Randomised trial of sequential pretreatment for Nd:YAG laser iridotomy in dark irides

D Julian de Silva,1 Alexander C Day,1,2 Catey Bunce,1 Gus Gazzard,1 Paul J Foster1,2,3

ABSTRACT
Aims To compare iridotomy outcomes in dark irides by 1064 nm pulsed Nd:YAG laser with and without 532 nm continuous-wave Nd:YAG (frequency-doubled) green laser pretreatment.
Methods 30 patients with occludable anterior chamber angles underwent bilateral standard pulsed 1064 nm Nd:YAG laser iridotomy with one eye randomly assigned to sequential pretreatment with 532 nm continuous-wave Nd:YAG laser. Outcome measures were iridotomy patency and complications including haemorrhage and elevated intraocular pressure (IOP).
Results Median pulsed YAG power in the standard treatment group was 37.5 mJ (IQR 25–77) and 22.5 mJ (IQR 14–32) in the sequential treatment group (p=0.0079). Iris haemorrhage occurred in 43% of the standard treatment group and 13% of the sequential treatment group (p=0.0128). All iridotomies were patent at last follow-up of median 38.5 months (IQR 32.0–42.3).
Conclusions This study provides evidence that iridotomy with pretreatment using a continuous-wave Nd:YAG laser is safer and more effective than pulsed Nd:YAG-only laser iridotomy for dark irides and should be considered as the preferred technique.

INTRODUCTION
The use of laser peripheral iridotomy (PI) for the treatment and prevention of primary angle-closure is well established.1–4 Although pulsed 1064 nm Nd:YAG (photodisruption) laser PI is an effective technique in light coloured irides, it is less effective in dark irides.2,5,6 This is presumably because dark irides have thicker stroma with fewer iris crypts7 and thus higher Nd:YAG laser energies are required for a patent iridotomy.2,8 Argon laser (photocoagulation) iridotomy is also less effective in these irides,7,9,6 and consequently a sequential argon–Nd:YAG iridotomy5,6,10–15 has been proposed as a possible solution that confers the advantages of each laser without their respective drawbacks, that is, pretreatment with argon laser causes iris contraction and coagulation of nearby vessels thus reducing tissue thickness and minimising iris haemorrhage and the Nd:YAG laser is used for final iris penetration with minimal pigment dispersion and a low closure rate. Most argon lasers have now been replaced by frequency-doubled Nd:YAG or diode lasers due to technical advantages. The aim of this randomised controlled trial was to evaluate the outcomes of laser iridotomy using a standard 1064 nm pulsed Nd:YAG laser with and without pretreatment using a 532 nm (frequency-doubled) continuous-wave Nd:YAG green laser.

METHODS
Thirty patients of predominantly African or Asian descent with thick dark irides were enrolled between June 2006 and May 2007. An absence of radial vascular/muscle structures visible in the peripheral 2 mm of the superior iris was the criterion to identify eligible patients. All patients had either appositional and/or synechial closure of 180 degrees or more in both eyes and were listed for elective primary, bilateral PI. Patients were excluded if there was a history of acute primary angle closure, uveitis, previous intraocular surgery or any intracocular pathology unrelated to primary angle closure. The study was approved by Moorfields Eye Hospital Research Committee and the Moorfields/Whittington NHS Ethics Committee. The study was carried out in accordance with the tenets of the Declaration of Helsinki. The trial was registered with the International Standard Randomised Controlled Trials (http://www.controlled-trials.com/ISRCTN8266926). Written informed consent was obtained in all cases. Participants were evaluated for eligibility and baseline data were collected at a preliminary glaucoma clinic appointment. The hospital research department provided an independent, logged telephone randomisation service (using randomised permuted blocks of varying sizes) from which one eye of each patient was assigned to receive pretreatment with 532 nm continuous-wave (frequency-doubled) Nd:YAG green laser prior to standard 1064 nm Nd:YAG laser iridotomy. All patients were reviewed 1 week later with subsequent clinical care as required. The sequential laser iridotomy technique used has been previously described10 and is summarised below. Topical pilocarpine (4%) and apraclonidine (0.5%) were administered 30 min before the procedure, with a second dose immediately before treatment. A Wise iridotomy contact lens (Ocular Instruments, Bellevue, Washington, DC, USA) was used for all treatments. All iridotomies were performed between 11 and 1 o’clock positions in the peripheral iris. Where possible, an iris crypt was selected. Continuous-wave 532 nm (frequency-doubled) Nd:YAG laser was applied in two stages. Twenty to 40 shots (120 mW, 0.05 s, 50 μm diameter) were applied to create a circular pitted iris stroma of approximately 250 μm diameter. Next,
Clinical science

