CLINICAL STUDY

Frequency-doubled Nd:YAG laser for the treatment of exudative diabetic maculopathy

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Abstract

Purpose **To determine the clinical efficacy of frequency-doubled Nd:YAG (FD YAG) laser for the treatment of diabetic clinically significant macular oedema (CSMO).**

Methods **A prospective pilot study was carried out on 55 eyes with CSMO. FD YAG laser exposures were applied in a focal or grid pattern. The results were evaluated by Snellen visual acuity, slit-lamp biomicroscopy, colour photography and fundus fluorescein angiography.**

Results **At mean review of 5.3 months, macular oedema had resolved either completely or partly in 44 (80%) eyes, was unchanged in 10 (18%) eyes and progressed in 1 (2%) eye. Visual acuity improved in 11 (20%), stabilised in 40 (73%) and deteriorated in 4 (7%) eyes.**

Conclusion **FD YAG laser therapy is effective in the treatment of CSMO. It combines the ergonomic advantages of a solid-state laser with the benefits of its wavelength. A comparison between the clinical results of FD YAG and other lasers used in the treatment of CSMO is, however, required.**

Key words Clinically significant macular oedema, Diabetic maculopathy, Diabetic retinopathy, Frequency-doubled Nd:YAG laser, Laser photocoagulation

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Previously presented as a Free Paper at the Annual Congress of the Royal College of Ophthalmologists, Cardiff, May 1998

Received: 17 January 2001
Accepted in revised form: 11 June 2001

Proprietary interest: None

The efficacy of argon, diode and krypton lasers has already been proven in the treatment of clinically significant macular oedema (SMO).[1–5] Frequency-doubled Nd:YAG (FD YAG) laser (532 nm), like the argon green laser (514 nm), has the advantages of good absorption in the melanin of retinal pigment epithilium, reduced risk of extensive neuroretinal damage due to low absorption in xanthophyll and high absorption in oxyhaemoglobin, thereby causing direct closure of microaneurysms.[6,7] It is also a solid-state device, with all the attendant advantages of portability, efficiency and reliability. Diode (810 nm) and krypton (647 nm) lasers, on the other hand, offer the benefits of their longer wavelengths with ease of penetration through media opacities, but at the cost of poor absorption in melanin and haemoglobin.[4,5] FD YAG combines the advantages of solid-state lasers with the emission of green wavelength.[8] L'Esperance[9] first demonstrated the photocoagulation effect of FD YAG laser on rabbit and human eyes. Histological studies show no difference between the morphology of chorioretinal burns caused by FD YAG laser and argon green laser.[6,10,11]

FD YAG laser has been used in the treatment of a variety of retinal disorders, including retinal vein occlusion, diabetic retinopathy, retinal tears, Eales' disease, Coats' disease and age-related macular degeneration.[12] Its efficacy in panretinal photocoagulation (PRP) has been proven.[7] There are, however, fewer data available on the treatment of CSMO with FD YAG laser. In 1995, Okuyama *et al.*[13] carried out a comparative study between FD YAG, diode and krypton lasers for CSMO in 26 eyes (divided into three groups). In the FD YAG group (6 eyes) the central 30° visual sensitivity was maintained better than in the diode laser group.

This study investigates the clinical effectiveness of FD YAG laser therapy for CSMO in a substantive sample size.

Patients and methods

Thirty-nine consecutive patients (55 eyes) referred to the Ophthalmology Department of King's College Hospital, London, were recruited for this prospective pilot study. All eyes had CSMO according to the Early Treatment Diabetic Retinopathy Study (ETDRS) classification.[11]

Table 1. *Patient data*

Total no. of patients	39
No. of eyes	55
Males	23
Females	17
Type I diabetes mellitus	19
Type II diabetes mellitus	21
Age range	42–82 years
Mean age	63.7 years
Fovea involved	44 eyes

