cataracts and suspected progressive retinal atrophy (PRA).

Animals studied: 54 client-owned dogs.

Procedures: A multicentre, retrospective study was performed including ECS with suspected PRA which underwent phacoemulsification. PRA was suspected on ophthalmic examination before and after surgery, and/or after electroretinography (ERG) was performed. Visual outcome was assessed by menace response per eye at seven time periods post-surgery (P1=25-90 days, P2=91-180 days, P3=181-364 days, P4=365-549 days, P5=550-729 days, P6=730-1094 days, P7≥1095 days). Descriptive statistics were performed. Generalized estimating equations were used to identify predictors associated with vision after surgery. Odds ratio and confidence intervals were reported. Significance was set at $p<0.05$. Owners were invited to participate in a questionnaire.

Results: Phacoemulsification was performed in 85 eyes. Median age at surgery was 9.09 years (min. 2.17 years, max. 13.49 years). At all re-examinations, up to and including P5, significantly more eyes were visual than before surgery ($p\leq0.003$). Odds for vision were significantly increased for eyes that underwent surgery. Electroretinograms were performed in 75/85 eyes that underwent surgery, demonstrating low b-wave amplitudes. There was no significant effect of the age, gender, vision before surgery, presence of dazzle reflex, cataract stage or abnormality on gonioscopy on visual outcome. The questionnaire response rate was 48.2%. Most participants (92.5%) felt that cataract surgery led to improvement of the dog's quality of life.

Conclusions: English Cocker Spaniels with suspected PRA may benefit from phacoemulsification with vision up to two years following surgery.

Key words: PRA, progressive retinal atrophy, cataract, phacoemulsification

Introduction

Cataracts are a common cause of blindness in dogs. Possible causes of cataract include inherited, congenital, aging, progressive retinal atrophy (PRA) and diabetes mellitus.(1-8) As the cataract progresses, secondary complications such as lens-induced uveitis and secondary glaucoma can develop, which may cause ocular discomfort or pain.(1-3) Surgical removal of the cataract holds the best prognosis for restoring vision and improving the overall ocular health, compared to medical management only or no treatment at all.(3) Surgical success rates of 85-90 % have been reported. (4-6) Long-term complications after phacoemulsification include posterior capsular opacification, corneal lipid opacity, intraocular haemorrhage, glaucoma and retinal detachment, which may lead to blindness or enucleation. (4,6-9)

Progressive retinal atrophy is a broad term for a variety of progressive, inherited diseases of the retina, that manifest as degeneration of the photoreceptor layer and/or the retinal pigmented epithelium in many different dog breeds.(10,11) It has been reported to be the third most common cause of cataracts accounting for 7.6 % and 12.5 % of cases in two retrospective studies.(12,13) Cataracts secondary to PRA have been described to develop at advanced stages of PRA in some breeds.(11,14) Historically, cataract surgery has not been recommended routinely in dogs affected by PRA, as these dogs will progressively lose vision despite the surgery.(15) Disease onset and progression, as well as the underlying genetic mutations causative of PRA, vary between and within breeds.(16-18) Many breeds are affected by a progressive rod-cone degeneration (prcd) with an identical mutation in the prcd locus, which is responsible for a late-onset form PRA.(17) Interestingly, phenotypic differences have also been reported between breeds affected by the same prcd mutation. The English Cocker Spaniel (ECS) demonstrated a slower rate of photoreceptor degeneration histologically, compared to the Miniature Poodle (MP) and American Cocker Spaniel

(ACS).(17,19) Furthermore, ECS showed a mosaic of disease stages across the meridians of the fundus, with areas of delayed retinal degeneration. On ERG examination, MP's lost their remaining b-wave function twice as fast as ECS.(19) Supported by these findings in the ECS, the frequent presentation of this breed with cataracts and anecdotal clinical experiences of late onset vision loss, the authors have performed cataract surgery in ECS following careful owner counselling.

The main objective of this retrospective study was to describe the visual outcome at various re-examination periods following phacoemulsification in ECS with suspected PRA. The second objective was to investigate any predictors associated with a positive visual outcome following surgery.

