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Long Term Visual Outcomes of Glaucoma Patients Following a Single Episode of Transscleral Cyclodiode Laser Treatment

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Objectives: To investigate the efficacy of a single cyclodiode laser photocoagulation treatment for refractory glaucoma and its effect on visual outcome in patients with good visual potential as well as to evaluate possible predictive factors in establishing optimal treatment parameters.

Design: Retrospective observational study

Setting: Tertiary referral centre

Participants: The notes of 87 patients with refractory glaucoma who underwent cyclodiode photocoagulation as a first surgical intervention over a 7-year period.

Main outcome measures: Maintenance of intraocular pressure reduction, number of medications and visual acuity outcomes post-treatment.

Results: The mean intraocular pressure (IOP) after a single treatment decreased from 39.5 +/-1.3 mmHg to 17.8+/-1.5 mmHg after a 6-week follow-up period (P<0.0001). This reduction in IOP was maintained over a 3-year period. Here 61.5% of the patients were able to reduce the number of medications used, with mean reduction from 2.6 to 1.5 medications (P<0.05). Mean initial visual field loss prior to treatment was 8.74dB and at 6 months post-treatment was measured at 9.06dB (P>0.05) suggesting no significant overall change. The visual acuity remained unchanged or improved for 83.6% of the patients (P>0.05) with relatively good visual potential (average vision preoperatively was 0.57 logMAR). Hypotony occurred in 5.3% of the patients. No patients required enucleation or evisceration.

Conclusion: A single session of cyclodiode laser therapy was sufficient to achieve IOP reduction in the majority of the patients with refractory glaucoma. The majority were able to maintain the IOP reduction over a 3-year period without the need for a

further surgical intervention. Additionally, over 80% of the patients in our study were able to maintain their baseline visual acuity. These results support the view that a single cyclodiode treatment can be sufficient in achieving long term IOP control and may be considered in eyes with relatively good visual potential.

Introduction:

Transscleral diode laser cyclophotocoagulation (cyclodiode) has been established as a relatively safe and effective intervention for glaucoma.[1-6] Cyclodiode is often used in refractory glaucoma, where alternative surgical approaches, such as antiproliferative augmented trabeculectomy and tube shunt surgery, may sometimes be judged less appropriate, for example in eyes with poor visual potential. Additionally, cyclodiode has been shown to be safer than other cyclodestructive procedures, such as Nd:YAG laser cyclophotocoagulation and cyclocryotherapy, which present a greater risk of hypotony and phthisis resulting from excessive ciliary body ablation.[7–9] However, the outcome of cyclodiode therapy is unpredictable and multiple treatments may be required to achieve long term intraocular control.[10-11]

Currently there is no general consensus for an optimum treatment protocol for cyclodiode. Data for outcomes following cyclodiode laser vary considerably in the literature.[12] Parameters such as total delivered energy per eye, number of laser applications per treatment, pulse power, pulse duration and proportion of circumference treated have been analysed with varying results.[13–17] Furthermore, cyclodiode therapy has often been reserved for eyes with poor vision due to reports that it can lead to decrease in visual acuity.[18]

The purpose of this study was to evaluate the long-term safety and efficacy of a single episode of transscleral diode laser cyclophotocoagulation for raised intraocular pressure in patients with good visual potential at a UK tertiary glaucoma referral centre. Additionally, we aim to identify possible predictive factors that could establish optimal treatment parameters by investigating the relation between laser energy delivered and degrees treated to the long-term maintenance in IOP reduction.

Methods:

The departmental electronic medical record system (Medisoft Ophthalmology, Medisoft Ltd Leeds UK) and operating theatre log books were examined for the period 09/2004 to 06/2011 to identify patients who had undergone cyclodiode treatment as a first surgical intervention.

All patients were assessed for their response to treatment and those who did not achieve the target IOP reduction were taken as treatment failures. The patients who required either repeat cyclodiode or alternative treatments for IOP control during the follow up period were also considered as treatment failures from the time of the additional surgical intervention. They were not further assessed for maintenance of post-operative IOP as any additional surgical interventions would interfere with the interpretation of the IOP maintenance data.

Cyclophotocoagulation was performed in the Operating Theatre under subtenon, peribulbar or general anaesthesia using a standard treatment protocol. A lid speculum was placed to achieve adequate exposure for probe placement all around the limbus and a squint hook was used to rotate the globe to achieve exposure in those with narrow palpebral apertures. All treatments were performed using Oculight Sx semiconductor diode 810nm laser and the contact G Probe™ (IRIS Medical

Instruments, Inc.). Standard settings were 1500ms duration and 1500mW power. The energy levels were not routinely titrated for ‘pops’ and the power settings were left at 1500mW. Transillumination was performed for ciliary body identification. Usually 10 applications were applied per quadrant for 180 to 360°, with the applications spaced approximately one-half width of the probe tip apart. The 3 and 9 o’clock positions were avoided to spare the long ciliary nerves. Postoperative steroid drops were used for 4 weeks. Glaucoma medications were continued after cyclodiode treatment and adjusted later as required.

Success was defined as an intraocular pressure (IOP) of 6–21 mmHg at the last follow-up visit without the need for oral acetazolamide and an IOP reduction of at least 30% compared with pre-treatment. Hypotony was defined as an IOP of 5 mmHg or less. The laser energy used was classified as either low energy (median value 45 +/- 11.47 J, range 22.5-67.5J) or high energy (median value 90 +/- 13.42 J, range 67.5-130J). The follow up period in IOP measurements was 3 years. Visual acuity (VA) prior to treatment was assessed for all patients using LogMAR scale. Visual field testing was performed with the Humphrey Visual Field Analyser™ using the SITA 24-2 threshold programme. Mean deviation of visual field sensitivity loss in decibels (MD) was taken as our surrogate measure of visual field loss.

Data was analysed using Microsoft Excel™ and where appropriate a Student’s t-test was used to calculate p-values. R^2 values were derived from linear regression analyses using the same programme. Kaplan-Meier ‘survival’ analysis was done using GraphPad Prism 5.0™. Approval for the audit was granted by the Cambridge

University Hospitals NHS Foundation Trust Ethics Committee. The tenets of the Declaration of Helsinki were observed.

Results:

From our records, we were able to identify 104 patients who underwent cyclodiode therapy as a first surgical treatment modality in the period from 09/2004 to 06/2011 at Addenbrooke's Hospital, Cambridge. Of these, complete medical records were available for 87 patients with follow up data available for up to 3 years. Preoperative patient data is summarised in **Table 1**.

Table 1. Baseline demographics and clinical parameters

	Category	Cases (n=87)
Mean age, yrs		66.3
Sex (n (%))	Male	49 (56.3%)
	Female	38 (43.7%)
Preoperative VA, mean		0.57 LogMAR
IOP (mmHg), mean (SD)		39.5 +/- 1.3 mmHg
Mean number of glaucoma medications		2.6
Glaucoma type (n (%))	Primary open angle glaucoma (POAG)	33 (37.9%)
	Primary angle closure glaucoma (PACG)	6 (6.9%)
	Neovascular glaucoma	25 (28.7%)
	Uveitic glaucoma	5 (5.7%)
	Secondary open angle glaucoma (SOAG)- Other	18 (20.8%)

Change in Intraocular Pressure (Fig.1A)

Mean intraocular pressure (IOP) decreased significantly from 39.5 mmHg (SE 1.26) before cyclodiode therapy to 17.8 mmHg (SE 1.51) at 6 weeks post-treatment, an observable reduction of 45.1 % (P<0.0001). There was a mild linear correlation between preoperative IOP and observed IOP reduction (R^2 = 0.32).

Safety and Efficacy of Cyclodiode Treatment (Fig.1B)

An IOP reduction greater than 30% of initial IOP was achieved at 6 weeks in 67.7 % of the patients, while hypotony occurred in only 5 cases or 5.3% of patients ($p<0.05$). None of the patients experienced post-treatment uveitis or required further treatment or enucleation for pain symptoms. The data for the patients who developed hypotony such as initial diagnosis, treatment settings, IOP measurements and VA outcome is summarised in **Table 2**.

Table 2. Details of hypotony patients

	Diagnosis	Energy used	Degrees treated	Peak IOP (mmHg)	Postop IOP (mmHg)	Hypotony duration	Last IOP (mmHg)	Preop VA (LogMAR)	Last VA (LogMAR)
PT1	Neovascular	90J	180	58	2	6 months	10	0.78	PL
PT2	Neovascular	90J	360	41	4	6 months	32	PL	NPL
PT3	Neovascular	120J	360	40	2	6 months	9	0.6	HM
PT4	SOAG(other)	120J	360	26	3	6 months	8	1.0	CF
PT5	SOAG(other)	120J	360	48	2	-	3	HM	HM

Long term maintenance of IOP reduction after a single cyclodiode treatment (Fig.1C)

The IOP reduction was maintained long term over the period of 3 years in the majority of our patients. Measurements were taken pre-operatively (39.5+/-1.3 mmHg) as well as post-operatively at 6 weeks (17.8+/-1.5 mmHg) and 6 months (19.6+/-1.5 mmHg) for all patients. Patients who required additional procedures in that eye post-treatment were excluded from further analysis from the time point of additional intervention as it would artificially lower their IOP measurements The follow-up measurements at 1 year (18.9 mmHg), 2 year (22.1 mmHg) and 3 years (21.7 mmHg) were all after a single cyclodiode treatment.

Kaplan-Meier analysis of IOP reduction 'survival' following a single cyclodiode treatment (Fig.2)

Success was defined as an intraocular pressure (IOP) of 6–21 mmHg at the last follow up visit without the need for oral acetazolamide and an IOP reduction of at least 30% compared with preoperatively. The proportion of patients to maintain the desired IOP reduction after a single cyclodiode treatment without the need for further IOP lowering intervention in our study was 67.7% at 6 weeks post-operatively, 66.2% at 6 months, 63% at 1 year, 61.2% at 2 years and 61.2% at 3 years. Of the patients who responded to treatment at 6 weeks, 90.4% were able to maintain the IOP reduction over a period of 3 years.