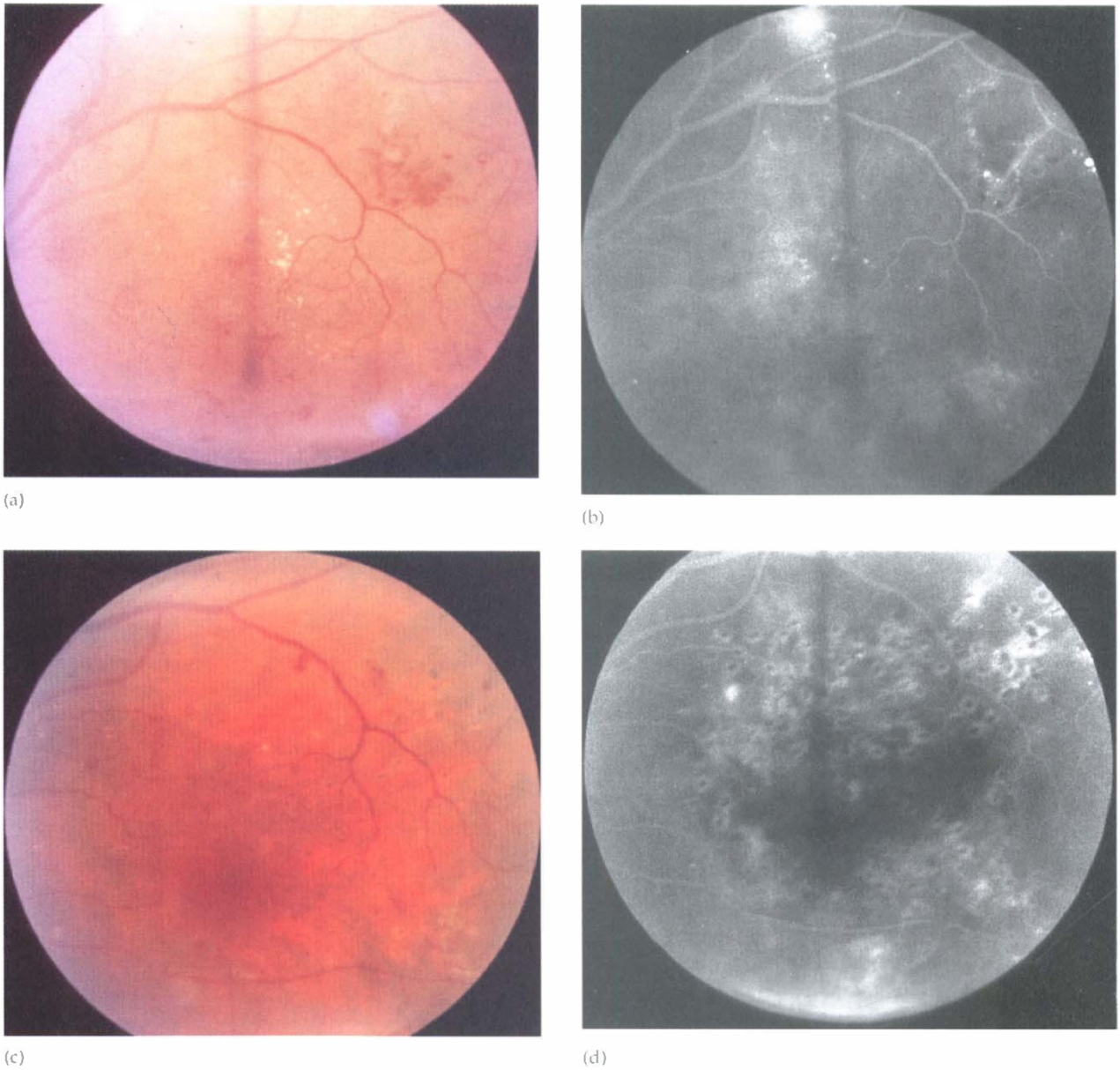

Fig. 1(a)–(d). *Eye no. 14. FD YAG laser applied in a modified grid pattern resulted in resolution of CSMO and closure of microaneurysms. Vision improved from 6/24 to 6/12, 19 weeks after FD YAG laser treatment.*

None of the patients had had laser treatment for diabetic retinopathy within the previous 2 years. One patient died from ischaemic heart disease following laser treatment for his maculopathy. His follow-up at 8 weeks showed marked resolution of macular oedema and improvement in vision. Table 1 shows the demographic data of the patients. Informed consent was obtained from the participating patients prior to the treatment. Visual acuity and fundus examination were performed before, 1 month, 3 months and finally 6 months after the treatment. In addition, colour photographs and intravenous fluorescein angiograms were obtained before the laser treatment and again at the last follow-up visit.