Materials and Methods

A retrospective multicentre study was performed. Databases of the Royal Veterinary College (RVC), the Animal Health Trust (AHT) and Dick White Referrals (DWR) were searched for ECS with suspected progressive retinal atrophy and cataracts, which underwent phacoemulsification between 2002 and 2017. Ethical approval was obtained from the RVC Clinical Research Ethical Review Board (CRERB, URN: M2015 0073) and AHT Clinical Research Ethics Committee (41-2016).

Dogs were included if they underwent a full ophthalmic examination including slit-lamp biomicroscopy, indirect binocular ophthalmoscopy and tonometry before and after surgery by a diplomate or a resident under the supervision of a diplomate of the European College of Veterinary Ophthalmologists (ECVO). Gonioscopy (Koeppe lens, Ocular instruments inc., Washington, USA) and ocular ultrasound results were reported from examinations before

surgery. Furthermore, information about the presence of concurrent systemic disease or ocular diseases was collected.

A diagnosis or suspicion of PRA was made based on the patient history, signalment, full ophthalmic examination before or after surgery and, in the majority of cases, supported by the ERG results. In all referral centres, a short 'yes/no' ERG protocol was employed to assess gross photoreceptor function. The protocols used among the centres varied. A summary of the ERG protocols used is demonstrated in *table 1*. ERGs were performed in conscious dogs at the AHT and at DWR and under general anaesthesia at the RVC. The ERG machines used were, HMsERG system (Model 2000 OcuScience, Henderson, NV) at the RVC and DWR, and Photic stimulator (SLE, CPS-20; Medilec Synergy, VIASYS, Madison, USA) at the AHT. Dogs with a b-wave amplitude below 40mV were included. The b-wave amplitude of the mixed/rod cone response was used at the RVC and the b-wave amplitude of a cone dominated ERG curve was assessed at the AHT and DWR. The cases with no ERG, but with suspected PRA, were included following careful selection based on their history, signalment, full ophthalmic examination, the presence of attenuated retinal vascularization and tapetal hyper-reflectivity on funduscopy and if visual deficits in low light were reported. ECS with uni-or bilateral phacoemulsification were evaluated.

Visual outcome post-surgery was assessed in all ECS presented at re-examinations by ophthalmic examination, particularly the menace response, at seven time-periods post-surgery (P1 = 25-90 days, P2 = 91-180 days, P3 = 181-364 days, P4 = 365-549 days, P5 = 550-729 days, P6 = 730-1094 days, p7 ≥ 1095 days). Other methods of visual assessment (obstacle/maze tests, tracking response and visual placing response) were also reported in a number of cases, but not consistently in all dogs. The results of genetic testing were reported if available.

Owners were invited to participate in a simple questionnaire by email, letter or telephone call, asking:

1) Is your pet still visual or how long has he/she been visual in your opinion?

2) Do you feel that cataract surgery has improved your pet's quality of life?

Frequencies and percentages were reported for the categorical variables: gender, operated eye, menace response per eye, ERG, the presence of a flat trace and postoperative complications. The RVC databank RxWorks 5.2.4195 was searched to investigate the frequency of ECS presented to the RVC in general and to the ophthalmology department between 2002 and 2017. Medians (minimum, maximum) were reported for numerical variables like age and ERG b-wave amplitudes per eye. McNemar's tests were performed to compare visual outcome before and after surgery. Generalized estimating equations (GEE) with binomial logit link function were used to assess association between age, gender, centre, presence of a dazzle reflex, cataract grade, abnormalities on gonioscopy or ocular ultrasound, presence of vision before surgery or a flat trace on ERG with the postoperative visual outcome. Odds ratio (OR) and 95% confidence intervals (CI) are presented for results of the generalized estimating equation. Statistical significance was set at $p < 0.05$. All analyses were performed with IBM SPSS Statistics (Version 24; IBM Corp., Armonk, NY, USA). Graphic illustrations were created with GraphPad Prism (Version 7.00 for Windows, GraphPad Software, La Jolla California USA) and R (Version 3.4.2, R Foundation for Statistical Computing, Vienna, Austria).

