## The National Diabetic Retinopathy Laser Treatment Audit. II. Proliferative retinopathy

### Abstract

The National Diabetic Retinopathy Laser Treatment Audit is a prospective survey of laser treatment for diabetic retinopathy throughout the United Kingdom. This paper presents data on 284 patients who were undergoing their first panretinal photocoagulation for proliferative retinopathy during a 2 month period in 1995, describing the demographic features, the level of systematic screening, the sources of referral, and the waiting times. For those cases where proliferative retinopathy was present at the first ophthalmology outpatient visit, the retinopathy was detected as a result of systematic screening in 46.8%, whilst 28.7% presented symptomatically. Of these patients 28.4% waited for more than 12 weeks from referral to the time of laser treatment, but once the patient had been listed for laser treatment this was performed within 8 weeks in 95.3%. The retinopathy features and the type of treatment given are also described. Compared with the DRS and ETDRS recommendations, at least 32.5-40.2% of eyes may be undertreated initially, and for those with highrisk characteristics these figures were at least 30.8-38.5%.

*Key words* Diabetic retinopathy, Proliferative retinopathy, Laser, Panretinal photocoagulation, Process, Screening

The effectiveness of photocoagulation in the treatment of proliferative diabetic retinopathy has been demonstrated in a number of studies.<sup>1-4</sup> Despite the availability of an effective treatment many patients do still go blind from diabetic retinopathy, and it remains a leading cause of blindness in patients of working age in the Western world.<sup>5-8</sup> The Saint Vincent Declaration, endorsed by the British Diabetic Association and the Department of Health, set as one of its targets reducing blindness due to diabetes by one-third or more.<sup>9</sup>

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Whether this can be achieved depends on a number of factors including screening and the efficacy of treatment.

This national audit was designed to examine the processes of delivery of photocoagulation treatment for diabetic retinopathy throughout the United Kingdom. This paper presents data on patients with proliferative retinopathy.

## Methods

The full description of the methodology for this audit is described elsewhere.<sup>10</sup> In brief, all consultant ophthalmologists in the UK who undertake laser treatment for diabetic retinopathy were invited to participate. Eligible for inclusion were those patients with proliferative diabetic retinopathy undergoing panretinal photocoagulation for the first time in a particular eye during June and July 1995. The ophthalmologist performing the laser treatment was asked to complete a confidentially coded questionnaire containing questions on retinopathy features, visual acuity prior to photocoagulation, grade of ophthalmologist performing the treatment, and the treatment given. The questionnaire also asked for the sources of referral, the mode of detection of the retinopathy, and waiting times for the clinic and laser treatment.

For those patients who were undergoing bilateral simultaneous treatment (n = 20), the eye with the worse visual acuity was included in the audit. Where the vision was equal in the two eyes, the right or left eye was randomly chosen for further analysis.

## Results

#### Patient characteristics

Two hundred and eighty-four patients undergoing the first panretinal

photocoagulation in one eye were recruited into the audit. Their mean age was 54.8 years, range 17–85 years; 42.1% were female, and 57.9% were C.C. Bailey ⊠ J.M. Sparrow R.H.B. Grey H. Cheng The Royal College of Ophthalmologists 17 Cornwall Terrace London NW1 4QW, UK

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#### Table 1. Source of referral to the ophthalmology clinic

	n	%
Hospital physician	116	41.3
General practitioner	79	28.1
Optometrist	37	13.2
Hospital ophthalmologist	37	13.2
Self-referral	10	3.6
Ophthalmic medical practitioner	2	0.7
Total	281	100

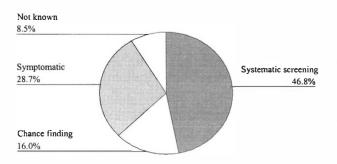
male (chi-squared = 6.96, p < 0.01). The right eye was recruited into the audit in 54.6% of patients, and the left eye was recruited in 45.4%.

Diabetes mellitus was diagnosed before the age of 30 years and required insulin treatment (younger-onset) in 31.2% (64) of these patients. Diabetes mellitus was diagnosed after the age of 30 years (older-onset) in 68.8% (141). Of the older-onset group, 43.3% (61) required insulin treatment, 50.3% (71) required oral hypoglycaemic agents, and 6.4% (9) were controlled with diet alone.

The mean duration of diagnosed diabetes for these cases with proliferative retinopathy was 16.8 years (range 0.1–54.9 years). For those with younger-onset diabetes mellitus, the mean duration of diabetes was 24.7 years (range 7.3–54.9 years). For the older-onset group, the mean duration of diagnosed diabetes was 13.1 (range 0.1–34.1 years).