Best corrected visual acuity was recorded in all cases using the same Snellen chart in the same examination room. A change of 2 or more lines in Snellen visual acuity was considered as significant in evaluating the results. Use of an ETDRS chart would have been the ideal method for evaluation of visual acuity, but unfortunately the department did not have an ETDRS chart at the time of this study. Mydriasis was achieved using guttae tropicamide 1%. Fundoscopy was carried out with a 78 dioptre condensing lens (Volk, USA) using a slit-lamp (Haag Streit, Switzerland). As this is purely a clinical study, macular oedema was first assessed on the basis of retinal thickening by exercising clinical judgement alone. This was later confirmed by fundus fluorescein angiography (FFA). Patients with pure exudative maculopathy as well as those with mixture of exudative and ischaemic maculopathy were considered suitable for laser treatment. Patients with pure ischaemic maculopathy were excluded. A solid state FD Nd:YAG laser (Iris Medical, USA), emitting at 532 nm, continuous wave, was used for the treatment of macular oedema. A slit-lamp-mounted laser delivery system was used and the applications were delivered through a fundus contact lens (Area Centralis, Volk, USA). Threshold burns were produced using powers of between 70 and 210 mW

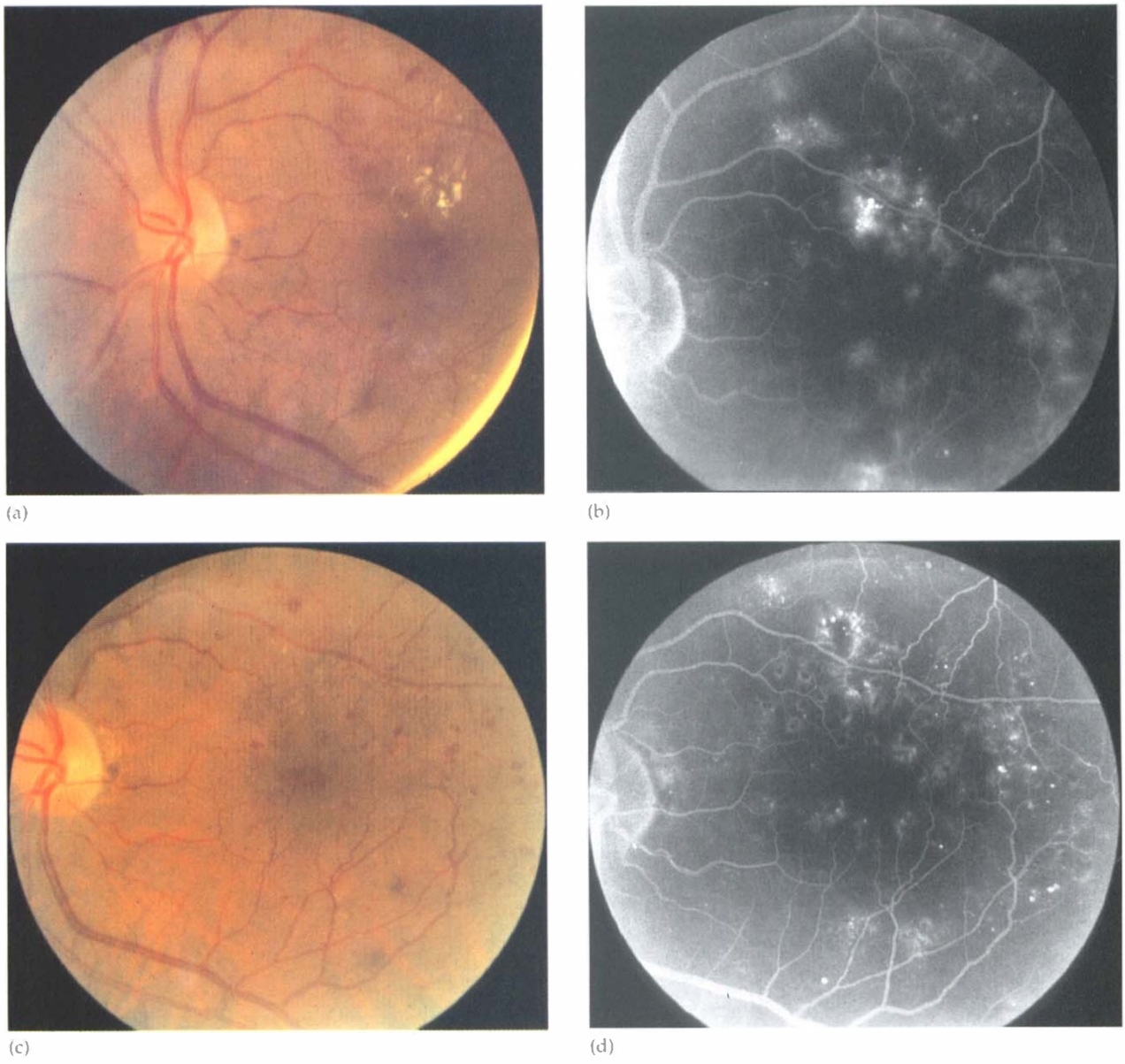

Fig. 2(a)–(d). *Eye no. 29. There is complete resolution of macular oedema after prophylactic laser therapy with FD YAG. Vision remained stable at 6/9, 24 weeks after treatment.*