Table 1  Diagnosis by group (PACS, PAC, PACG)\(^1\)\(^4\) and median laser energies used

<table>
<thead>
<tr>
<th></th>
<th>PACS (eyes/30)</th>
<th>PAC (eyes/30)</th>
<th>PACG (eyes/30)</th>
<th>Median 532 nm Nd:YAG pretreatment</th>
<th>Median 1064 nm Nd:YAG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard treatment</td>
<td>7</td>
<td>15</td>
<td>8</td>
<td>—</td>
<td>37.5 mJ* (IQR 25–77)</td>
</tr>
<tr>
<td>Sequential treatment</td>
<td>7</td>
<td>14</td>
<td>9</td>
<td>1.24 J (IQR 0.996–1.498)</td>
<td>22.5 mJ* (IQR 14–32)</td>
</tr>
</tbody>
</table>

\(^{1}p=0.0079.\)

PAC, primary angle closure; PACG, primary angle closure glaucoma; PACS, primary angle closure suspect.

15–20 shots (700 mW, 0.1 s, 50 μm diameter) were used to produce a crater to the level of the radial muscle fibres and vasculature. The iridotomy was then completed with a 1064 nm Nd:YAG laser, 0.8–2 mJ shots, using 2–40 laser shots to achieve a full-thickness iridotomy, enlarged circumferentially to minimum 200 μm diameter. All procedures were performed by the senior author. Eyes randomised to pulsed YAG laser alone (standard treatment) were treated with identical management of the peripheral 2 mm of the superior iris. Mean age was 60 years with an absence of radial vascular/muscle structures visible in the peripheral 2 mm of the superior iris. Mean age was 60 years old (SD 11 years) with 10 male and 20 female subjects. Underlying diagnoses are shown in table 1. Total median follow-up was 38.5 months (IQR 32.0–42.3).

Of the 30 patients enrolled, 13 were of Afro-Caribbean descent, 12 Asian descent, 2 South American descent, 2 Middle Eastern descent and 1 Southern European descent. All had dark irides with some patients having large IOP rises. In the standard treatment group 6/30 patients (20%) had an IOP rise of 10 mm Hg or more. Of these, the highest IOP rises (14, 14 and 24 mm Hg) were associated with iris haemorrhage and uveitis and change in anterior chamber angle configuration. The study was not masked to patient or treating clinicians.

Sample size and power

The primary outcome variable was mean utilised energy. For a two-sided \(x\) of 0.05, a sample size of 30 patients was calculated to provide greater than 95% power to detect a difference of 24 mJ (based on previous reports)\(^4\)\(^6\) allowing for a 15% loss to follow-up or unforeseen events. The signed rank test was used to assess the statistical significance of an observed difference between the total energy utilised in treating each eye. Paired t tests were used to determine any statistical significance in IOP between groups. McNemar’s test was conducted to assess whether there was evidence of a difference in incidence of iris haemorrhage between fellow eyes. A non-parametric method was adopted because of marked skewness in the distribution of utilised energy. Analyses were conducted using Stata 11, and \(p\) values of <0.05 were considered statistically significant.

RESULTS

Of the 30 patients enrolled, 13 were of Afro-Caribbean descent, 12 Asian descent, 2 South American descent, 2 Middle Eastern descent and 1 Southern European descent. All had dark irides with an absence of radial vascular/muscle structures visible in the peripheral 2 mm of the superior iris. Mean age was 60 years old (SD 11 years) with 10 male and 20 female subjects. Underlying diagnoses are shown in table 1. Total median follow-up was 38.5 months (IQR 32.0–42.3).

Mean IOP before laser iridotomy was 19.0 mm Hg (SD 4.9) in the standard treatment group and 19.8 mm Hg (SD 4.7) in the sequential treatment group (p=0.223) (table 2). Mean IOP at 1 h post-laser iridotomy was 14.4 mm Hg (SD 5.2) in the standard treatment group and 13.3 mm Hg (SD 4.8) in the sequential treatment group. Both were significantly lower than the pre-laser iridotomy values (p<0.001). The IOP reduction in the sequential treatment group was significantly lower than that of the standard treatment group (–6.2 mm Hg (SD 5.7) vs –4.7 mm Hg (SD 6.7) respectively; p=0.042). At 1 week, mean IOP was 21.3 mm Hg (SD 6.4 mm Hg) in the standard treatment group and 20.8 mm Hg (SD 5.4 mm Hg) in the sequential treatment group. Neither of these was significantly different from baseline values; however, there was a marked variation with some patients having large IOP rises. In the standard treatment group 6/30 patients (20%) had an IOP rise of 10 mm Hg or more. Of these, the highest IOP rises (14, 14 and 24 mm Hg) were associated with iris haemorrhage at the time of the iridotomy. In the sequential treatment group, 2/30 (7%) had an IOP rise of ≥10 mm Hg (10, 22 mm Hg). There was no iris haemorrhage at the time of iridotomy in either of these and