Results:

There were 54 ECS included in this study (RVC 14 cases, AHT 32 cases and DWR 8 cases), comprising 28 (51.9 %) males and 26 (48.1 %) females. Phacoemulsification was performed

in 85 of 108 eyes, comprising 41 right eyes (48.2 %) and 44 left eyes (51.8 %). Bilateral phacoemulsification was performed in 31 dogs (57.4 %) and unilateral in 23 dogs (42.6 %). Seventy-three (85.9 %) intraocular lenses (IOL) were placed. Phacoemulsification was performed on separate days in 8/54 dogs (14.8 %) and on the same day in 46/54 dogs (85.2 %). The median age at surgery was 9.09 years (Min. 2.17 years, Max. 13.49 years).

The ECS was the fourth most common breed (4 % of the total population), presented to the RVC between 2002 and 2017 and the second most common breed (7 % of the total population) presented to the ophthalmology department of the RVC during the same time period. Funduscopy supported the suspicion of PRA in all operated eyes either before surgery (4/85, 4.7%) or at re-examinations (81/85, 95.3%) following surgery. Funduscopic details like tapetal hyperreflectivity (78/85, 91.8%), attenuated retinal vascularisation (67/85, 78.8%) and a pale or atrophied optic nerve head (11/85, 12.9%) were described in most patient records. Clinicians have used the general term progressive retinal atrophy to describe funduscopic findings in all cases.

An ERG was performed in 75/85 (88.2 %) operated eyes. All ERGs were consistent with reduced retinal function and the median ERG b wave amplitude was 10mV (Min. 0mV, max 40mV) in all eyes. A flat ERG trace was found in 30 (40 %) of the operated eyes. One dog was tested positive for the prcd gene mutation (Optigen, Ithaka, NY, USA). Ten eyes of eight patients did not undergo an ERG, all of which demonstrated tapetal hyperreflectivity, attenuated retinal vessels on funduscopy and all of these patients were nyctalopic.

A concurrent diagnosis of diabetes mellitus was not reported in any dog. Eight dogs had been diagnosed with keratoconjunctivitis sicca (KCS, 14.8 %) at the time of the first examination. Cataracts were described as incipient (1/85, 1.2%), immature (40/85, 47.1%), mature (38, 44.7%) and hypermature (6/85, 7.1%). The cataract stage was significantly associated with blindness before the surgery ($p = 0.004$). Following the surgery there was no association

between previous cataract grade and visual outcome. There were statistically significant associations at P4 ($p = 0.003$) and P5 ($p = 0.029$). However, these were considered questionable, due to the loss to follow up, as there were only 1 and 3 blind patients that presented for each period. A higher number of re-examined patients would be required to avoid bias. Gonioscopy was performed in 27 (25%) of 108 eyes in total with 16 (59.2%) abnormal findings of the iridocorneal angle (ICA). There were descriptions of seven narrow ICAs (7/27, 25.9%), six eyes with narrow ICAs alongside pectinate ligament dysplasia (PLD) (6/27, 22.2%), three eyes with PLD only (3/27, 11.1%) and 11 normal findings (11/27, 40.7%). An abnormal finding on gonioscopy did not affect the visual outcome of operated eyes in this study statistically and none of these cases developed glaucoma following surgery ($p < 0.001$). Ocular ultrasound was performed in 93 (86.1%) of 108 eyes and abnormalities were reported in 24 (22.2%) eyes. The most frequent finding was vitreal degeneration ($n = 22$, 20.3%). There was a single case of lenticonus and one suspected persistent tunica vasculosa lentis, which was not confirmed following surgery. There were no cases of retinal detachment.

Before surgery, 19 (22.4%) of the operated eyes demonstrated a positive menace response and 66 (77.6%) eyes had a negative response. However, significantly more eyes had a positive menace response post operatively from re-examination period P1 until and including P5 ($p \leq 0.003$), compared to the menace response before surgery. See *table2 / figure 1 and figure 2*

Thirty eyes (40 %) undergoing cataract surgery demonstrated a flat trace on ERG. Before surgery, five (16.7 %) of these eyes had a positive menace response and 25 eyes (83.3 %) had a negative menace response. Of the five eyes with flat trace readings and positive menace responses, two ERGs were measured consciously, three ERGs were measured under general

anaesthesia. Despite the flat ERG traces in 30 eyes, there was significant improvement of vision from P1 to P4 ($p \leq 0.031$). *See table 3/figure 3*