(mean 108 mW), pulse duration 50 ms and a spot size of 75 μm. Burns were applied in a scatter pattern over the areas of retinal thickening and also focused on leaking microaneurysms. A single surgeon (M.S.) delivered laser treatment to all the patients in this study.

Patients were reviewed at 4 weeks, 12 weeks and finally at 24 weeks after the laser treatment. In some patients complete resolution of macular oedema and visual recovery was noted before 24 weeks and was considered the end point.

Treatment results were evaluated by assessing the visual acuity and macular oedema at the last follow-up.

Results

A change of up to 2 lines in Snellen visual acuity was considered significant. On this basis 11 (20%) eyes showed improvement, 40 (72%) remained stable whereas in 4 (7%) eyes, vision continued to deteriorate. The best improvement in vision was up to 3 Snellen lines and it was interesting to note that the patients who showed maximum improvement did so in the earlier phase of the follow-up (8–24 weeks). This included 1 patient (patient 32) who died during the follow-up. This last examination 8 weeks after the laser treatment showed partial resolution of macular oedema but 3 lines improvement in vision. Table 2 shows the details of treatment results.

Table 3 summarises the 4 eyes that showed visual deterioration. One of these 4 eyes had persistent leakage for which more laser was applied (eye 6). The remaining 3 eyes were noted to have macular ischaemia; one developed vitreous haemorrhage due to neovascularisation of the peripheral retina (new vessels elsewhere, NVE) and this necessitated PRP treatment of the ischaemic sector of retina (eye 48). The macular oedema did not resolve in this eye.