#### Sources of referral and level of systematic screening

The sources of referral to the ophthalmology clinic are shown in Table 1. A total of 69.4% of patients were referred by their hospital physician or general practitioner, while in 13.2% of cases the referral was initiated by the optometrist. Proliferative retinopathy was present at the first ophthalmology clinic appointment in 35.9% (94), and for this group (excluding self-referrals) the presence of proliferative retinopathy was correctly identified by the referrer in 48.2% of cases.



**Fig. 1.** Mode of detection of the retinopathy that led to referral to the ophthalmology outpatient clinic, for those patients in whom proliferative retinopathy was present at the first ophthalmology outpatient visit (n = 94). In this context, systematic screening refers to the detection of retinopathy as a result of at least annual, planned, dilated fundal examination by an optometrist or doctor. A chance finding refers to the detection of the pathology in a patient who did not undergo systematic screening as defined above, and who did not present symptomatically.

#### Table 2. Retinopathy features (n = 284)

Retinopathy feature present	n	%
NVD	144	50.7
NVE	169	59.5
Concurrent maculopathy	86	30.3
Previously treated maculopathy	76	26.7
Vitreous haemorrhage	73	25.7
Rubeosis	10	3.5
Traction	16	5.6
Traction retinal detachment	2	0.7

NVD, new vessels on the disc; NVE, new vessels elsewhere.

For all the cases undergoing panretinal photocoagulation, the detection of retinopathy that led to referral to the ophthalmology clinic was the result of systematic screening in 55.3%. In this context, systematic screening was defined as at least annual, dilated fundal examination by an optometrist or doctor. This group also included those patients who had maculopathy detected or treated prior to the development of proliferative retinopathy, and was not therefore a true reflection of the detection rate from screening for preproliferative or proliferative retinopathy per se. Fig. 1 is a truer reflection of the mode of detection of retinopathy for those in whom proliferative retinopathy was present at the first ophthalmology outpatient visit. For this group, 28.7% presented symptomatically, and the retinopathy was detected by systematic screening in 46.8%.

#### Retinopathy features present

The retinopathy features are described in Table 2. Patients who had new vessels on the disc (NVD) comprised 50.7%, whilst 59.5% had new vessels elsewhere (NVE). Overall 61.2% of patients had either NVD and/or NVE associated with vitreous haemorrhage, broadly equivalent to the 'high-risk characteristics' as defined by the Diabetic Retinopathy Study.<sup>2</sup>

In the fellow eye, 53.1% had proliferative retinopathy, 38.5% had maculopathy, 27.3% had background retinopathy only, and 1.1% had no diabetic retinopathy.

Table 3. Best-recorded vi	visual acuity	prior to	treatment <sup>a</sup>
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		51				
		uity in the e treated	Visual acuity in the better eye			
Visual acuity	n	%	n	%		
6/5	32	11.3	43	15.2		
6/6	52	18.4	68	24.0		
6/9	73	25.7	87	30.7		
6/12	46	16.2	37	13.1		
6/18	28	9.9	26	9.2		
6/24	15	5.3	5	1.8		
6/36	10	3.5	8	2.8		
6/60	6	2.1	4	1.4		
<6/60	21	7.4	5	1.8		
Total	283	100	283	100		

<sup>a</sup>The best-recorded visual acuity using spectacles and/or pinhole if required.

**Table 4.** Waiting times to be seen in the ophthalmology clinic and for the laser treatment

Wait (weeks)	n	%	Cumulative %
For laser treatment			
Treatment on same day	52	18.9	18.9
1–4 weeks	166	60.4	79.3
5–8	44	16.0	95.3
9–12	11	4.0	99.3
>12	2	0.7	100
Total	275	100	
For clinic appointment <sup>a</sup>			
Up to 4	41	48.8	48.8
5-8	23	27.4	76.2
9–12	11	13.1	89.3
1316	5	5.9	95.2
>16	4	4.8	100
Total	84	100	
Overall <sup>b</sup>			
Up to 4	24	29.6	29.6
5-8	21	26.0	55.6
912	13	16.0	71.6
13-16	11	13.6	85.2
>16	12	14.8	100
Total	81	100	

<sup>a</sup>Refers to cases where proliferative retinopathy was present at the first ophthalmology outpatient visit.