There were increased odds for vision if an eye underwent phacoemulsification compared to eyes not undergoing surgery at P1 ($p < 0.001$, OR = 12.89, CI = 4.33, 38.8), P2 ($p < 0.001$, OR = 23.70, CI = 5.18, 108.39) and P3 ($p < 0.001$, OR = 157.55, CI = 17.34, 1431.43). The GEE could not be performed for P4, P5, P6 and P7 as there were zero visual eyes in the group that had not undergone surgery. Abnormalities on ocular ultrasound did not have any statistical effect on the presence of a flat line on ERG or on the visual outcome of operated eyes in this study. The presence of a dazzle reflex before surgery did not have a significant effect on vision post-surgery. The presence or absence of an IOL did not have an effect on the presence of vision statistically. There was no significant effect of referral centre, age, gender or vision before surgery on visual outcome.

Of all 85 eyes operated, 39 (45.9%) presented with complications throughout the re-examination time periods. Complications included KCS (n = 17, 20.0%, not including previously diagnosed patients), glaucoma (n = 11, 12.9%), corneal ulceration (n = 6, 7.1%), mineral or lipid deposits in the cornea (n = 3, 3.5%), corneal endothelial disease (n = 4, 4.7%), endophthalmitis (n = 3, 3.5%) and intraocular artificial lens luxation (n = 1, 1.2%). Four eyes of three dogs were enucleated due to secondary glaucoma. One eye was removed at day one following surgery; however, glaucoma was present in this eye before surgery. Two eyes of the same dog (only the left eye was operated) were enucleated 2.5 years and one eye 3.5 years following surgery. *See figure 4*

Twenty-seven owners replied to the brief questionnaire (27/56, 48.2% reply rate). Most owners felt positive about the surgery and reported that the quality of life of their pet had improved (25/27 replies, 92.5%). The question for vision was not answered uniformly with

yes or no and some patients were deceased, therefore this question was excluded from the results.

Discussion

Historically, due to the inevitable progressive loss of vision, reports that cataracts develop in the late stages of PRA and that phacoemulsification does not benefit patients with underlying PRA, surgery has not been recommended routinely.(11,14,15). The risks and complications of the surgery always need to be outweighed by the advantages, which could be improved vision and overall ocular health. Cataracts are not only an opacity leading to blindness, but may lead to lens-induced uveitis, lens luxation or glaucoma.(1-3,20) Therefore, in a study by Lim et al. it was discussed that phacoemulsification could be performed to decrease risks of ocular disease secondary to the cataracts. (3) In patients with PRA, it is expected that vision will be gradually lost, even after phacoemulsification of their secondary cataracts. However, there are breed-related differences in the onset and progression of PRA. It has been reported that ECS are affected by a relatively late onset and slowly progressive form of PRA, as demonstrated by late changes on funduscopy, areas of delayed retinal degeneration on histology and delayed loss of the b wave function on ERG in comparison to other breeds.(17,19) There is a relatively high prevalence of prcd mutations in this breed, which is a late onset form of PRA.(16,21) In the present study, all of the dogs included were ECS which is a very popular breed in the United Kingdom and one of the most common dog breeds presented to the RVC during the period of the study. When counselling the owners, it was discussed, that the visual outcome and how long the dog could remain visual post-surgery, were unknown at the time. The decision to operate one or both eyes was based on the clinician's recommendation and the owner's decision.

In this study, six eyes regained and maintained vision after surgery for over three years. The improvement of vision was significant until P5, which was the time period between 1.5 and 2 years post-surgery. *(See figure 1, figure 2)* Considering that dogs affected by PRA were not routinely operated in the past, the authors were encouraged that many dogs in this study benefitted from vision improvement for such a long time.