Cyclodiode effect on glaucoma medications (Fig.3A)

A significant proportion of the patients (61.5%) were able to decrease the number of medications they are taking for IOP control following cyclodiode. A decrease of 2 medications or more was achieved by 34.6% of patients, while 26.9% of patients decreased their medication by one. Overall, the average number of medications decreased from 2.6 before cyclodiode treatment to 1.5 medications after cyclodiode treatment ($P<0.05$).

Change in visual acuity (Fig.3B)

A single episode of cyclodiode treatment had no significant effect on visual acuity (VA). Mean VA measurements changed from 0.5720 Log MAR units before cyclodiode therapy to 0.5408 Log MAR units post treatment, which was not statistically significant ($P>0.05$). The data analysis was performed on 47 patients (54.1%), who had clearly annotated numerical values for their VA measurements both preoperatively and postoperatively. The boxed numerals in the graph represent the number of values at the same point.

Change in visual fields (Fig.3C)

The average visual field sensitivity remained almost unchanged with an average MD value of -8.74 dB pre-treatment compared to MD value of -9.05 dB at 6 months post-treatment, which was not statistically significant (P>0.05). The data analysis was performed on 36 patients (41.3%), who had clearly annotated numerical values for their visual fields measurements both pre-operatively and post-operatively.

Effect of laser energy on IOP reduction (Fig.4A)

Of the patients that received high energy treatment (90J), 80.3% obtained pressure reduction of >30% of initial IOP compared with 56.8% in the patients that received low energy treatment (45J).

Effect of laser energy on visual acuity (Fig.4B)

Of the patients that received high energy treatment (90J), 18.6% noted improvement of the equivalent of at least 1 Snellen line compared with 6.7% in the patients that received low energy treatment.

Effect of degrees treated on IOP reduction (Fig.4C)

Of the patients that underwent 360 degrees treatment, 71.4% obtained pressure reduction greater than 30% of initial IOP compared with 55% of the patients that underwent 180 degree treatment.

Effect of degrees treated on visual acuity (Fig.4D)

Of the patients that underwent 360 degrees treatment, 20.9% noted improvement of the equivalent of at least 1 Snellen line compared with 5.5% of the patients underwent 180 degree treatment.

Discussion:

The results of this retrospective analysis are supportive of a single cyclodiode treatment being effective in management of refractory glaucoma. Although this is a retrospective rather than a prospective study, we aimed to avoid selection bias by including all patients either as success or failure of treatment. The patients who required additional surgical interventions were taken as failure from the time of additional intervention.

Our data show that 67.7% of the patients achieved an IOP reduction greater than 30% of presenting IOP at 6 weeks and 61.5% could reduce the number of medications by at least 1. Hypotony appears to be related to the type of glaucoma (with neovascular glaucoma associated with worse outcome) as well as to the number of degrees treated and total energy used. Indeed, the patients with neovascular glaucoma in our cohort were almost 4 times more likely to develop hypotony compared to any other types of glaucoma.

In our patients, the mean intraocular pressure (IOP) decreased significantly from 39.5 mmHg (SE 1.26) before cyclodiode therapy to 17.8 mmHg (SE 1.51) at 6 weeks post-treatment, an observable reduction of 45.1 % ($P<0.05$). The results of the linear regression analysis indicate that there might be some predictive value in determining

IOP reduction based on initial IOP measurements such as the greatest reduction in IOP is likely to be seen in patients with the highest IOP at the time of treatment (R^2 = 0.32). A similar relationship was reported by Vernon et al., where eyes with IOP greater than 30 mmHg were more likely to exhibit a pressure drop greater than 30% of initial IOP.[19]

The IOP reduction was maintained long term in 61.2% of all patients in our study after a single cyclodiode treatment. Of the patients who responded to treatment at 6 weeks, 90.4% were able to maintain the IOP reduction over a period of 3 years. Similar sustainability of the mean IOP reduction postoperatively is also reported by Bloom et al. and Kosoko et al., although in both these studies the follow up was considerably shorter, the average time being less than 2 years.[18,20] The results from our patient cohort suggest that a single session of cyclodiode therapy could potentially be a viable initial treatment modality for maintaining a longer term IOP control in patients with refractory glaucoma.

In our study, of the patients that received high energy treatment (90J), 80.3% obtained an IOP reduction of greater than 30% of the initial IOP compared with 56.8% in the patients receiving low energy treatment (45J). This is consistent with a meta-analysis by Iliev et al., where comparing different laser protocols from different studies suggested that the use of a low energy protocol potentially could result in the lowest IOP reduction, the highest postoperative IOP and the highest retreatment rate overall.[17] We also observed similar relationship when patients were assessed in regard to the degrees treated rather than energy used. Here, of the patients that underwent

360 degrees treatment, 71.4% obtained pressure reduction greater than 30% of initial IOP compared with 55% of the patients that underwent 180 degrees treatment.

Hypotony was the most common long-term complication in our study (5.3%), which is in accordance with other published reports.[14] In our cohort, the incidence of hypotony was much more likely with an eye with neovascular glaucoma (**Table 2**). Murphy et al. also found a higher risk of hypotony in eyes with neovascular glaucoma, particularly if preoperative IOP was high and energy level used was greater.[14] This correlation between hypotony and higher energy used in cyclodiode is also observed in several other studies.[12] However, univariate regression analysis done by Murphy et al. shows that very high pre-treatment IOP alone, possibly causing ciliary body ischaemia, could be responsible for the high incidence of hypotony in the patients receiving high-energy treatment in their study. [14]

Additionally, in a retrospective analysis of 209 eyes by Bloom et al., a very low incidence of hypotony (1%) was observed with a high energy protocol when the mean energy used was 90J.[18] Furthermore, Iliev et al. report in their study that eyes developing hypotony had not received higher energies compared with eyes that maintained normal IOP.[17] Therefore, the intention to reduce hypotony risk by using a lower laser power and fewer applications per treatment should be weighed against the possibility for a lower efficacy of the cyclodiode treatment.

Visual acuity (VA) remained unchanged for the majority of our patients who underwent cyclodiode treatment (69.9%). In our study 16.4% reported deterioration in VA of 1 Snellen line, while 13.7% of the patients reported an improvement in VA of

1 Snellen line after 6 weeks. The latter probably resulted either from resolution of preoperative corneal oedema or inter-observer variation in visual acuity testing. Similar results are also reported in a study by Murphy et al., where the VA remained the same in 74.6% of the patients at 6 months following cyclodiode treatment.[14] In our study most patients with difficult to manage glaucoma retained their good VA in the long-term following cyclodiode treatment. The proportion losing two Snellen lines is actually better than that reported after trabeculectomy or tube surgery.[21] These results suggest a possible role for the use of transscleral cyclodiode treatment in eyes with relatively good visual potential, however, further controlled prospective studies would be required to better define this role.

This study is the first to measure the mean deviation (MD) values for the patients both pre-operatively and post-operatively in order to provide a more objective assessment of glaucoma related visual loss. The MD values in our patients remained virtually unchanged after cyclodiode treatment from -8.74dB preoperatively to -9.05 dB postoperatively. Previously it has been reported that the most frequent cause of visual loss was further progression of glaucoma, which was an attributable cause in over half of the cases.[22] The peri-operative visual field assessment presented in this study suggests that the maintenance of VA observed in the majority of the patients following cyclodiode treatment could be due to a good postoperative IOP control. There are no previous retrospective or prospective studies evaluating visual field measurements peri-operatively in patients undergoing cyclodiode treatment and this most likely reflects the difficulties associated with performing the tests in patients with poor VA. Our study therefore is the first to provide a standardised measurable evidence of maintenance of patients' visual fields as a marker of glaucoma progression following a single cyclodiode treatment. Our study's main limitations are its retrospective nature and the absence of a control group to distinguish the adverse effects of the treatment from the natural history of the underlying disease.

The results of this study suggest that the IOP reduction after cyclodiode treatment could potentially prevent further deterioration in the glaucoma patients' vision. Currently, according to the UK National Cyclodiode Survey Study only 60% of practitioners would perform cyclodiode procedure in the presence of good visual acuity.[12] Until recently, cyclodiode treatment has been associated with subsequent loss of VA in significant percentage of the patients.[18,23,24] However, cyclodiode use in eyes with useful vision has already been proposed in several studies.[19,22-25] Furthermore, the risk of VA loss in patients after multiple cyclodiode treatments does not appear to be any greater than that after any other surgical modality used for treating patients with glaucoma as reported in a study by Rotchford et al.[24]

In our study, the better outcome in visual acuity was most pronounced in the high energy group, probably due to the more effective IOP control. Of the patients that received high energy treatment (90J), 18.6% noted improvement of at least 1 Snellen line compared with 6.7% in the patients that received low energy treatment (45J). Similar results are observed when patients were assessed in regard to the degrees treated. Here, of the patients that underwent 360 degrees treatment, 20.9% noted improvement of the equivalent of at least 1 Snellen line compared with 5.5% of the patients underwent 180 degrees treatment.

In conclusion, conventional diode cyclophotocoagulation is a safe and effective treatment for refractory glaucoma characterised by low incidence of complications. IOP pressure can be effectively reduced in patients with glaucoma after a single cyclodiode treatment without adverse effects on VA over a 3 year period in majority of the patients. Hypotony is the main risk of treatment and might be limited by reducing the laser energy applied to less than 90J, particularly for patients with neovascular glaucoma**.**

Figure and Table Legends

Figure 1 (A) Change in Intraocular Pressure following a single Cyclodiode treatment (**B**) Safety and Efficacy of Cyclodiode Treatment (**C**) IOP reduction was maintained long-term over the period of 3 years after single treatment

Figure 2 Kaplan-Meier analysis for cumulative proportion of success in IOP control after a single Cyclodiode treatment. Survival was defined as sustained IOP drop of at least 30% compared with pre-treatment or sustained intraocular pressure (IOP) of 6–21 mmHg without the need for additional IOP lowering medications or further surgical interventions.