<sup>b</sup>Refers to the overall wait from the time of referral to the laser treatment for those cases where proliferative retinopathy was present at the first ophthalmology outpatient visit.

#### Best-recorded visual acuity in the eye to be treated

The best-recorded visual acuity in the eye prior to treatment is shown in Table 3, which reveals that 55.4% of eyes to be treated had a best-recorded visual acuity of 6/9 or better, whilst 18.3% had a best-recorded visual acuity of 6/24 or worse. Where the visual acuity was less than 6/9 in the treated eye, 24.2% had some degree of cataract sufficient to cause a reduction in visual acuity. In the better eye, 70.0% of patients had a visual acuity of 6/9 or better, whilst 7.8% had a visual acuity of 6/24 or worse.

## Waiting times to be seen in the ophthalmology outpatient clinic and for the laser treatment

The waiting times to be seen in the ophthalmology clinic and for the laser treatment are shown in Table 4. The median wait for the laser treatment from listing was 2 weeks (range 0–14 weeks), 79.3% being treated within 4 weeks whilst 4.7% waited for more than 8 weeks from listing for their laser treatment. For those patients in whom proliferative retinopathy was present at the first ophthalmology outpatient visit, the median wait for the clinic appointment was 5 weeks (range 0–30 weeks), 48.8% being seen within 4 weeks of referral, while 10.7% waited for more than 12 weeks for their clinic appointment. For these cases, the overall wait from the time of referral to the time of laser treatment was a median 7 weeks (range 0–31 weeks), and 28.4% waited for more than 12 weeks from the time of referral.

**Table 5.** Grade of ophthalmologist performing the panretinal photocoagulation

Grade of ophthalmologist	n	%
Consultant	100	35.6
Associaté specialist	35	12.5
Staff grade	30	10.7
Clinical assistant	19	6.8
Fellow	4	1.4
Senior registrar	31	11.0
Registrar	44	15.7
Senior house officer	10	3.6
SHO or other under supervision	8	2.8
Total	281	100

# Grade of ophthalmologist performing panretinal photocoagulation

The grade of ophthalmologist performing panretinal photocoagulation is shown in Table 5. A consultant ophthalmologist performed 35.6% of the photocoagulation.

## Treatment given

In 41.2% of cases it was considered that the ophthalmologist intended to give the initial panretinal photocoagulation in one sitting. This was based upon the statement that the next appointment was for reassessment rather than specifically for further treatment. In 55.6% of cases it was intended to divide the initial treatment into more than one session, whilst in 3.2% of cases this information was not recorded. The spot sizes used for the panretinal photocoagulation are shown in Table 6 and the number of burns given at the first treatment is shown in Table 7. For the group in which the intention was to give the initial panretinal photocoagulation treatment in one session (n = 117), the median number of burns given at the first session was 1146 (range 325-2686). 3.4% of eyes were given fewer than 500 burns, and 18.8% of eyes were given fewer than 800 burns.

A peri- or retrobulbar injection of anaesthetic was given in 6.9% of all patients undergoing panretinal photocoagulation, and in 5.7% of those who were given the initial treatment in one session.

Table 6. Spot size used for the laser treatment<sup>a</sup>

Spot size used (µm)	n	%
100	2	0.7
150	5	1.8
200	108	38.3
250	10	3.5
300	19	6.7
350	1	0.4
400	29	10.3
500	107	37.9
600	1	0.4
Total	282	100

<sup>a</sup>Does not necessarily represent the size of the laser spot on the retina, in view of the range of possible lenses used for the treatment. Refers to the most frequently used spot size for the treatment.

No. of burns	Cases (%) for whom intention was to give PRP in one session (n = 117)	Cases (%) for whom intention was to give PRP in more than one session (n = 158)	All cases (%) ( <i>n</i> = 284)	Cases (%) with NVD and/or NVE associated with vitreous haemorrhage, <sup>a</sup> for whom the intention was to give PRP in one session (n = 65)
<500	3.4	9.5	7.4	0
500-999	26.5	44.9	36.3	24.6
1000-1499	41.0	31.7	35.2	47.7
15001999	17.1	11.4	14.4	20.0
2000-2500	10.3	2.5	5.6	7.7
>2500	1.7	0	1.1	0

<sup>a</sup>Broadly equivalent to the high-risk characteristics as defined by the DRS.