Several eyes with an initial flat trace did regain vision after surgery, as reported in the results, which was found significant from P1 to P4. However, these findings raise questions about the accuracy of the different ERG readings and subjectivity of the menace response for vision testing. The ERG readings were likely affected by positioning, state of consciousness, type of anaesthesia, severity of the cataracts and noise, making it challenging to distinguish between a reduced b-wave amplitude and a flat line. (22-24) This is considered a limitation of this study, as it was performed retrospectively and at different centres with various ERG protocols and ERG machines and various states of consciousness, which need to be considered when comparing ERG results with each other as it may have affected the results.(24) In order to assess the validity of the ERG result in eyes with reduced photoreceptor function, the ERG protocols require standardisation in several aspects. Ideally, the same ERG machines and the same protocol should have been used. The recommended protocols for diagnosis of photoreceptor disorders imply that all ERGs include twenty minutes dark adaption, testing of a mixed rod cone response, testing of cone function after ten minutes of light adaption and a flicker test. (25,26) These protocols, together with a standardized approach to perform the ERG either sedated or anaesthetized, in the same room and with the same ERG machine, would improve the validity of the ERG results, to allow a more accurate investigation into the presence of a photoreceptor disorder. This was a clinical study. A suspicion of PRA was made based on the history, signalment, full ophthalmic examination before or after surgery and, in the majority of cases, supported by the ERG

results. In this study, the suspicion of PRA was further supported in one case by genetic testing. The cases without an ERG were included following careful selection based on their history, signalment, full ophthalmic examination, the presence of attenuated retinal vascularization and tapetal hyper-reflectivity on funduscopy and if nyctalopia was reported. The ERGs were performed to add weight to the suspicion of PRA. Repeating ERGs at later stages as well as using the standardized protocol for diagnosis of photoreceptor disorders, could have further supported the diagnosis of PRA and aided in the assessment of the progression of vision loss. However, this would have meant, that the patient would require several anaesthesias or sedations, which is not feasible in a clinical setting, it may elicit phototoxic effects on the diseased retina and, in the authors opinion, would not have been in the best interest of the patient.

Many clients mentioned that the photopic vision had returned, however these observations were not reported routinely for every case and therefore these results were not used to report the visual outcome post-surgery. For consistency, the visual outcome was reported based on the presence or absence of menace responses in clinical examinations. However, the menace response is only a crude test for vision and cannot provide detailed information about the degree of photoreceptor degeneration. Furthermore, it would be interesting to analyse the effect of the phototoxic effect of the operating microscope light on retinas with PRA as well as safe exposure time. The use of an ultraviolet radiation filter or a yellow filter could be considered to reduce phototoxicity in patients with PRA, however there is no strong evidence in the literature that this measure would decrease photoreceptor destruction during surgery in cases with PRA. (27,28)

There was no statistical effect of the referral centre, age, gender, abnormality on gonioscopy or ocular ultrasound, cataract stage, dazzle reflex, vision before surgery or IOL placement on

the visual outcome post-surgery as assessed by GEE. The association of funduscopic findings with visual outcome could not be evaluated statistically. The detailed description of findings on fundoscopy varied between clinicians and therefore, funduscopic findings were described only. For the same reasons, it was not possible to establish a standardized approach to assess the progression of the degree of funduscopic changes and their association with the visual outcome in this retrospective study, however this would be an interesting question for future studies. The use of diagnostic imaging like fundus photography or OCT could be considered for standardisation of the findings and to assess for progression of the degree of retinal atrophy.

In this study, owners were contacted and asked about the perceived quality of life of their dog after surgery. The response rate to the questionnaire was 48.2 %. This lies just below the mean response rate for academic studies, which could be explained by the long study period and that some dogs were already deceased at the time of the questionnaire.(29) We cannot base conclusions out of this low response rate. However, we would like to report that, of all responses, 92.5 % owners replied that the quality of life of their dog had improved significantly after surgery.

There are further limitations to this study, due to its retrospective nature, which may have influenced the results. There was loss to follow up, which increased with each re-examination time period and as demonstrated in the tables. Due to the descriptive nature of this study, we decided to still report all long-term results, even though this holds a small potential for overreaching conclusions. Furthermore, we described the PRA diagnosis as ‘suspected’, as most cases were diagnosed by history, signalment, clinical examination and short ERG, but were not confirmed by the recommended protocol for diagnosis of photoreceptor disorders, multiple ERGs, or gene tests in the majority of cases. To address this, we only included cases

with a sufficient follow up and repeatedly confirmed suspicion/diagnosis by diplomates or residents under supervision of diplomates of the ECVO.