Figure 3 (A) Cyclodiode effect on antiglaucoma medications (**B**) Preoperative and postoperative visual acuity measurements in LogMAR units after a single Cyclodiode treatment (**C**) Preoperative and postoperative visual field loss taken from MD values (dB) on the HVF analyser after a single Cyclodiode treatment

Figure 4 (A) Effect of laser energy on IOP reduction **(B)** Effect of laser energy on visual acuity (VA) **(C)** Effect of degrees treated on IOP reduction **(D)** Effect of degrees treated on visual acuity (VA)

Table 1 Baseline demographics of the patients and clinical parameters including diagnostic features, pre-operative IOP and visual acuity assessments.

Table 2 Details of the patients who developed hypotony including diagnostic and treatment features, peri-operative IOP assessments and duration of hypotony

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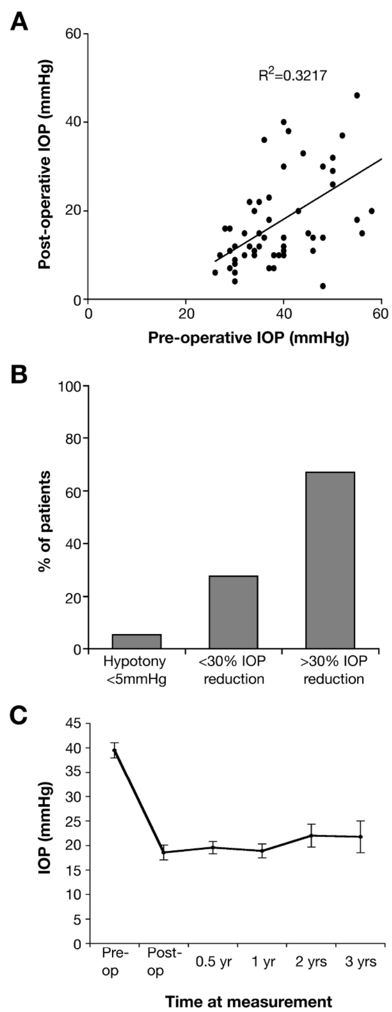

Figure 1

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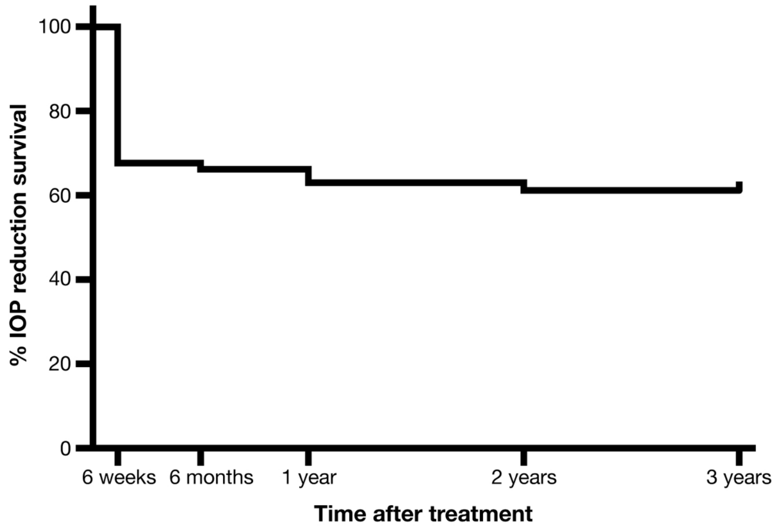

Figure 2

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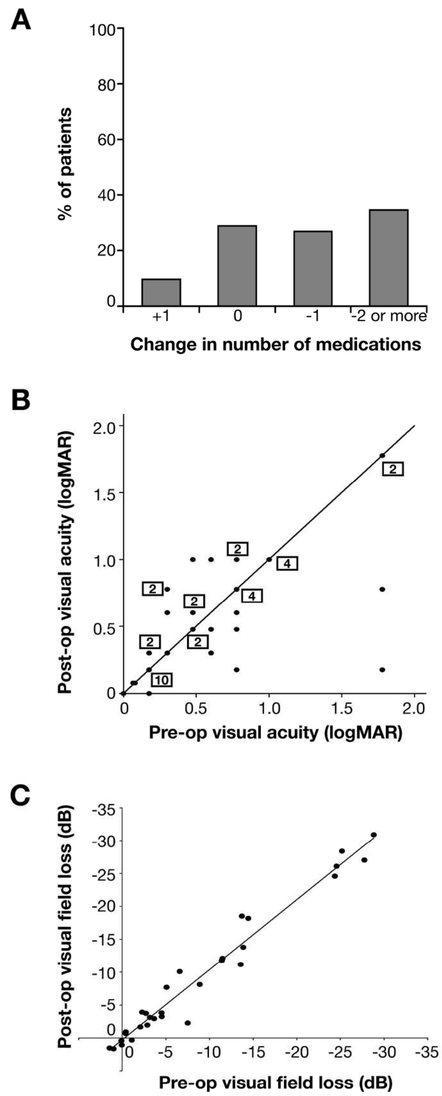

Figure 3

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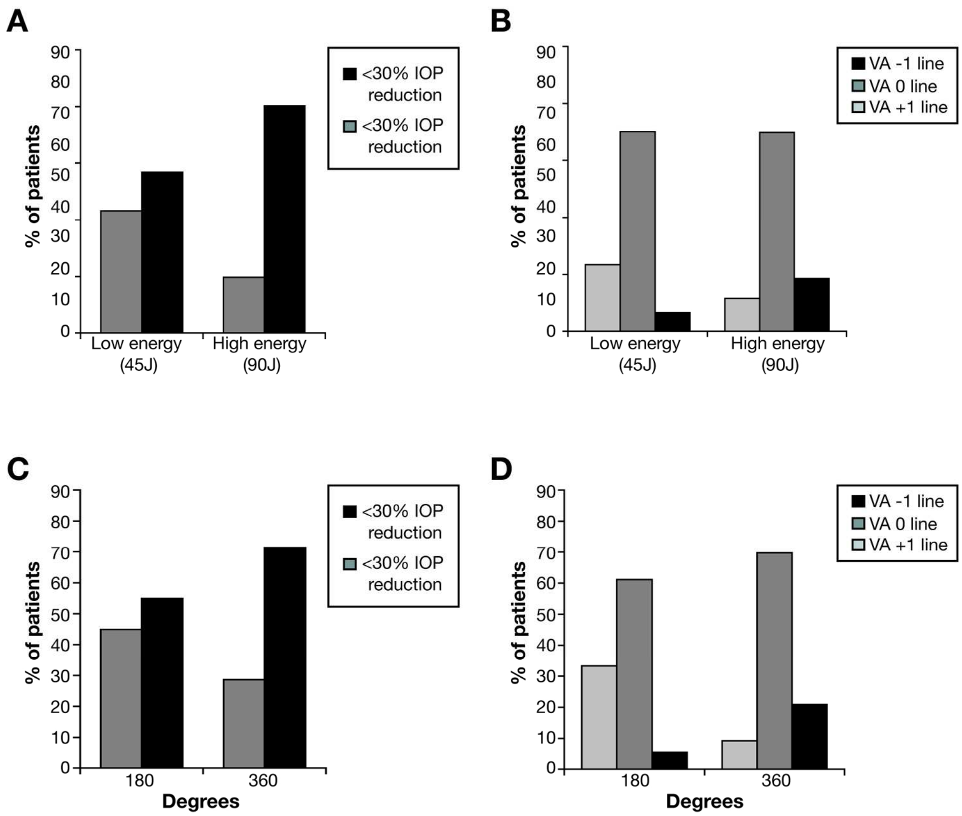

Figure 4

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A Retrospective Analysis of Long Term Outcomes Following a Single Episode of Transscleral Cyclodiode Laser Treatment in Glaucoma Patients

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Main outcome measures: Maintenance of intraocular pressure reduction, number of medications and visual acuity outcomes post-treatment.

Results: The mean intraocular pressure (IOP) after a single treatment decreased from 39.5 +/-1.3 mmHg to 17.8+/-1.5 mmHg after a 6-week follow-up period ($P<0.0001$). This reduction in IOP was maintained over a 3-year period. Here 61.5% of the patients were able to reduce the number of medications used, with mean reduction from 2.6 to 1.5 medications ($P<0.05$). Mean initial visual field loss prior to treatment was 8.74dB and at 6 months post-treatment was measured at 9.06dB ($P>0.05$) suggesting no significant overall change. The visual acuity remained unchanged or improved for 83.6% of the patients ($P>0.05$) with relatively good visual potential (average vision preoperatively was 0.57 logMAR). Hypotony occurred in 5.3% of the patients. No patients required enucleation or evisceration.

Conclusion: A single session of cyclodiode laser therapy was associated with significant IOP reduction in the majority of the patients with refractory glaucoma. The

majority were able to maintain the IOP reduction over a 3-year period without the need for a further surgical intervention. Additionally, over 80% of the patients in our study were able to maintain their baseline visual acuity. These results support the view that a single cyclodiode treatment can be sufficient in achieving long term IOP control and may be considered in eyes with relatively good visual potential.