## Treatment for concurrent maculopathy

For those patients in whom maculopathy was present concurrently with proliferative retinopathy (n = 86), 26.7% (23) had undergone treatment for the maculopathy prior to the panretinal photocoagulation, whilst 45.3% (39) had the maculopathy treated at the same session. In 22.1% of cases (19) the maculopathy was to be treated after the panretinal photocoagulation, whilst in 5.8% (5) there was no specific intention to treat the maculopathy. For those in whom treatment of the maculopathy was to be after the panretinal photocoagulation, this was intended to be within 1 month of the panretinal photocoagulation in 10.5%, within 1-2 months in 31.6% and had not been decided in 57.9%. For those whose concurrent maculopathy was treated prior to panretinal photocoagulation, this was performed between 0.4 and 109 weeks before, with a median value of 18 weeks.

#### Follow-up

When the next appointment was specifically for further treatment (n = 158), the median interval was 2 weeks (range 1–11 weeks). Further treatment was to be given within 2 weeks in 60.3%, within 3–4 weeks in 28.8%, whilst 8.3% were to be brought back for further treatment after 5–6 weeks and 2.6% were to be brought back for further treatment after 6 weeks. When the next appointment was for reassessment rather than specifically for further treatment (n = 117), the median follow-up was 6 weeks (range 1–13 weeks). Reassessment was to be within 4 weeks in 30.2%, within 5-8 weeks in 55.1%, whilst 14.7% were to be brought back for reassessment within 9–13 weeks.

#### Discussion

#### Patient characteristics

The sample had significantly more men than women. The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) showed a significant association between male gender and the development of proliferative retinopathy in those patients in whom diabetes was diagnosed before the age of 30 years and required insulin treatment, where diabetes had been present for more than 10 years,<sup>11</sup> but this was not found for those patients with older-onset diabetes.<sup>12</sup> The excess of male patients with proliferative retinopathy probably reflects the fact that diabetes is now more common in men than women in the UK. The 1993 Health Survey of England<sup>13</sup> reported a prevalence of diabetes of 3% in men compared with 2% in women, and in the UK Prospective Diabetes Study the ratio of men to women was 3:2.<sup>14</sup>

In this audit, 32% of the patients with proliferative retinopathy had diabetes of younger onset (diagnosed before the age of 30 years and requiring insulin treatment). This may be compared with the estimate that 10-25% of adults with diabetes in the UK have type 1 diabetes.

The mean duration of diabetes from diagnosis to the time of recruitment into the audit was lower for the older-onset than the younger-onset groups. For those with younger-onset diabetes, 1.8% had a duration of disease of less than 10 years, with a mean of 24.7 years. For the older-onset group, 40.7% had had diabetes for less than 10 years with a mean duration from diagnosis of 13.2 years. This is in accordance with expectations based upon the WESDR, which showed that during the first 9 years of diabetes the rates of panretinal photocoagulation treatment were higher in older-onset compared with younger-onset patients,<sup>15</sup> and in the UK Prospective Diabetes Study diabetic retinopathy was present at the time of diagnosis in at least 18% of patients with type 2 diabetes.<sup>16</sup> These observations probably reflect the fact that type 2 diabetes may have been present for several years before diagnosis.

The number of patients treated for new proliferative retinopathy during the study period can be extrapolated to represent about 2260 patients annually, which takes into account a level of participation of just over 75% as indicated by the validation exercise.<sup>10</sup> The 1993 Health Survey for England estimated that there are 1 380 000 adults with diabetes in the UK.<sup>13</sup> Thus it would appear that about 0.16% of adults with diabetes in the UK develop proliferative retinopathy in one eye that is detected and treated each year. The WESDR estimated the incidence of progression to proliferative retinopathy to be 2.7% per year for the first 4 years for those patients with younger-onset diabetes, whilst this was 2.0% for the older-onset group not requiring insulin.<sup>17</sup> In the UK,

the incidence of sight-threatening retinopathy is thought to be 1.2–1.5%.<sup>18,19</sup> A comparison of the number of patients expected to undergo first panretinal photocoagulation treatment per annum in the UK and the numbers actually treated would suggest that there is a significant amount of sight-threatening retinopathy that is not currently being detected or treated.

## Level of systematic screening

For those patients in whom proliferative retinopathy was present at the first outpatient clinic, the retinopathy was detected by systematic screening in 46.8%, and 28.7% of patients presented symptomatically. This large percentage of patients presenting symptomatically suggests that a significant amount of proliferative disease is not being detected or treated. The presence of the proliferative retinopathy was correctly diagnosed by the referrer in only 48.2% of cases compared with 80.8% for maculopathy, when the disease was noted at first presentation to the ophthalmology clinic.<sup>10</sup> Moreover, 64.8% of maculopathy was detected by systematic screening, and 13.5% presented symptomatically. It would therefore appear that primary screening is less efficient at detecting proliferative retinopathy than maculopathy. Since the detection of proliferative retinopathy relies on screening in the asymptomatic stage, the sensitivity of primary screening needs to improve.