Table 2  Intraocular pressures (IOPs) before peripheral iridotomy (PI) and at 1 h and 1 week following iridotomy

<table>
<thead>
<tr>
<th></th>
<th>IOP pre-PI mm Hg (SD)</th>
<th>IOP 1 h post-PI mm Hg (SD)</th>
<th>IOP reduction at 1 h post-PI mm Hg (SD)</th>
<th>IOP at 1 week post-PI mm Hg (SD)</th>
<th>IOP change pre—post-PI at 1 week, mm Hg (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard treatment</td>
<td>19.0 (4.9)</td>
<td>14.4 (5.2)</td>
<td>–4.7 (6.7)</td>
<td>21.3 (6.4)</td>
<td>+2.3 (7.7)</td>
</tr>
<tr>
<td>Sequential treatment</td>
<td>19.8 (4.7)</td>
<td>13.8 (4.8)</td>
<td>–6.2 (5.7)</td>
<td>20.8 (5.4)</td>
<td>+1.0 (6.6)</td>
</tr>
<tr>
<td>p Value</td>
<td>0.223</td>
<td>0.277</td>
<td>0.042</td>
<td>0.513</td>
<td>0.054</td>
</tr>
</tbody>
</table>

In the sequential treatment group, the median (IQR) number of low power and high power 532 nm laser shots (as described in the Methods section) were 30 (25–35) and 15 (12–19), respectively. The total median 532 nm Nd:YAG pretreatment energy was 1.24 J (IQR 0.996–1.498).

Iris haemorrhage occurred in 13/30 eyes (43%) in the standard treatment group as compared with 4/30 eyes (13%) in the sequential treatment group (p=0.0126). Of the 30 patients, 2 had haemorrhages in both eyes, 2 had haemorrhage only in eyes that underwent sequential treatment and 11 had haemorrhages only in eyes that underwent standard treatment. All iridotomies were patent at the end of the procedure in the sequential treatment group, while 2/30 (7%) in the standard treatment group were abandoned due to significant haemorrhage.

All completed iridotomies in both groups were patent at the 1-week follow-up appointment. The two iridotomies that were not completed at the initial sitting in the standard treatment group due to iris haemorrhage underwent routine repeat procedures at 1 week. Two patients had iridotomies that were deemed patent but too small and these were enlarged by 1064 nm YAG laser without complication (one patient, both standard and sequential treatment iridotomies at 2 weeks, and one patient, sequential treatment iridotomy only at 6 months). All iridotomies were patent at the last follow-up appointment with a median follow-up of 38.5 months (IQR 32.0–42.3). There were no significant complications including corneal decompensation.

Br J Ophthalmo 2012; 96: 263–266. doi: 10.1136/bjo.2010.200030
the same two patients had an IOP rise of ≥10 mm Hg in the other eye. At 1 week, three eyes of two patients (one eye standard treatment and two eyes sequential treatment, p=1.0) had symptomatic, mild anterior uveitis requiring further treatment. These settled without further complication.

In 59/60 (65%) eyes at 1 week, PI opened the anterior chamber angle sufficiently (>180 degrees posterior pigmented trabecular meshwork seen on gonioscopy); 21/60 (35%) eyes had anterior chamber angles that remained closed.

**DISCUSSION**

There is a significant geographic variation in the preferred laser iridotomy technique\(^5\) which is only partially explained by the perceived iris characteristics of predominant local populations.

In the UK, 1064 nm Nd:YAG only laser iridotomy is the standard technique\(^6\); while in Singapore it is sequential argon–Nd: YAG iridotomy\(^5\) and in Japan it is argon only laser iridotomy.\(^5\)

There is little evidence comparing laser PI techniques, and even less for dark irides specifically. A number of studies have previously looked at the use of sequential argon–YAG as an alternative treatment for dark irides,\(^6\)^\(^7\)^\(^8\)^\(^9\)^\(^10\)^\(^11\)^\(^12\)^\(^13\) with the cumulative evidence suggesting an advantage, although there are no previous randomised trials for dark irides. We are aware of only one randomised prospective trial for sequential argon–Nd:YAG versus Nd:YAG only iridotomy,\(^12\) one for sequential argon–Nd: YAG versus argon laser only iridotomy\(^7\) and three clinical trials for 1064 nm Nd:YAG only versus argon only iridotomy.\(^1\)\(^3\)\(^4\)

The randomised trials of 1064 nm Nd:YAG only versus argon only laser iridotomy showed that both methods are effective at forming a patent iridotomy.\(^1\)\(^4\) Nd:YAG only iridotomy has a significantly lower rate of closure compared with argon laser iridotomy (0% vs 16%–50%, respectively) but is associated with a significantly higher risk of iris haemorrhage (34%–45% vs 0%, respectively).\(^1\)\(^3\)\(^4\) As previously reported\(^11\) and seen in our results, the iris haemorrhage in 1064 nm Nd:YAG only iridotomy may be severe and warrant postponing the procedure or re-siting the iridotomy position.