Finally, the quality of life questionnaire answered by clients was subjective and further studies to validate a quality of life tool for this purpose are required.

Conclusion:

Phacoemulsification in ECS with suspected PRA and secondary cataract development can be recommended. Visual improvement can be obtained for some time, but as expected the day vision will be lost eventually. No predictor for a successful visual outcome following surgery could be identified. However, vision was present for up to two years in this study population and this was significant when comparing to vision before surgery. ERGs were useful in supporting the suspicion of PRA but no conclusion on visual outcome associated with ERG results could be drawn, as the ERGs were not standardized. The response rate of the questionnaire was low; however, most participants reported an improved quality of life of their dogs.

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Table 1. Summary of ERG protocols used at the RVC, AHT and DWR

Centre	State of consciousness	Dark adaption	ERG protocols
RVC 1 **5 dogs**	Anaesthetized	No dark adaption Light off Five minute dark adaption	1) 3000 mcd.s/m^2, 1 flash each 0s 2) 3000 mcd.s/m^2, 1 flash each 0s 3) 3000 mcd.s/m^2, 4 flashes, 1 each 10s 4) 3000 mcd.s/m^2, 4 flashes, 1 each 10s 5) 3000 mcd.s/m^2, 4 flashes, 1 each 10s 6) 3000 mcd.s/m^2, 4 flashes, 1 each 10s 7) 10000 mcd.s/m^2, 4 flashes, 1 each 20s 8) 10000 mcd.s/m^2, 4 flashes, 1 each 20s 9) Flicker 3000 mcd.s/m^2, 128 flashes, 1 each 0.033s 10) Flicker 3000 mcd.s/m^2, 128 flashes,1 each 0.033s
RVC 2 **9 dogs**	Anaesthetized	One minute dark adaption	1) 0 mcd.s/m^2, 4 flashes, 1 each 1s, 2) 0 mcd.s/m^2, 4 flashes,1 each 1s 3) 10 mcd.s/m^2, 10 flashes,1 each 2s 4) 10 mcd.s/m^2, 10 flashes, 1 each 2s 5) 3000 mcd.s/m^2, 4 flashes, 1 each 10s 6) 3000 mcd.s/m^2, 4 flashes, 1 each 10s 7) 10000 mcd.s/m^2, 4 flashes, 1 each 20s 8) 10000 mcd.s/m^2, 4 flashes,1 each 20s 9) Flicker 3000 mcd.s/m^2, 128 flashes, 1 each 0.033s 10) Flicker 3000 mcd.s/m^2, 128 flashes, 1 each 0.033s
AHT **30 dogs**	Conscious	One minute dark adapted	64 lx.s at a distance of 30 cm, 10 flashes (averaged), manually elicited, flash duration of 10 ms Intensitiy control: 7 steps linear control. Used: Step 7
DWR **2 dogs**	Conscious	Not dark adapted	9000 mcd, 10 flashes (averaged) each 400 ms (2.59Hz)

Legend: mcd.s/m^2 = millicandelas.second/square metre, s = second, ms = millisecond, Hz = Herz

Table 2. Summary of visual outcome per eye before and after surgery and significance of visual improvement compared to before surgery

Time	All eyes n	Visual	Percent (%)	Blind	Percent (%)	Missing	McNemar p
Before surgery	85	19	22.4	66	77.6		
P1*	85	75	88.2	10	11.8		0.000
P2*	63	58	92.1	5	7.9	22	0.000
P3*	46	44	96.7	2	4.3	39	0.000
P4*	32	31	96.9	1	3.1	53	0.000
P5*	19	16	84.2	3	15.8	66	0.003
P6	15	9	60.0	6	40.0	70	0.289
P7	10	6	60.0	4	40.0	75	0.453

P = time period, p = significance level

Table 3. Summary of visual outcome following surgery, of eyes that had a flat ERG trace before surgery and significance of visual improvement compared to before surgery