## Waiting times

While the median wait for treatment was only 2 weeks and 79.3% of patients were treated within 4 weeks of listing, 23.8% of patients with established disease still had to wait for more than 8 weeks to be seen in the outpatient clinic and the overall wait for treatment from referral was more than 12 weeks in 28.4%. Improvement of the waiting time to be seen in the ophthalmology clinic is indicated.

## Treatment given at the first session

The Diabetic Retinopathy Study (DRS) protocol for panretinal photocoagulation recommended 800–1600 argon laser burns of 500  $\mu$ m spot size extending to or beyond the vortex ampullae for eyes with high-risk characteristics.<sup>2</sup> The ETDRS protocol for full scatter treatment was developed from this and recommended 1200–1600 argon laser burns of 500  $\mu$ m spot size.<sup>20</sup> The ETDRS recommended that the treatment should be performed in two or more episodes, which were no more than 2 weeks apart, and that no more than 900 burns were to be applied in one session.

An estimate of the area of retina ablated can be described using the standard formula of  $\pi r^2$  multiplied by the number of burns (Fig. 2). Fig. 3 shows the results of this calculation for eyes with NVD and/or NVD associated with vitreous haemorrhage (broadly equivalent to the 'high-risk characteristics' as defined by the DRS). To avoid complexity the type of lens used in treatment was not specified in the questionnaire. However, since the quadraspheric lens gives the greatest possible magnification of the commonly available contact lenses used in treatment (by a factor of 1.9), one can assume a range of magnification of the areas of treated retina.

For the group in whom the intention was to give the initial panretinal photocoagulation in one session (n = 117), the median retinal area treated was 98.2 mm<sup>2</sup>

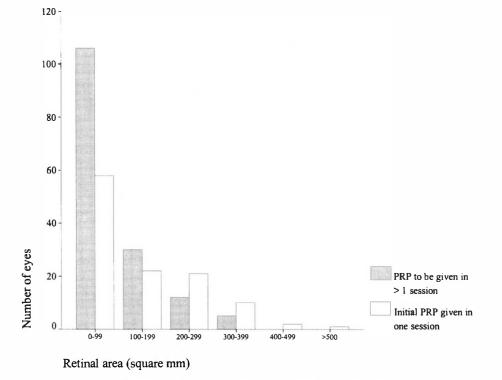
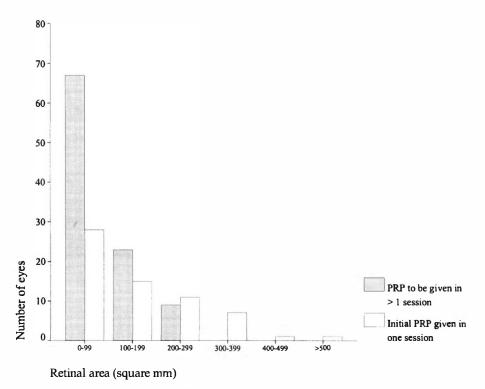


Fig. 2. Estimate of the area of retina ablated at the first treatment session.



**Fig. 3.** Estimate of the area of retina ablated for eyes with new vessels on the disc and/or new vessels elsewhere associated with vitreous haemorrhage (broadly equivalent to 'high-risk characteristics' as defined by the DRS).

(range 6.7–682.5 mm<sup>2</sup>), or 354.4 mm<sup>2</sup> (range 24.3-2464 mm<sup>2</sup>) based upon a calculation assuming use of the quadraspheric lens for all cases. For the subgroup with the equivalent of high-risk characteristics who were to be given their initial panretinal photocoagulation in one session (n = 65), the median retinal area treated was 104.6 mm<sup>2</sup> (range 10.4–682.5 mm<sup>2</sup>), or 377.6 mm<sup>2</sup> (range 37.6-2464 mm<sup>2</sup>) if the quadraspheric lens had been used for all cases. According to the DRS protocol, the recommended amount of retina treated is equivalent to an area of 157 to 314 mm<sup>2</sup>, whilst the lower limit for the full panretinal photocoagulation treatment as recommended by the ETDRS is equivalent to an area of 236 mm<sup>2</sup>. In this study, for those eyes in which the intention was to give the initial panretinal photocoagulation in one sitting, 64.1% of eyes received less than the lower limit of the DRS protocol, and 81.2% received less than the lower limit of the ETDRS protocol. For the subgroup with the equivalent of high-risk characteristics who were given their initial treatment in one session (n = 65), the corresponding figures were 60% and 80% respectively. If a spot magnification factor of 1.9 is taken for all cases, then 32.5% of eyes received less than the lower limit of the DRS protocol, and 40.2% of eyes received less than the lower limit of the ETDRS protocol. For the subgroup with the equivalent of highrisk characteristics who were treated in one sitting these results were 30.8% and 38.5% respectively.