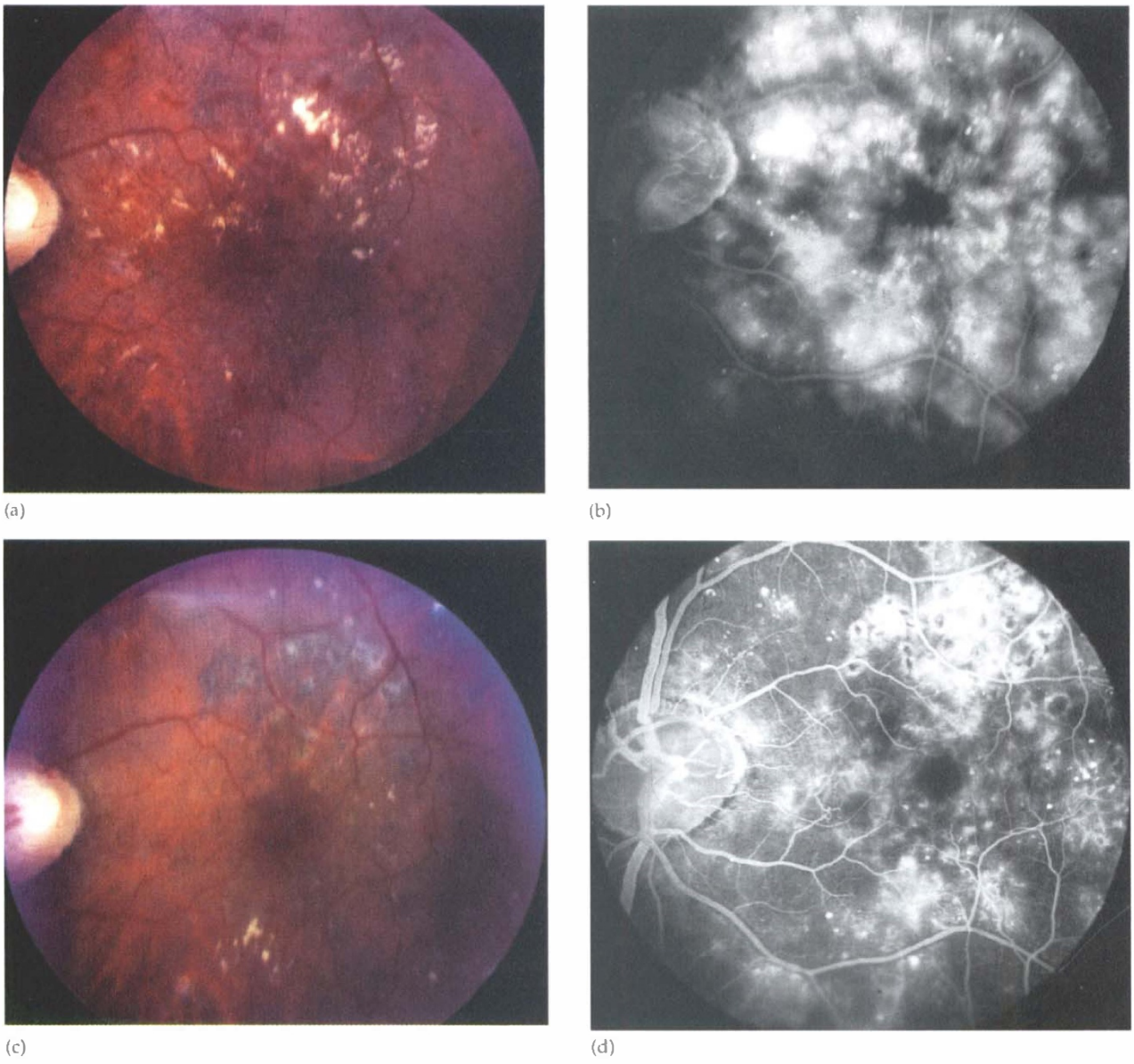

Fig. 3(a)–(d). *Eye no. 36. Extensive macular oedema that has recurred 4 years after argon laser treatment. Note the marked resolution in oedema and closure of dilated microaneurysms after FD YAG laser therapy. Vision improved from 6/36 to 6/12, 24 weeks after treatment.*

Ten eyes failed to show any signs of resolution of macular oedema, whereas 1 eye showed worsening of macular oedema. Three of these 10 eyes required PRP laser later due to either NVE or new vessels at disc (NVD). These 3 eyes had significant visual loss after focal laser treatment due to macular ischaemia and the remaining 7 maintained stable vision. Four eyes in the non-resolving group were considered suitable for more focal laser with FD YAG laser after an interval of 24–28 weeks. Re-treatment was considered necessary because there was still a significant amount of oedema clinically visible at a stage when resolution was to be expected.

Laser-related complications were not observed, but a few eyes developed complications as a result of diabetic retinopathy or other ocular condition. One eye (eye 47) developed neovascularisation at the optic disc (NVD), whereas 3 eyes (eyes 17, 31 and 48) developed NVE. One eye (no. 4) had impending central retinal vein occlusion (CRVO), which was observed in the form of tortuous veins and extensive arteriovenous nipping, 20 weeks after the laser treatment. This patient was hypertensive. There were no signs of proliferative or pre-proliferative retinopathy clinically, or on FFA. Following laser treatment, there was partial resolution of oedema with a 1 line improvement in vision.