Time	Flat ERG before surgery n	Visual	Percent (%)	Blind	Percent (%)	Missing	McNemar p
Before surgery	30	5	16.7	25	83.3		
P1*	30	22	73.3	8	26.7		0.000
P2*	21	17	81.0	4	19.0	9	0.000
P3*	10	8	80.0	2	6.7	20	0.031
P4*	8	7	87.5	1	12.5	22	0.031
P5	5	4	80.0	1	3.3	25	0.250
P6	4	2	50.0	2	50.0	26	1.000
P7	3	2	66.7	1	33.3	27	1.000

P = time period, p = significance level

Figure 1. Summary of visual and blind eyes before and after surgery. Missing eyes were lost to follow up. Significant improvement of visual outcome was marked with *

Figure 2. Operated vs not operated eyes. One box represents the visual outcome of one eye per exam period. Development of an eye can be followed from left to right. Black boxes stand for blind eyes, grey boxes for visual eyes, white boxes stand for loss to follow up or menace response not specified

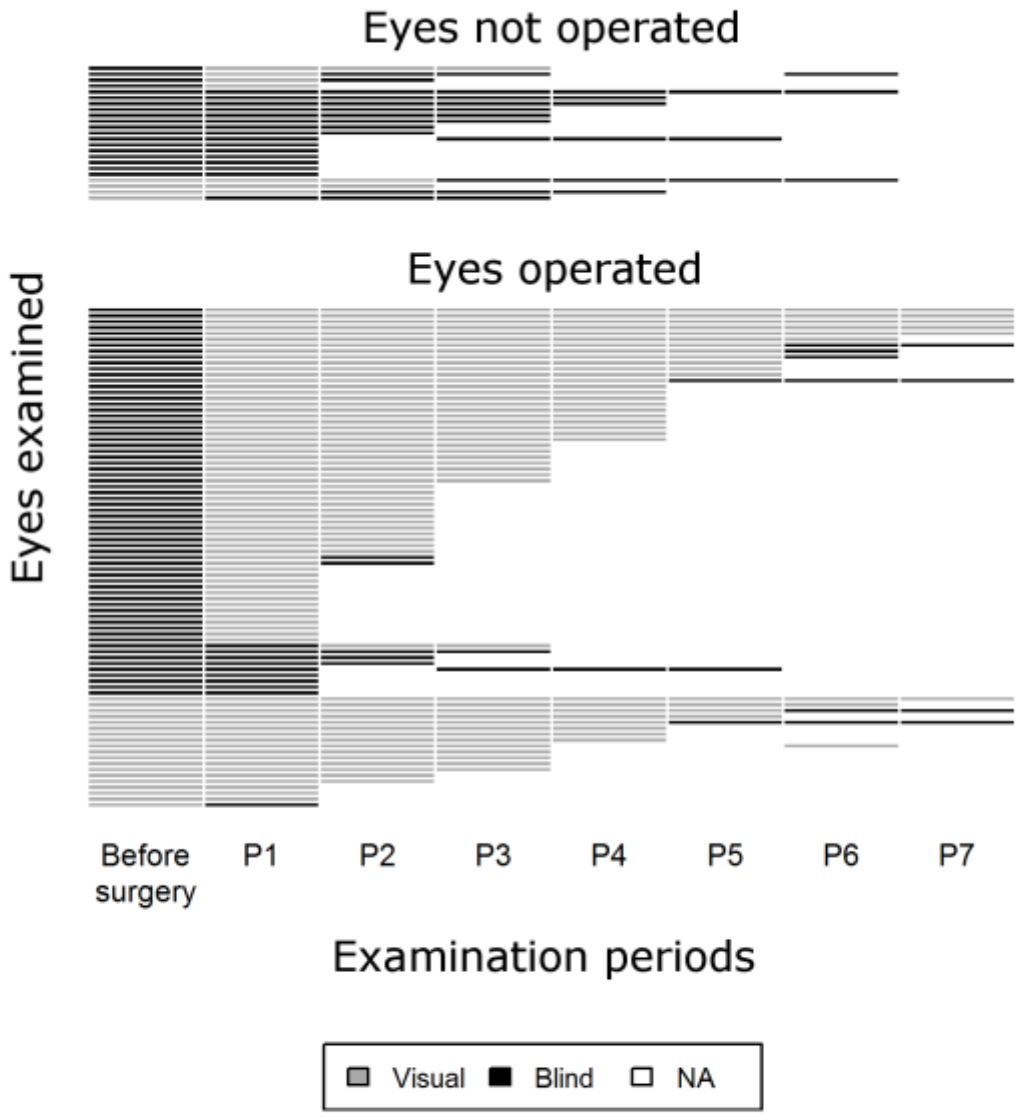

Figure 3. Summary of visual outcome of eyes that had a flat ERG trace before surgery.