Introduction:

Transscleral diode laser cyclophotocoagulation (cyclodiode) has been established as a relatively safe and effective intervention for glaucoma.[1-6] Cyclodiode is often used in refractory glaucoma, where alternative surgical approaches, such as antiproliferative augmented trabeculectomy and tube shunt surgery, may sometimes be judged less appropriate, for example in eyes with poor visual potential. Additionally, cyclodiode has been shown to be safer than other cyclodestructive procedures, such as Nd:YAG laser cyclophotocoagulation and cyclocryotherapy, which present a greater risk of hypotony and phthisis resulting from excessive ciliary body ablation.[7–9] However, the outcome of cyclodiode therapy is unpredictable and multiple treatments may be required to achieve long term intraocular control.[10-11]

Currently there is no general consensus for an optimum treatment protocol for cyclodiode. Data for outcomes following cyclodiode laser vary considerably in the literature.[12] Parameters such as total delivered energy per eye, number of laser applications per treatment, pulse power, pulse duration and proportion of circumference treated have been analysed with varying results.[13–17] Furthermore, cyclodiode therapy has often been reserved for eyes with poor vision due to reports that it can lead to decrease in visual acuity.[18]

The purpose of this study was to evaluate the long-term safety and efficacy of a single episode of transscleral diode laser cyclophotocoagulation for raised intraocular pressure in patients with good visual potential at a UK tertiary glaucoma referral centre. The retrospective nature of the study design reflected the need to analyse multiple clinical variables and evaluate different types of outcomes as well as their progression over several years. Additionally, such a study could facilitate the identification predictive factors for optimal treatment parameters by investigating the relation of laser energy delivered and degrees treated to the long-term maintenance in IOP reduction.

Methods:

The departmental electronic medical record system (Medisoft Ophthalmology, Medisoft Ltd Leeds UK) and operating theatre log books were examined for the period 09/2004 to 06/2011 to identify patients who had undergone cyclodiode treatment as a first surgical intervention.

All patients were assessed for their response to treatment and those who did not achieve the target IOP reduction were taken as treatment failures. The patients who required either repeat cyclodiode or alternative treatments for IOP control during the follow up period were also considered as treatment failures from the time of the additional surgical intervention. They were not further assessed for maintenance of post-operative IOP as any additional surgical interventions would interfere with the interpretation of the IOP maintenance data.

Cyclophotocoagulation was performed in the Operating Theatre under subtenon, peribulbar or general anaesthesia using a standard treatment protocol. A lid speculum was placed to achieve adequate exposure for probe placement all around the limbus and a squint hook was used to rotate the globe to achieve exposure in those with narrow palpebral apertures. All treatments were performed using Oculight Sx semiconductor diode 810nm laser and the contact G Probe™ (IRIS Medical Instruments, Inc.). Standard settings were 1500ms duration and 1500mW power. The energy levels were not routinely titrated for 'pops' and the power settings were left at 1500mW. Transillumination was performed for ciliary body identification. Usually 10 applications were applied per quadrant for 180 to 360°, with the applications spaced approximately one-half width of the probe tip apart. The 3 and 9 o'clock positions were avoided to spare the long ciliary nerves. Postoperative steroid drops were used for 4 weeks. Glaucoma medications were continued after cyclodiode treatment and adjusted later as required.

Success was defined as an intraocular pressure (IOP) of 6–21 mmHg at the last follow-up visit without the need for oral acetazolamide and an IOP reduction of at least 30% compared with pre-treatment. Hypotony was defined as an IOP of 5 mmHg or less. The laser energy used was classified as either low energy (median value 45 +/- 11.47 J, range 22.5-67.5J) or high energy (median value 90 +/- 13.42 J, range 67.5-130J). The follow up period in IOP measurements was 3 years. Visual acuity (VA) prior to treatment was assessed for all patients using LogMAR scale. Visual field testing was performed with the Humphrey Visual Field Analyser™ using the SITA 24-2 threshold programme. Mean deviation of visual field sensitivity loss in decibels (MD) was taken as our surrogate measure of visual field loss.

Data was analysed using Microsoft Excel™ and where appropriate a Student's t-test was used to calculate p-values. R^2 values were derived from linear regression analyses using the same programme. Kaplan-Meier 'survival' analysis was done using GraphPad Prism 5.0™. Approval for the audit was granted by the Cambridge University Hospitals NHS Foundation Trust Ethics Committee. The tenets of the Declaration of Helsinki were observed.

Results:

From our records, we were able to identify 104 patients who underwent cyclodiode therapy as a first surgical treatment modality in the period from 09/2004 to 06/2011 at Addenbrooke's Hospital, Cambridge. Of these, complete medical records were available for 87 patients with follow up data available for up to 3 years. Preoperative patient data is summarised in **Table 1**.

Table 1. Baseline demographics and clinical parameters

	Category	Cases (n=87)
Mean age, yrs		66.3
Sex (n (%))	Male	49 (56.3%)
	Female	38 (43.7%)
Preoperative VA, mean		0.57 LogMAR
IOP (mmHg), mean (SD)		39.5 +/- 1.3 mmHg
Mean number of glaucoma medications		2.6
Glaucoma type (n (%))	Primary open angle glaucoma (POAG)	33 (37.9%)
	Primary angle closure glaucoma (PACG)	6 (6.9%)
	Neovascular glaucoma	25 (28.7%)
	Uveitic glaucoma	5 (5.7%)
	Secondary open angle glaucoma (SOAG)- Other	18 (20.8%)

Change in Intraocular Pressure (Fig.1A)

Mean intraocular pressure (IOP) decreased significantly from 39.5 mmHg (SE 1.26) before cyclodiode therapy to 17.8 mmHg (SE 1.51) at 6 weeks post-treatment, an observable reduction of 45.1 % (P<0.0001). There was a mild linear correlation between preoperative IOP and observed IOP reduction ($R^2 = 0.32$).

Safety and Efficacy of Cyclodiode Treatment (Fig.1B)

An IOP reduction greater than 30% of initial IOP was achieved at 6 weeks in 67.7 % of the patients, while hypotony occurred in only 5 cases or 5.3% of patients (p<0.05). None of the patients experienced post-treatment uveitis or required further treatment or enucleation for pain symptoms. The data for the patients who developed hypotony such as initial diagnosis, treatment settings, IOP measurements and VA outcome is summarised in **Table 2**.

Table 2. Details of hypotony patients

	Diagnosis	Energy used	Degrees treated	Peak IOP (mmHg)	Postop IOP (mmHg)	Hypotony duration	Last IOP (mmHg)	Preop VA (LogMAR)	Last VA (LogMAR)
PT1	Neovascular	90J	180	58	2	6 months	10	0.78	PL
PT2	Neovascular	90J	360	41	4	6 months	32	PL	NPL
PT3	Neovascular	120J	360	40	2	6 months	9	0.6	HM
PT4	SOAG(other)	120J	360	26	3	6 months	8	1.0	CF
PT5	SOAG(other)	120J	360	48	2	-	3	HM	HM

Long term maintenance of IOP reduction after a single cyclodiode treatment (Fig.1C)

The IOP reduction was maintained long term over the period of 3 years in the majority of our patients. Measurements were taken pre-operatively (39.5+/-1.3 mmHg) as well as post-operatively at 6 weeks (17.8+/-1.5 mmHg) and 6 months

(19.6+/-1.5 mmHg) for all patients. Patients who required additional procedures in that eye post-treatment were excluded from further analysis from the time point of additional intervention as it would artificially lower their IOP measurements The follow-up measurements at 1 year (18.9 mmHg), 2 year (22.1 mmHg) and 3 years (21.7 mmHg) were all after a single cyclodiode treatment.

Kaplan-Meier analysis of IOP reduction 'survival' following a single cyclodiode treatment (Fig.2)

Success was defined as an intraocular pressure (IOP) of 6–21 mmHg at the last follow up visit without the need for oral acetazolamide and an IOP reduction of at least 30% compared with preoperatively. The proportion of patients to maintain the desired IOP reduction after a single cyclodiode treatment without the need for further IOP lowering intervention in our study was 67.7% at 6 weeks post-operatively, 66.2% at 6 months, 63% at 1 year, 61.2% at 2 years and 61.2% at 3 years. Of the patients who responded to treatment at 6 weeks, 90.4% were able to maintain the IOP reduction over a period of 3 years.

Cyclodiode effect on glaucoma medications (Fig.3A)

A significant proportion of the patients (61.5%) were able to decrease the number of medications they are taking for IOP control following cyclodiode. A decrease of 2 medications or more was achieved by 34.6% of patients, while 26.9% of patients decreased their medication by one. Overall, the average number of medications decreased from 2.6 before cyclodiode treatment to 1.5 medications after cyclodiode treatment ($P<0.05$).

Change in visual acuity (Fig.3B)

A single episode of cyclodiode treatment had no significant effect on visual acuity (VA). Mean VA measurements changed from 0.5720 Log MAR units before cyclodiode therapy to 0.5408 Log MAR units post treatment, which was not statistically significant (P>0.05). The data analysis was performed on 47 patients (54.1%), who had clearly annotated numerical values for their VA measurements both preoperatively and postoperatively. The boxed numerals in the graph represent the number of values at the same point.

Change in visual fields (Fig.3C)

The average visual field sensitivity remained almost unchanged with an average MD value of -8.74 dB pre-treatment compared to MD value of -9.05 dB at 6 months post-treatment, which was not statistically significant (P>0.05). The data analysis was performed on 36 patients (41.3%), who had clearly annotated numerical values for their visual fields measurements both pre-operatively and post-operatively.

Effect of laser energy on IOP reduction (Fig.4A)

Of the patients that received high energy treatment (90J), 80.3% obtained pressure reduction of >30% of initial IOP compared with 56.8% in the patients that received low energy treatment (45J).

Effect of laser energy on visual acuity (Fig.4B)

Of the patients that received high energy treatment (90J), 18.6% noted improvement of the equivalent of at least 1 Snellen line compared with 6.7% in the patients that received low energy treatment.