Discussion

The ETDRS has confirmed the benefit of laser photocoagulation in diabetic retinopathy. The use of laser photocoagulation reduces the risk of significant visual loss due to macular oedema by 50% or more.[2] In the ETDRS, argon green laser (514 nm) was used due to its favourable wavelength characteristics. It is effective due to its good absorption in the melanin of the retinal pigment epithelium, and safe due to relatively poor absorption in macular xanthophyll compared with blue wavelength. Subsequent studies have tested the efficacy

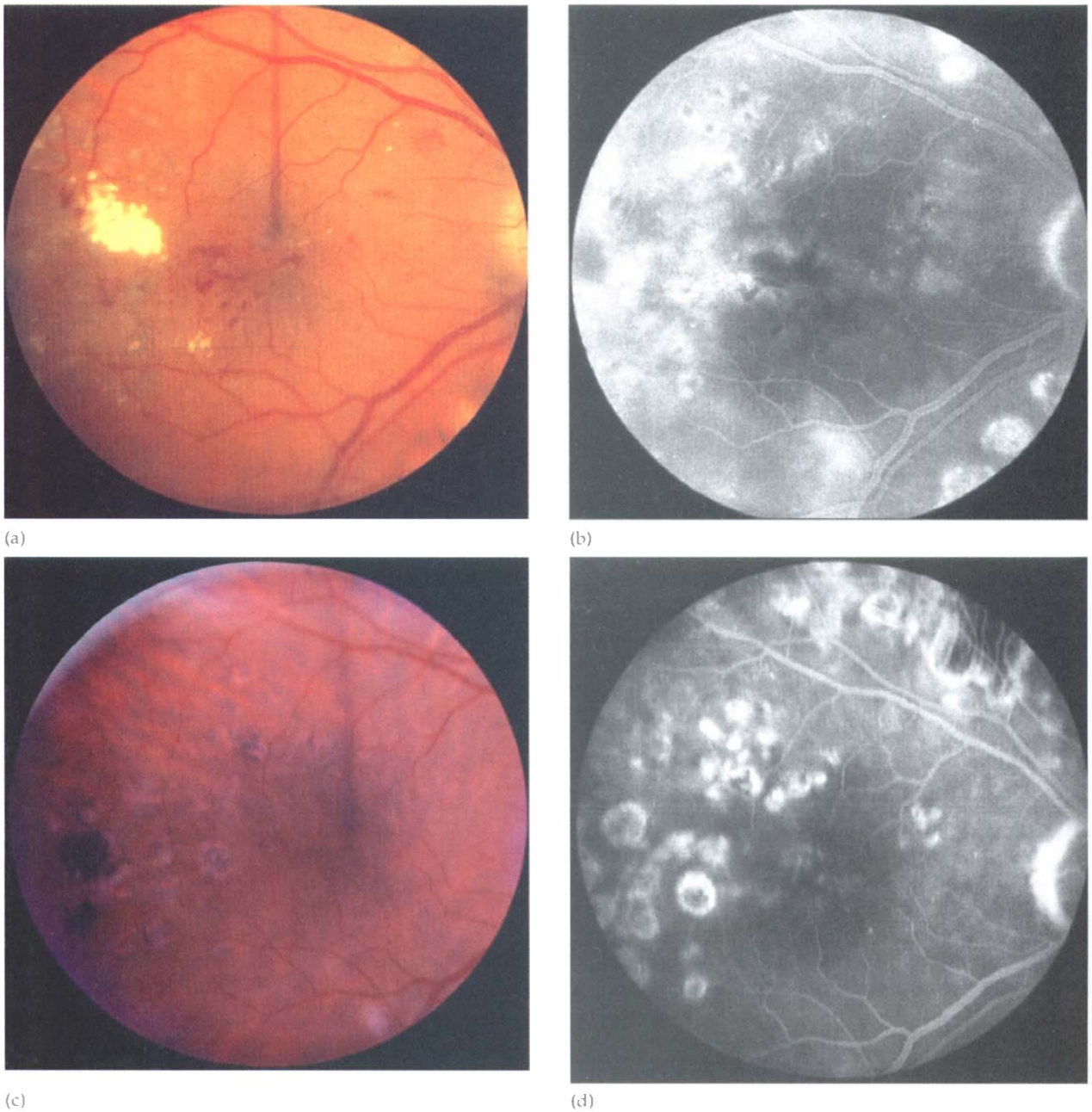

Fig. 4(a)–(d). *Eye no. 42. Recurrence of macular oedema more than 2 years after focal argon laser treatment. Macular oedema has an almost cystoid appearance on fluorescein angiography (b). Exudates have disappeared after FD YAG laser therapy (c), with marked reduction in leakage (d). Vision improved from 6/12 to 6/9, 24 weeks after treatment.*