Significant improvement of visual outcome was marked with *

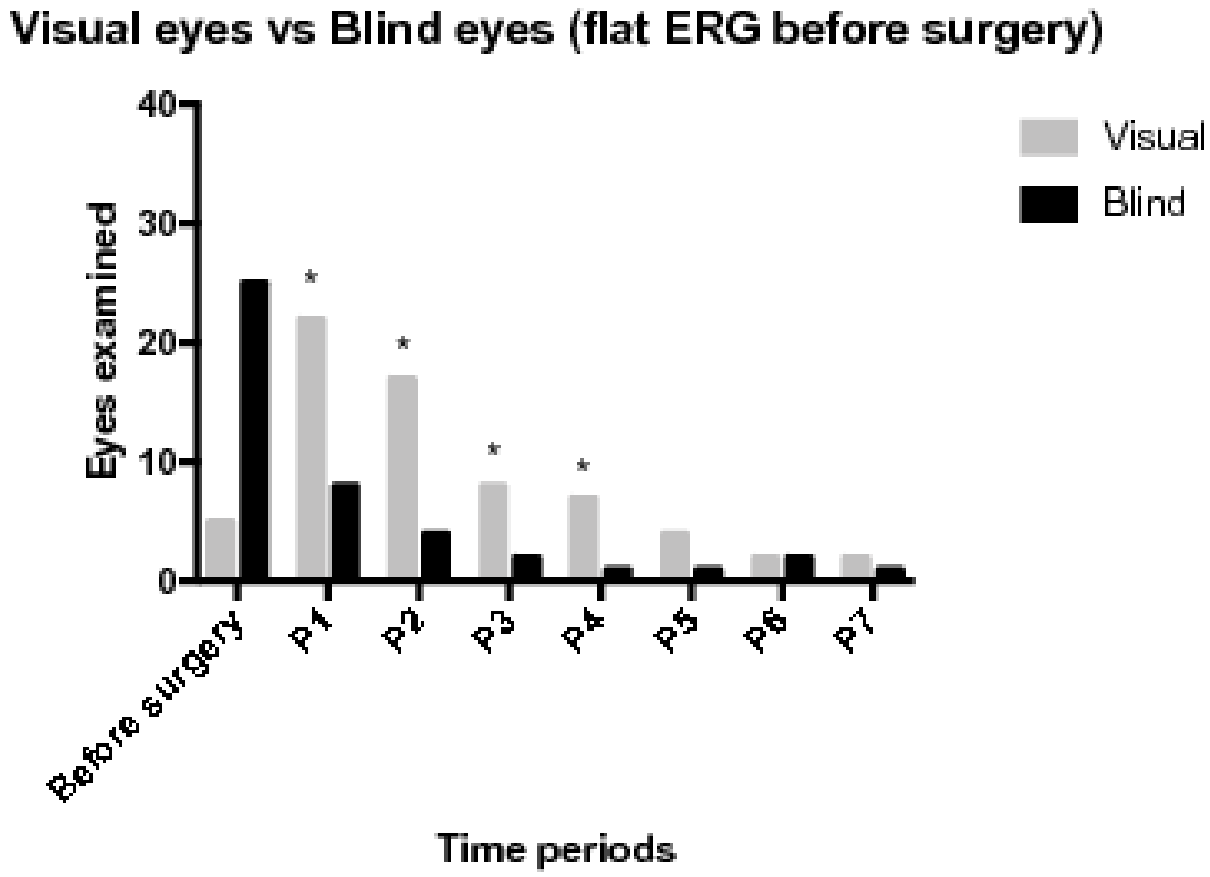

Figure 4. Summary of complications diagnosed at re-examinations at all time periods post-surgery