Effect of degrees treated on IOP reduction (Fig.4C)

Of the patients that underwent 360 degrees treatment, 71.4% obtained pressure reduction greater than 30% of initial IOP compared with 55% of the patients that underwent 180 degree treatment.

Effect of degrees treated on visual acuity (Fig.4D)

Of the patients that underwent 360 degrees treatment, 20.9% noted improvement of the equivalent of at least 1 Snellen line compared with 5.5% of the patients underwent 180 degree treatment.

Discussion:

The results of this retrospective analysis are supportive of a single cyclodiode treatment being effective in management of refractory glaucoma. Although this is a retrospective rather than a prospective study, we aimed to avoid selection bias by including all patients either as success or failure of treatment. The patients who required additional surgical interventions were taken as failure from the time of additional intervention.

Our data show that 67.7% of the patients achieved an IOP reduction greater than 30% of presenting IOP at 6 weeks and 61.5% could reduce the number of medications by at least 1. Hypotony appears to be related to the type of glaucoma (with neovascular glaucoma associated with worse outcome) as well as to the number of degrees treated and total energy used. Indeed, the patients with neovascular glaucoma in our cohort were almost 4 times more likely to develop hypotony compared to any other types of glaucoma.

In our patients, the mean intraocular pressure (IOP) decreased significantly from 39.5 mmHg (SE 1.26) before cyclodiode therapy to 17.8 mmHg (SE 1.51) at 6 weeks post-treatment, an observable reduction of 45.1 % ($P<0.05$). The results of the linear regression analysis indicate that there might be some predictive value in determining IOP reduction based on initial IOP measurements such as the greatest reduction in IOP is likely to be seen in patients with the highest IOP at the time of treatment (R^2 = 0.32). A similar relationship was reported by Vernon et al., where eyes with IOP greater than 30 mmHg were more likely to exhibit a pressure drop greater than 30% of initial IOP.[19]

The IOP reduction was maintained long term in 61.2% of all patients in our study after a single cyclodiode treatment. Of the patients who responded to treatment at 6 weeks, 90.4% were able to maintain the IOP reduction over a period of 3 years. Similar sustainability of the mean IOP reduction postoperatively is also reported by Bloom et al. and Kosoko et al., although in both these studies the follow up was considerably shorter, the average time being less than 2 years.[18,20] The results from our patient cohort suggest that a single session of cyclodiode therapy could potentially be a viable initial treatment modality for maintaining a longer term IOP control in patients with refractory glaucoma.

In our study, of the patients that received high energy treatment (90J), 80.3% obtained an IOP reduction of greater than 30% of the initial IOP compared with 56.8% in the patients receiving low energy treatment (45J). This is consistent with a meta-analysis by Iliev et al., where comparing different laser protocols from different studies suggested that the use of a low energy protocol potentially could result in the lowest IOP reduction, the highest postoperative IOP and the highest retreatment rate overall.[17] We also observed similar relationship when patients were assessed in regard to the degrees treated rather than energy used. Here, of the patients that underwent 360 degrees treatment, 71.4% obtained pressure reduction greater than 30% of initial IOP compared with 55% of the patients that underwent 180 degrees treatment.

Hypotony was the most common long-term complication in our study (5.3%), which is in accordance with other published reports.[14] In our cohort, the incidence of hypotony was much more likely with an eye with neovascular glaucoma (**Table 2**). Murphy et al. also found a higher risk of hypotony in eyes with neovascular glaucoma, particularly if preoperative IOP was high and energy level used was greater.[14] This correlation between hypotony and higher energy used in cyclodiode is also observed in several other studies.[12] However, univariate regression analysis done by Murphy et al. shows that very high pre-treatment IOP alone, possibly causing ciliary body ischaemia, could be responsible for the high incidence of hypotony in the patients receiving high-energy treatment in their study.[14]

Additionally, in a retrospective analysis of 209 eyes by Bloom et al., a very low incidence of hypotony (1%) was observed with a high energy protocol when the mean energy used was 90J.[18] Furthermore, Iliev et al. report in their study that eyes developing hypotony had not received higher energies compared with eyes that maintained normal IOP.[17] Therefore, the intention to reduce hypotony risk by using a lower laser power and fewer applications per treatment should be weighed against the possibility for a lower efficacy of the cyclodiode treatment.

Visual acuity (VA) remained unchanged for the majority of our patients who underwent cyclodiode treatment (69.9%). In our study 16.4% reported deterioration in VA of 1 Snellen line, while 13.7% of the patients reported an improvement in VA of 1 Snellen line after 6 weeks. The latter probably resulted either from resolution of preoperative corneal oedema or inter-observer variation in visual acuity testing. Similar results are also reported in a study by Murphy et al., where the VA remained the same in 74.6% of the patients at 6 months following cyclodiode treatment.[14] In our study most patients with difficult to manage glaucoma retained their good VA in the long-term following cyclodiode treatment. The proportion losing two Snellen lines is actually better than that reported after trabeculectomy or tube surgery.[21] These results suggest a possible role for the use of transscleral cyclodiode treatment in eyes with relatively good visual potential, however, further controlled prospective studies would be required to better define this role.

This study is the first to measure the mean deviation (MD) values for the patients both pre-operatively and post-operatively in order to provide a more objective assessment of glaucoma related visual loss. The MD values in our patients remained virtually unchanged after cyclodiode treatment from -8.74dB preoperatively to -9.05 dB postoperatively. Previously it has been reported that the most frequent cause of visual loss was further progression of glaucoma, which was an attributable cause in over half of the cases.[22] The peri-operative visual field assessment presented in this study suggests that the maintenance of VA observed in the majority of the patients following cyclodiode treatment could be due to a good postoperative IOP control. There are no previous retrospective or prospective studies evaluating visual field measurements peri-operatively in patients undergoing cyclodiode treatment and this most likely reflects the difficulties associated with performing the tests in patients with poor VA. Our study therefore is the first to provide a standardised measurable evidence of maintenance of patients' visual fields as a marker of glaucoma progression following a single cyclodiode treatment. Our study's main limitations are its retrospective nature and the absence of a control group to distinguish the adverse effects of the treatment from the natural history of the underlying disease.

The results of this study suggest that the IOP reduction after cyclodiode treatment could potentially prevent further deterioration in the glaucoma patients' vision. Currently, according to the UK National Cyclodiode Survey Study only 60% of practitioners would perform cyclodiode procedure in the presence of good visual acuity.[12] Until recently, cyclodiode treatment has been associated with subsequent loss of VA in significant percentage of the patients.[18,23,24] However, cyclodiode use in eyes with useful vision has already been proposed in several studies.[19,22-25] Furthermore, the risk of VA loss in patients after multiple cyclodiode treatments does not appear to be any greater than that after any other surgical modality used for treating patients with glaucoma as reported in a study by Rotchford et al.[24]

In our study, the better outcome in visual acuity was most pronounced in the high energy group, probably due to the more effective IOP control. Of the patients that received high energy treatment (90J), 18.6% noted improvement of at least 1 Snellen line compared with 6.7% in the patients that received low energy treatment (45J).

Similar results are observed when patients were assessed in regard to the degrees treated. Here, of the patients that underwent 360 degrees treatment, 20.9% noted improvement of the equivalent of at least 1 Snellen line compared with 5.5% of the patients underwent 180 degrees treatment.

In conclusion, conventional diode cyclophotocoagulation is characterised by low incidence of complications and therefore appears to be a safe and effective treatment for refractory glaucoma. In our study the IOP pressure was effectively reduced in glaucoma patients after a single cyclodiode treatment without adverse effects on VA in the majority of the patients over a 3 year period. Hypotony seems to be the main risk of treatment and could be limited by reducing the laser energy applied to less than 90J, particularly in the patients with neovascular glaucoma.

Figure and Table Legends

Figure 1 (**A**) Change in Intraocular Pressure following a single Cyclodiode treatment (**B**) Safety and Efficacy of Cyclodiode Treatment (**C**) IOP reduction was maintained long-term over the period of 3 years after single treatment

Figure 2 Kaplan-Meier analysis for cumulative proportion of success in IOP control after a single Cyclodiode treatment. Survival was defined as sustained IOP drop of at least 30% compared with pre-treatment or sustained intraocular pressure (IOP) of 6–21 mmHg without the need for additional IOP lowering medications or further surgical interventions.

Figure 3 (**A**) Cyclodiode effect on antiglaucoma medications (**B**) Preoperative and postoperative visual acuity measurements in LogMAR units after a single Cyclodiode treatment (**C**) Preoperative and postoperative visual field loss taken from MD values (dB) on the HVF analyser after a single Cyclodiode treatment

Figure 4 (A) Effect of laser energy on IOP reduction **(B)** Effect of laser energy on visual acuity (VA) **(C)** Effect of degrees treated on IOP reduction **(D)** Effect of degrees treated on visual acuity (VA)

Table 1 Baseline demographics of the patients and clinical parameters including diagnostic features, pre-operative IOP and visual acuity assessments.

Table 2 Details of the patients who developed hypotony including diagnostic and treatment features, peri-operative IOP assessments and duration of hypotony

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A Retrospective Analysis of Long Term Outcomes Following a Single Episode of Transscleral Cyclodiode Laser Treatment in Glaucoma Patients

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Objectives: To investigate the efficacy of a single cyclodiode laser photocoagulation treatment for refractory glaucoma and its effect on visual outcome in patients with good visual potential as well as to evaluate possible predictive factors in establishing optimal treatment parameters.

Design: Retrospective observational study

Setting: Tertiary referral centre

Participants: The notes of 87 patients with refractory glaucoma who underwent cyclodiode photocoagulation as a first surgical intervention over a 7-year period.

Main outcome measures: Maintenance of intraocular pressure reduction, number of medications and visual acuity outcomes post-treatment.