of longer-wavelength lasers such as the diode (810 nm)[5,15–17] and krypton (647 nm)[4,13,18,19] lasers. Longer wavelengths are absorbed relatively poorly by the lens and blood and thus are useful in the presence of nuclear sclerosis or vitreous haemorrhage. They have minimal absorption by the macular xanthophyll. The photocoagulation effect of these longer wavelengths is quite different from that of argon green. The energy absorption in the case of the krypton laser, and particularly the diode laser, is more at the level of the choroid. The burn caused is at a deeper level and clinically much less white in appearance. There is more risk of potential damage to Bruch's membrane and choroidal haemorrhage if these lasers are used at higher energy levels.

The 532 nm wavelength of the FD YAG laser, being longer than the 514 nm of argon green, has a theoretical advantage, which may be clinically significant: it undergoes less scattering and results in a better-focused beam,[20] which is an important consideration in the treatment of the macula. FD YAG laser has the time-tested benefit of green wavelength that has been shown to be very effective in the treatment of diabetic retinopathy including exudative maculopathy. Its good absorption by the retinal melanin is comparable to that of the argon green laser. Due to a slightly longer wavelength than argon green it may possibly be absorbed less by the macular xanthophyll, which is a protective feature. For the same reason the potential damage to the Henle's nerve fibre layer is less, which is relevant in the treatment of the macula.[21,22]

Table 2. *Patient data, FD YAG laser treatment parameters and results*

Eye no.	Patient no.	Age (years)	Sex	Eye (R/L)	Focal or grid (F/G)	Av. power (mW)	VA pre-laser	VA post-laser	VA change +/−	CSMO (R/PR/UR/W)	Complication/ outcome
1	1	64	F	R	F	75	6/6	6/5	0	R	
2	1			L	F	75	6/5	6/5	0	R	
3	2	67	F	L	F	80	6/12	6/6	+	R	
4	3	82	M	L	F	150	6/24	6/18	0	PR	Imp. CRVO
5	4	65	F	R	F	100	6/18	6/24	0	UR	AION
6	4			L	FG	112	6/18	6/36	–	W	More focal
7	5	68	M	R	F	120	6/9	6/6	0	R	
8	5			L	F	90	6/9	6/6	0	PR	
9	6	51	M	L	F	100	6/9	6/5	+	R	
10	6			R	F	75	6/6	6/5	0	R	
11	7	55	M	R	F	70	6/9	6/6	0	R	
12	7			L	F	100	6/9	6/6	0	R	
13	8	72	F	R	F	160	6/9	6/6	0	R	
14	9	69	M	L	FG	135	6/24	6/12	+	R	
15	10	68	M	L	G	180	6/12	6/18	0	R	
16	10			R	F	135	6/12	6/6	+	R	
17	11	49	M	R	FG	100	6/9	6/9	0	UR	NVE/PRP
18	11			L	F	90	6/9	6/9	0	R	
19	12	61	F	L	F	105	6/12	6/12	0	R	Macular ischaemia
20	12			R	F	120	6/9	6/18	–	R	Macular ischaemia
21	13	48	F	L	F	80	6/5	6/6	0	R	
22	13			R	F	80	6/5	6/6	0	R	
23	14	55	M	R	FG	85	6/6	6/6	0	R	
24	15	67	F	R	FG	180	6/36	6/12	+	R	
25	15			L	F	180	6/24	6/18	0	R	
26	16	69	M	R	F	130	6/6	6/9	0	PR	
27	17	77	M	L	F	180	6/12	6/12	0	PR	
28	18	63	M	R	F	90	6/18	6/18	0	UR	More focal
29	19	66	F	L	F	100	6/6	6/6	0	R	
30	20	78	M	L	FG	205	6/36	6/60	0	R	Macular ischaemia
31	21	56	F	R	F	90	6/24	6/12	+	R	NVE/PRP
32	21			L	F	100	6/12	6/9	0	R	
33	22	81	F	L	F	110	6/9	6/9	0	R	
34	23	60	F	R	F	130	6/12	6/18	0	PR	
35	24	64	M	R	F	160	6/12	6/12	0	PR	More focal
36	25	59	F	L	FG	80	6/36	6/12	+	R	
37	26	60	M	L	F	90	6/6	6/6	0	R	
38	27	71	M	L	F	80	6/18	6/6	+	R	
39	27			R	F	85	6/18	6/9	+	R	
40	28	63	M	L	F	75	6/12	6/12	0	R	
41	29	79	M	R	F	105	6/36	6/24	0	UR	More focal
42	30	49	F	R	F	70	6/12	6/9	0	R	
43	30			L	F	70	6/12	6/12	0	R	
44	31	61	F	R	G	110	6/36	3/60	–	UR	Macular ischaemia
45	31			L	F	110	6/18	6/12	0	PR	
46	32	77	M	L	G	110	5/60	6/24	+	PR	Deceased
47	33	77	M	R	F	90	6/6	6/9	0	UR	NVD/PRP
48	33			L	G	120	6/9	6/18	–	UR	VH, NVE/PRP
49	34	65	M	R	FG	110	6/18	6/18	0	UR	More focal
50	35	76	F	R	F	120	6/12	6/12	0	R	
51	36	65	F	R	F	90	6/18	6/6	+	R	
52	37	64	F	L	F	110	6/12	6/12	0	R	
53	38	76	M	R	F	115	6/12	6/18	0	UR	
54	38			L	F	160	6/9	6/12	0	UR	
55	39	42	M	L	F	80	6/6	6/6	0	R	