Both argon\(^5\)\(^9\) and Nd:YAG\(^2\)\(^9\) iridotomies are less effective in dark irides and require higher energy levels. Quigley reported that 58% of patients with dark brown irides needed two or more sittings to achieve a patent argon iridotomy,\(^9\) while Schwartz showed a 20% failure rate of penetration in brown eyes.\(^15\) Both techniques are also associated with corneal damage including endothelial cell loss. The latter is thought to be greater in argon iridotomy\(^4\) and cases of corneal decompensation have been reported.\(^15\) As a higher laser power is needed for brown irides, endothelial cell loss due to both direct and indirect thermal effects\(^15\) of the laser would be expected to be higher. The reduction in endothelial cell count following a 1064 nm Nd:YAG iridotomy is related to the total laser energy used and distance of the iridotomy site from the endothelium.\(^15\) In the trial of sequential argon–YAG compared with argon laser only iridotomy,\(^5\) the total argon laser energy used was reported to be reduced by 2.65 times by using the sequential laser iridotomy technique. Thus, the sequential treatment technique may be of particular benefit in patients with very shallow anterior chambers and higher likelihood of endothelial cell density compromise such as that following a previous acute primary angle closure.\(^13\)

A greater pigment dispersion occurs in Nd:YAG iridotomies compared with argon iridotomies, and in dark irides this may be sufficient to cause a treatment delay while the pigment cloud disperses.\(^2\) Fewer laser shots are typically required for Nd:YAG iridotomy compared with argon iridotomy\(^7\) and so treatment times are typically less with better patient cooperation. Consequently, Nd:YAG only PI is usually preferred over argon only PI.

The randomised trial by Goins et al\(^1\) of argon laser pretreatment in 1064 nm Nd:YAG laser iridotomy was in light and dark irides. They randomised 24 eyes of 12 patients between treatment arms with the aims of examining iris haemorrhage and iridotomy closure rates. They showed that argon laser pretreatment significantly reduced the incidence of haemorrhage (67% vs 17%). This was consistent with our results of 43% versus 15% iris haemorrhage rates, standard versus sequential treatments, respectively (p=0.0126). In comparison with our results, which showed a 40% reduction (p=0.0079) in the 1064 nm Nd:YAG power required to create an iridotomy, they found no statistically significant difference. This is likely due to their low study numbers and their pretreatment method which used a uniform protocol of a single argon laser shot of 1 W, 50 µm spot size and 0.5-second pulse duration in all cases.

Direct comparison of total laser energies used between the standard and pretreatment groups is not possible as a 532 nm continuous-wave laser Nd:YAG has a thermal effect compared with the photodisruptive effect of a 1064 nm pulsed Nd:YAG laser. Certainly, a lower requirement for a 1064 nm pulsed laser to achieve a patent iridotomy is likely to result in less dispersion of iris pigment into the aqueous and thus there is a need for phagocytosis in already compromised outflow pathways.

Iridotomy with pretreatment using a continuous-wave Nd: YAG laser is by definition more time consuming to perform. However, we believe this is generally not the case in clinical practice due to the lower risk of iris haemorrhage and thus potential treatment delays. Moreover, any additional time can be minimised by using the newer combined continuous-wave and pulsed lasers that share the same laser delivery platform.

With these it is possible to complete both stages per eye without even removing the contact lens.

This study provides evidence that iridotomy with pretreatment using a continuous-wave Nd:YAG laser is safer and more effective than the pulsed Nd:YAG only laser iridotomy for dark irides and should be considered as the preferred technique.

**Competing interests** None.

**Ethics approval** This study was approved by the Moorfields Eye Hospital Research Committee and the Moorfields/Whittington NHS Ethics Committee.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**REFERENCES**

Randomised trial of sequential pretreatment for Nd:YAG laser iridotomy in dark irides

D Julian de Silva, Alexander C Day, Catey Bunce, et al.

Br J Ophthalmol 2012 96: 263-266 originally published online April 21, 2011
doi: 10.1136/bjo.2010.200030

Updated information and services can be found at:
http://bjo.bmj.com/content/96/2/263.full.html

References

These include:
This article cites 19 articles, 6 of which can be accessed free at:
http://bjo.bmj.com/content/96/2/263.full.html#ref-list-1

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/