Results: The mean intraocular pressure (IOP) after a single treatment decreased from 39.5 +/-1.3 mmHg to 17.8+/-1.5 mmHg after a 6-week follow-up period ($P<0.0001$). This reduction in IOP was maintained over a 3-year period. Here 61.5% of the patients were able to reduce the number of medications used, with mean reduction from 2.6 to 1.5 medications ($P<0.05$). Mean initial visual field loss prior to treatment was 8.74dB and at 6 months post-treatment was measured at 9.06dB ($P>0.05$) suggesting no significant overall change. The visual acuity remained unchanged or improved for 83.6% of the patients ($P>0.05$) with relatively good visual potential (average vision preoperatively was 0.57 logMAR). Hypotony occurred in 5.3% of the patients. No patients required enucleation or evisceration.

Conclusion: A single session of cyclodiode laser therapy was associated with significant IOP reduction in the majority of the patients with refractory

glaucoma. The majority were able to maintain the IOP reduction over a 3-year period without the need for a further surgical intervention. Additionally, over 80% of the patients in our study were able to maintain their baseline visual acuity. These results support the view that a single cyclodiode treatment can be sufficient in achieving long term IOP control and may be considered in eyes with relatively good visual potential.

Introduction:

Transscleral diode laser cyclophotocoagulation (cyclodiode) has been established as a relatively safe and effective intervention for glaucoma.[1-6] Cyclodiode is often used in refractory glaucoma, where alternative surgical approaches, such as antiproliferative augmented trabeculectomy and tube shunt surgery, may sometimes be judged less appropriate, for example in eyes with poor visual potential. Additionally, cyclodiode has been shown to be safer than other cyclodestructive procedures, such as Nd:YAG laser cyclophotocoagulation and cyclocryotherapy, which present a greater risk of hypotony and phthisis resulting from excessive ciliary body ablation.[7–9] However, the outcome of cyclodiode therapy is unpredictable and multiple treatments may be required to achieve long term intraocular control.[10-11]

Currently there is no general consensus for an optimum treatment protocol for cyclodiode. Data for outcomes following cyclodiode laser vary considerably in the literature.[12] Parameters such as total delivered energy per eye, number of laser applications per treatment, pulse power, pulse duration and proportion of circumference treated have been analysed with varying results.[13–17] Furthermore, cyclodiode therapy has often been reserved for eyes with poor vision due to reports that it can lead to decrease in visual acuity.[18]

The purpose of this study was to evaluate the long-term safety and efficacy of a single episode of transscleral diode laser cyclophotocoagulation for raised intraocular pressure in patients with good visual potential at a UK tertiary glaucoma referral centre. **The retrospective nature of the study design reflected the need to analyse multiple clinical variables and evaluate different types of outcomes as well as their progression over several years. Additionally, such a study could facilitate the identification predictive factors for optimal treatment parameters by investigating the relation of laser energy delivered and degrees treated to the long-term maintenance in IOP reduction.**

Methods:

The departmental electronic medical record system (Medisoft Ophthalmology, Medisoft Ltd Leeds UK) and operating theatre log books were examined for the period 09/2004 to 06/2011 to identify patients who had undergone cyclodiode treatment as a first surgical intervention.

All patients were assessed for their response to treatment and those who did not achieve the target IOP reduction were taken as treatment failures. The patients who required either repeat cyclodiode or alternative treatments for IOP control during the follow up period were also considered as treatment failures from the time of the additional surgical intervention. They were not further assessed for maintenance of post-operative IOP as any additional surgical interventions would interfere with the interpretation of the IOP maintenance data.

Cyclophotocoagulation was performed in the Operating Theatre under subtenon, peribulbar or general anaesthesia using a standard treatment protocol. A lid speculum was placed to achieve adequate exposure for probe placement all around the limbus and a squint hook was used to rotate the globe to achieve exposure in those with narrow palpebral apertures. All treatments were performed using Oculight Sx semiconductor diode 810nm laser and the contact G Probe™ (IRIS Medical Instruments, Inc.). Standard settings were 1500ms duration and 1500mW power. The energy levels were not routinely titrated for 'pops' and the power settings were left at 1500mW. Transillumination was performed for ciliary body identification. Usually 10 applications were applied per quadrant for 180 to 360°, with the applications spaced approximately one-half width of the probe tip apart. The 3 and 9 o'clock positions were avoided to spare the long ciliary nerves. Postoperative steroid drops were used for 4 weeks. Glaucoma medications were continued after cyclodiode treatment and adjusted later as required.

Success was defined as an intraocular pressure (IOP) of 6–21 mmHg at the last follow-up visit without the need for oral acetazolamide and an IOP reduction of at least 30% compared with pre-treatment. Hypotony was defined as an IOP of 5 mmHg or less. The laser energy used was classified as either low energy (median value 45 +/- 11.47 J, range 22.5-67.5J) or high energy (median value 90 +/- 13.42 J, range 67.5-130J). The follow up period in IOP measurements was 3 years. Visual acuity (VA) prior to treatment was assessed for all patients using LogMAR scale. Visual field testing was performed with the Humphrey Visual Field Analyser™ using the SITA 24-2 threshold programme. Mean deviation of visual field sensitivity loss in decibels (MD) was taken as our surrogate measure of visual field loss.

Data was analysed using Microsoft Excel™ and where appropriate a Student's t-test was used to calculate p-values. R^2 values were derived from linear regression analyses using the same programme. Kaplan-Meier 'survival' analysis was done using GraphPad Prism 5.0™. Approval for the audit was granted by the Cambridge University Hospitals NHS Foundation Trust Ethics Committee. The tenets of the Declaration of Helsinki were observed.

Results:

From our records, we were able to identify 104 patients who underwent cyclodiode therapy as a first surgical treatment modality in the period from 09/2004 to 06/2011 at Addenbrooke's Hospital, Cambridge. Of these, complete medical records were available for 87 patients with follow up data available for up to 3 years. Preoperative patient data is summarised in **Table 1**.

Table 1. Baseline demographics and clinical parameters

	Category	Cases (n=87)
Mean age, yrs		66.3
Sex (n (%))	Male	49 (56.3%)
	Female	38 (43.7%)
Preoperative VA, mean		0.57 LogMAR
IOP (mmHg), mean (SD)		39.5 +/- 1.3 mmHg
Mean number of glaucoma medications		2.6
Glaucoma type (n (%))	Primary open angle glaucoma (POAG)	33 (37.9%)
	Primary angle closure glaucoma (PACG)	6 (6.9%)
	Neovascular glaucoma	25 (28.7%)
	Uveitic glaucoma	5 (5.7%)
	Secondary open angle glaucoma (SOAG)- Other	18 (20.8%)

Change in Intraocular Pressure (Fig.1A)

Mean intraocular pressure (IOP) decreased significantly from 39.5 mmHg (SE 1.26) before cyclodiode therapy to 17.8 mmHg (SE 1.51) at 6 weeks post-treatment, an observable reduction of 45.1 % ($P<0.0001$). There was a mild linear correlation between preoperative IOP and observed IOP reduction ($R^2 = 0.32$).

Safety and Efficacy of Cyclodiode Treatment (Fig.1B)

An IOP reduction greater than 30% of initial IOP was achieved at 6 weeks in 67.7 % of the patients, while hypotony occurred in only 5 cases or 5.3% of patients ($p<0.05$). None of the patients experienced post-treatment uveitis or required further treatment or enucleation for pain symptoms. The data for the patients who developed hypotony such as initial diagnosis, treatment settings, IOP measurements and VA outcome is summarised in **Table 2**.

Table 2. Details of hypotony patients

	Diagnosis	Energy used	Degrees treated	Peak IOP (mmHg)	Postop IOP (mmHg)	Hypotony duration	Last IOP (mmHg)	Preop VA (LogMAR)	Last VA (LogMAR)
PT1	Neovascular	90J	180	58	2	6 months	10	0.78	PL
PT2	Neovascular	90J	360	41	4	6 months	32	PL	NPL
PT3	Neovascular	120J	360	40	2	6 months	9	0.6	HM
PT4	SOAG(other)	120J	360	26	3	6 months	8	1.0	CF
PT5	SOAG(other)	120J	360	48	2	-	3	HM	HM

Long term maintenance of IOP reduction after a single cyclodiode treatment (Fig.1C)

The IOP reduction was maintained long term over the period of 3 years in the majority of our patients. Measurements were taken pre-operatively (39.5+/-1.3 mmHg) as well as post-operatively at 6 weeks (17.8+/-1.5 mmHg) and 6 months

(19.6+/-1.5 mmHg) for all patients. Patients who required additional procedures in that eye post-treatment were excluded from further analysis from the time point of additional intervention as it would artificially lower their IOP measurements The follow-up measurements at 1 year (18.9 mmHg), 2 year (22.1 mmHg) and 3 years (21.7 mmHg) were all after a single cyclodiode treatment.

Kaplan-Meier analysis of IOP reduction 'survival' following a single cyclodiode treatment (Fig.2)

Success was defined as an intraocular pressure (IOP) of 6–21 mmHg at the last follow up visit without the need for oral acetazolamide and an IOP reduction of at least 30% compared with preoperatively. The proportion of patients to maintain the desired IOP reduction after a single cyclodiode treatment without the need for further IOP lowering intervention in our study was 67.7% at 6 weeks post-operatively, 66.2% at 6 months, 63% at 1 year, 61.2% at 2 years and 61.2% at 3 years. Of the patients who responded to treatment at 6 weeks, 90.4% were able to maintain the IOP reduction over a period of 3 years.

Cyclodiode effect on glaucoma medications (Fig.3A)

A significant proportion of the patients (61.5%) were able to decrease the number of medications they are taking for IOP control following cyclodiode. A decrease of 2 medications or more was achieved by 34.6% of patients, while 26.9% of patients decreased their medication by one. Overall, the average number of medications decreased from 2.6 before cyclodiode treatment to 1.5 medications after cyclodiode treatment ($P<0.05$).