Eye R/L, right or left; Av. power (mW), average laser power in milliwatts; VA pre-laser, vision before laser treatment; VA post-laser, vision after laser treatment; VA change +, 2 or more lines improvement in vision; VA change −, 2 or more lines deterioration in vision; CSMO (R/PR/UR/W), clinically significant macular oedema (resolved/partly resolved/unresolved/worse); Imp. CRVO, impending central retinal vein occlusion; AION, anterior ischaemic optic neuropathy; More focal, more focal laser treatment; VH, vitreous haemorrhage; NVE, new vessels elsewhere; NVD, new vessels at disc; PRP, panretinal photocoagulation.

FD YAG laser, in addition to its wavelength characteristics, has the benefit of being a solid-state laser and portable. Earlier versions of the FD YAG laser had unpredictable outputs and therefore were not as safe as the current versions. Advances in laser technology have resulted in the development of modern FD YAG laser equipment which incorporates potassium titamyl phosphate (KTP) as a frequency-doubling crystal and

Table 3. *Reduction in vision following FD YAG treatment*

Serial no.	Eye no.	Snellen lines reduction in VA	Cause
1	6	2	Progression of oedema
2	20	2	Macular ischaemia
3	44	4	Macular ischaemia
4	48	2	Vitreous haemorrhage, macular ischaemia, unresolved oedema

produces a continuous wave output.[23] It has simple operational requirements in terms of power supply and cooling.

In our experience, the FD YAG laser produced consistent and predictable clinical burns during the treatment. Other users of the same laser have independently supported this observation.

We conclude from this pilot study that the FD YAG laser is effective and safe for the treatment for diabetic macular oedema. There was no control group in this study as it was considered unsafe not to treat the macular oedema. ETDRS results showed that after 3 years of follow-up, focal laser reduced the risk of severe visual loss by 50% (only 12% of cases developed significant visual loss).[2] It is difficult to make a direct comparison between the results of our study and those of the ETDRS, but the outcome of the FD YAG laser treatment in our group of patients is also very encouraging, showing significant visual loss in only 7% of cases in a relatively short mean period of only 5.3 months. This number may possibly rise over a longer follow-up period due to progression of the retinopathy in a proportion of cases. A direct comparative analysis between the clinical effects of the FD YAG and other lasers is, however, required.

We thank Mr C. Clement, Ophthalmic Photographer, King's College Hospital, London; and Iris Medical for the loan of the frequency-doubled YAG laser.

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