Change in visual acuity (Fig.3B)

A single episode of cyclodiode treatment had no significant effect on visual acuity (VA). Mean VA measurements changed from 0.5720 Log MAR units before cyclodiode therapy to 0.5408 Log MAR units post treatment, which was not statistically significant (P>0.05). The data analysis was performed on 47 patients (54.1%), who had clearly annotated numerical values for their VA measurements both preoperatively and postoperatively. The boxed numerals in the graph represent the number of values at the same point.

Change in visual fields (Fig.3C)

The average visual field sensitivity remained almost unchanged with an average MD value of -8.74 dB pre-treatment compared to MD value of -9.05 dB at 6 months post-treatment, which was not statistically significant (P>0.05). The data analysis was performed on 36 patients (41.3%), who had clearly annotated numerical values for their visual fields measurements both pre-operatively and post-operatively.

Effect of laser energy on IOP reduction (Fig.4A)

Of the patients that received high energy treatment (90J), 80.3% obtained pressure reduction of >30% of initial IOP compared with 56.8% in the patients that received low energy treatment (45J).

Effect of laser energy on visual acuity (Fig.4B)

Of the patients that received high energy treatment (90J), 18.6% noted improvement of the equivalent of at least 1 Snellen line compared with 6.7% in the patients that received low energy treatment.

Effect of degrees treated on IOP reduction (Fig.4C)

Of the patients that underwent 360 degrees treatment, 71.4% obtained pressure reduction greater than 30% of initial IOP compared with 55% of the patients that underwent 180 degree treatment.

Effect of degrees treated on visual acuity (Fig.4D)

Of the patients that underwent 360 degrees treatment, 20.9% noted improvement of the equivalent of at least 1 Snellen line compared with 5.5% of the patients underwent 180 degree treatment.

Discussion:

The results of this retrospective analysis are supportive of a single cyclodiode treatment being effective in management of refractory glaucoma. Although this is a retrospective rather than a prospective study, we aimed to avoid selection bias by including all patients either as success or failure of treatment. The patients who required additional surgical interventions were taken as failure from the time of additional intervention.

Our data show that 67.7% of the patients achieved an IOP reduction greater than 30% of presenting IOP at 6 weeks and 61.5% could reduce the number of medications by at least 1. Hypotony appears to be related to the type of glaucoma (with neovascular glaucoma associated with worse outcome) as well as to the number of degrees treated and total energy used. Indeed, the patients with neovascular glaucoma in our cohort were almost 4 times more likely to develop hypotony compared to any other types of glaucoma.

In our patients, the mean intraocular pressure (IOP) decreased significantly from 39.5 mmHg (SE 1.26) before cyclodiode therapy to 17.8 mmHg (SE 1.51) at 6 weeks post-treatment, an observable reduction of 45.1 % ($P<0.05$). The results of the linear regression analysis indicate that there might be some predictive value in determining IOP reduction based on initial IOP measurements such as the greatest reduction in IOP is likely to be seen in patients with the highest IOP at the time of treatment (R^2 = 0.32). A similar relationship was reported by Vernon et al., where eyes with IOP greater than 30 mmHg were more likely to exhibit a pressure drop greater than 30% of initial IOP.[19]

The IOP reduction was maintained long term in 61.2% of all patients in our study after a single cyclodiode treatment. Of the patients who responded to treatment at 6 weeks, 90.4% were able to maintain the IOP reduction over a period of 3 years. Similar sustainability of the mean IOP reduction postoperatively is also reported by Bloom et al. and Kosoko et al., although in both these studies the follow up was considerably shorter, the average time being less than 2 years.[18,20] The results from our patient cohort suggest that a single session of cyclodiode therapy could potentially be a viable initial treatment modality for maintaining a longer term IOP control in patients with refractory glaucoma.

In our study, of the patients that received high energy treatment (90J), 80.3% obtained an IOP reduction of greater than 30% of the initial IOP compared with 56.8% in the patients receiving low energy treatment (45J). This is consistent with a meta-analysis by Iliev et al., where comparing different laser protocols from different studies suggested that the use of a low energy protocol potentially could result in the lowest IOP reduction, the highest postoperative IOP and the highest retreatment rate overall.[17] We also observed similar relationship when patients were assessed in regard to the degrees treated rather than energy used. Here, of the patients that underwent 360 degrees treatment, 71.4% obtained pressure reduction greater than 30% of initial IOP compared with 55% of the patients that underwent 180 degrees treatment.

Hypotony was the most common long-term complication in our study (5.3%), which is in accordance with other published reports.[14] In our cohort, the incidence of hypotony was much more likely with an eye with neovascular glaucoma (**Table 2**). Murphy et al. also found a higher risk of hypotony in eyes with neovascular glaucoma, particularly if preoperative IOP was high and energy level used was greater.[14] This correlation between hypotony and higher energy used in cyclodiode is also observed in several other studies.[12] However, univariate regression analysis done by Murphy et al. shows that very high pre-treatment IOP alone, possibly causing ciliary body ischaemia, could be responsible for the high incidence of hypotony in the patients receiving high-energy treatment in their study.[14]

Additionally, in a retrospective analysis of 209 eyes by Bloom et al., a very low incidence of hypotony (1%) was observed with a high energy protocol when the mean energy used was 90J.[18] Furthermore, Iliev et al. report in their study that eyes developing hypotony had not received higher energies compared with eyes that maintained normal IOP.[17] Therefore, the intention to reduce hypotony risk by using a lower laser power and fewer applications per treatment should be weighed against the possibility for a lower efficacy of the cyclodiode treatment.

Visual acuity (VA) remained unchanged for the majority of our patients who underwent cyclodiode treatment (69.9%). In our study 16.4% reported deterioration in VA of 1 Snellen line, while 13.7% of the patients reported an improvement in VA of 1 Snellen line after 6 weeks. The latter probably resulted either from resolution of preoperative corneal oedema or inter-observer variation in visual acuity testing. Similar results are also reported in a study by Murphy et al., where the VA remained the same in 74.6% of the patients at 6 months following cyclodiode treatment.[14] In our study most patients with difficult to manage glaucoma retained their good VA in the long-term following cyclodiode treatment. The proportion losing two Snellen lines is actually better than that reported after trabeculectomy or tube surgery.[21] These results suggest a possible role for the use of transscleral cyclodiode treatment in eyes with relatively good visual potential, however, further controlled prospective studies would be required to better define this role.

This study is the first to measure the mean deviation (MD) values for the patients both pre-operatively and post-operatively in order to provide a more objective assessment of glaucoma related visual loss. The MD values in our patients remained virtually unchanged after cyclodiode treatment from -8.74dB preoperatively to -9.05 dB postoperatively. Previously it has been reported that the most frequent cause of visual loss was further progression of glaucoma, which was an attributable cause in over half of the cases.[22] The peri-operative visual field assessment presented in this study suggests that the maintenance of VA observed in the majority of the patients following cyclodiode treatment could be due to a good postoperative IOP control. There are no previous retrospective or prospective studies evaluating visual field measurements peri-operatively in patients undergoing cyclodiode treatment and this most likely reflects the difficulties associated with performing the tests in patients with poor VA. Our study therefore is the first to provide a standardised measurable evidence of maintenance of patients' visual fields as a marker of glaucoma progression following a single cyclodiode treatment. Our study's main limitations are its retrospective nature and the absence of a control group to distinguish the adverse effects of the treatment from the natural history of the underlying disease.

The results of this study suggest that the IOP reduction after cyclodiode treatment could potentially prevent further deterioration in the glaucoma patients' vision. Currently, according to the UK National Cyclodiode Survey Study only 60% of practitioners would perform cyclodiode procedure in the presence of good visual acuity.[12] Until recently, cyclodiode treatment has been associated with subsequent loss of VA in significant percentage of the patients.[18,23,24] However, cyclodiode use in eyes with useful vision has already been proposed in several studies.[19,22-25] Furthermore, the risk of VA loss in patients after multiple cyclodiode treatments does not appear to be any greater than that after any other surgical modality used for treating patients with glaucoma as reported in a study by Rotchford et al.[24]

In our study, the better outcome in visual acuity was most pronounced in the high energy group, probably due to the more effective IOP control. Of the patients that received high energy treatment (90J), 18.6% noted improvement of at least 1 Snellen line compared with 6.7% in the patients that received low energy treatment (45J).

Similar results are observed when patients were assessed in regard to the degrees treated. Here, of the patients that underwent 360 degrees treatment, 20.9% noted improvement of the equivalent of at least 1 Snellen line compared with 5.5% of the patients underwent 180 degrees treatment.

In conclusion, conventional diode cyclophotocoagulation is characterised by low incidence of complications and therefore appears to be a safe and effective treatment for refractory glaucoma. In our study the IOP pressure was effectively reduced in glaucoma patients after a single cyclodiode treatment without adverse effects on VA in the majority of the patients over a 3 year period. Hypotony seems to be the main risk of treatment and could be limited by reducing the laser energy applied to less than 90J, particularly in the patients with neovascular glaucoma.

Figure and Table Legends

Figure 1 (A) Change in Intraocular Pressure following a single Cyclodiode treatment (**B**) Safety and Efficacy of Cyclodiode Treatment (**C**) IOP reduction was maintained long-term over the period of 3 years after single treatment

Figure 2 Kaplan-Meier analysis for cumulative proportion of success in IOP control after a single Cyclodiode treatment. Survival was defined as sustained IOP drop of at least 30% compared with pre-treatment or sustained intraocular pressure (IOP) of 6–21 mmHg without the need for additional IOP lowering medications or further surgical interventions.

Figure 3 (**A**) Cyclodiode effect on antiglaucoma medications (**B**) Preoperative and postoperative visual acuity measurements in LogMAR units after a single Cyclodiode treatment (**C**) Preoperative and postoperative visual field loss taken from MD values (dB) on the HVF analyser after a single Cyclodiode treatment

Figure 4 (A) Effect of laser energy on IOP reduction **(B)** Effect of laser energy on visual acuity (VA) **(C)** Effect of degrees treated on IOP reduction **(D)** Effect of degrees treated on visual acuity (VA)

Table 1 Baseline demographics of the patients and clinical parameters including diagnostic features, pre-operative IOP and visual acuity assessments.

Table 2 Details of the patients who developed hypotony including diagnostic and treatment features, peri-operative IOP assessments and duration of hypotony

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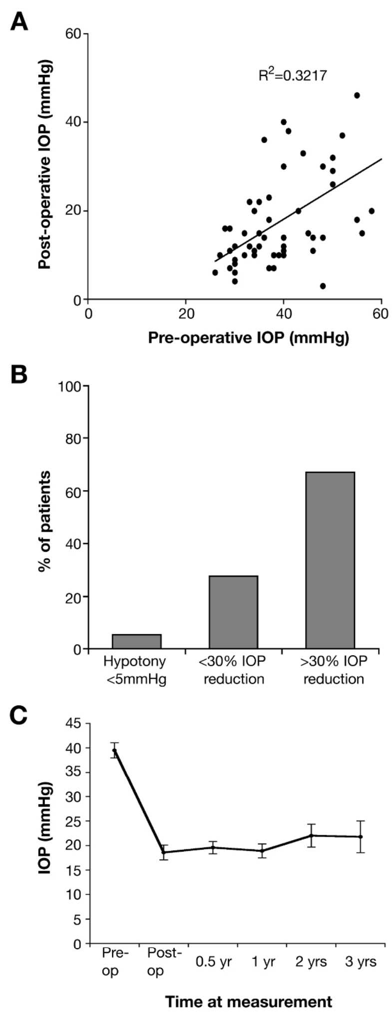

Figure 1

Figure 1 (A) Change in Intraocular Pressure following a single Cyclodiode treatment (B) Safety and Efficacy of Cyclodiode Treatment (C) IOP reduction was maintained long-term over the period of 3 years after single treatment
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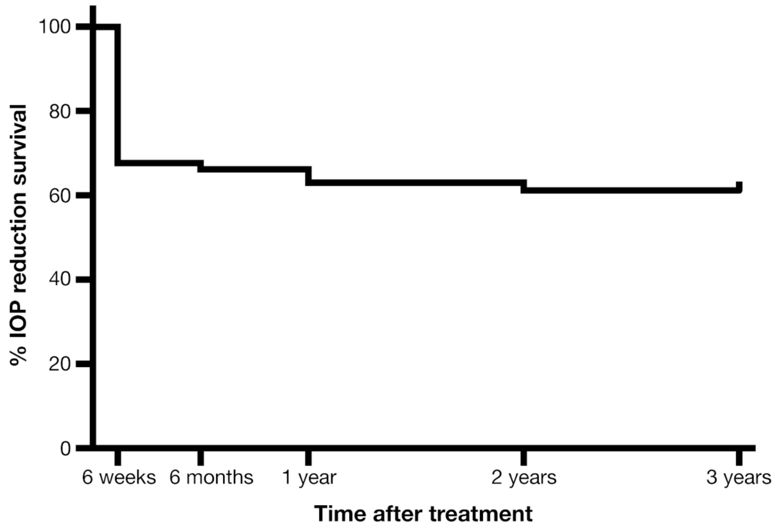

Figure 2

Figure 2 Kaplan-Meier analysis for cumulative proportion of success in IOP control after a single Cyclodiode treatment. Survival was defined as sustained IOP drop of at least 30% compared with pre-treatment or sustained intraocular pressure (IOP) of 6–21 mmHg without the need for additional IOP lowering medications or further surgical interventions.
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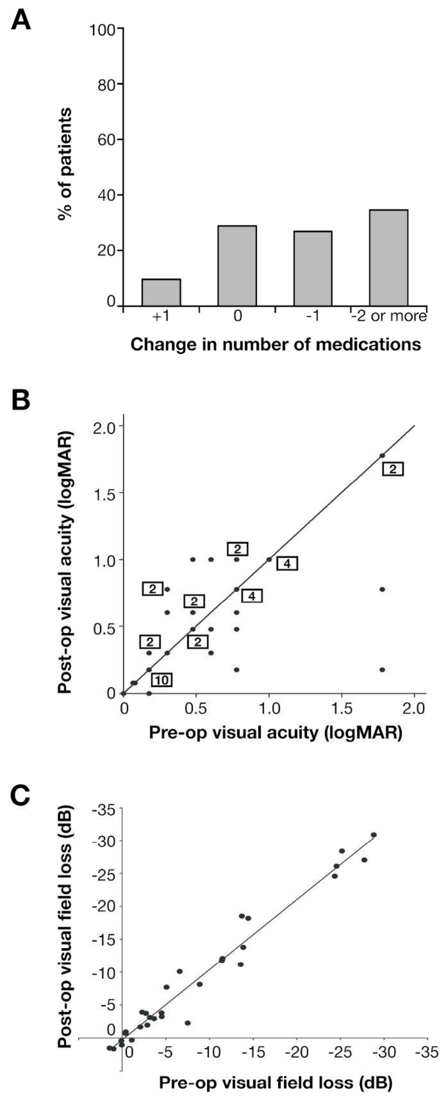

Figure 3

Figure 3 (A) Cyclodiode effect on antiglaucoma medications (B) Preoperative and postoperative visual acuity measurements in LogMAR units after a single Cyclodiode treatment (C) Preoperative and postoperative visual field loss taken from MD values (dB) on the HVF analyser after a single Cyclodiode treatment
171x234mm (300 x 300 DPI)

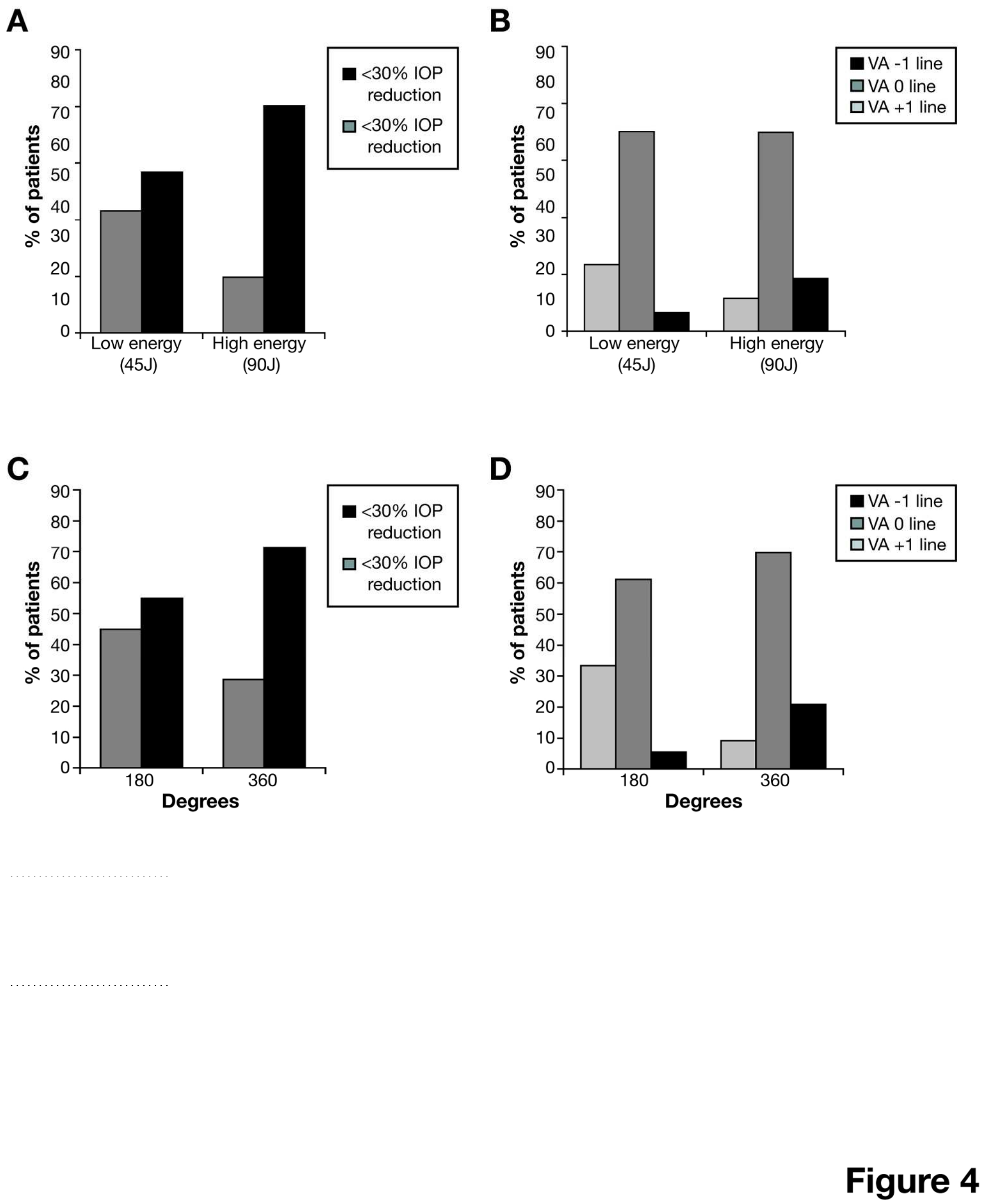

Figure 4 (A) Effect of laser energy on IOP reduction (B) Effect of laser energy on visual acuity (VA) (C) Effect of degrees treated on IOP reduction (D) Effect of degrees treated on visual acuity (VA)
175x216mm (300 x 300 DPI)