These smaller areas of retinal ablation would appear to result more from the spot size used than from the number of burns given, since only 18% of eyes that received the initial panretinal photocoagulation treatment in one session were given fewer than 800 burns. Hulbert and Vernon<sup>21</sup> reported their practice of using 200 µm size burns in the initial treatment protocol, since this was often easier for the patient to tolerate and for the operator to deliver. Moreover, they found that this had beneficial effects on the ability of patients to retain driving fields. They found that between 3000 and 3500 burns induced regression in all but the most severe cases. To ablate the same area of retina as the equivalent of 800 burns of 500 µm spot size would require 4997 burns of 200 µm spot size. In this audit for those patients treated with burns of 200  $\mu$ m spot size, in whom the intention was to give the initial treatment in one session, the mean number of burns given was 1190, and for those with high-risk characteristics in this category the mean number of burns was 1127 (n = 23). For those in whom a 500 µm spot size was used and the intention was to give the initial treatment in one session, the mean number of burns used was 1301, and was 1315 for those with highrisk characteristics. It would therefore appear that the number of burns given was not increased for those cases in which a smaller spot size was used, although it is possible that a more magnifying lens was used for those eyes in which a smaller spot size was recorded. For eyes with the equivalent of high-risk characteristics (n = 172), the most frequently used spot size was 200 µm in 41.2% of eyes, whilst this was 500 µm in 32.4% of eyes. It would not appear that the smaller spot size is being reserved specifically for lower-risk eyes in order to try to preserve field. It is possible that the DRS and ETDRS recommend more treatment than is actually needed in many cases, but in practice some eyes do require more treatment than described by these studies.<sup>22,23</sup> There therefore appears to be a tendency to undertreat initially, compared with

the DRS and ETDRS protocols. The follow-up study will show whether this is limited to the initial stages and whether outcome is affected.

It is interesting to note that for these patients undergoing the first panretinal photocoagulation for proliferative retinopathy in one eye, proliferative retinopathy and/or maculopathy was present in the other eye in 71.6% of cases.

## Presence and treatment of concurrent maculopathy

In the DRS, by a combination of clinical examination and fluorescein angiography, 15.2% of eyes had definite macular oedema, and a further 29.2% had questionable macular oedema.<sup>24</sup> In this audit, concurrent maculopathy was said to be present in 30.3%, and maculopathy that had been previously treated and had resolved was present in 26.7%. The ETDRS compared giving immediate panretinal photocoagulation with either simultaneous or delayed focal treatment, and found that the former strategy was associated with the least visual loss.<sup>4</sup> The DRS also discussed the timing of treatment for concurrent maculopathy and suggested that 'perhaps eliminating or reducing retinal thickening by applying focal photocoagulation for macular edema before beginning scatter treatment might reduce the risk of visual loss'.<sup>24</sup> Some ophthalmologists make an exception to this approach, especially for young patients with IDDM who have aggressive peripheral ischaemia associated with macular oedema that may resolve following panretinal photocoagulation.<sup>25</sup> In this audit, concurrent maculopathy was treated before or at the same session as the panretinal photocoagulation in 72%, whilst in 22% it was intended to treat the maculopathy after the panretinal photocoagulation. In the latter group, the mean age was 56.9 years (range 31-81 years), and these patients would not generally appear to fit into the category of young patients with aggressive disease in whom it may be best to perform panretinal photocoagulation first.

In conclusion, this audit has provided unique data concerning the processes of delivery of photocoagulation treatment for proliferative retinopathy throughout the United Kingdom. The issues that need to be addressed are:

- 1. The long waiting time for a clinic appointment for cases with established disease. This is an organisational issue that needs to be tackled locally.
- 2. The large proportion of eyes presenting symptomatically (28.7%), which suggests poor screening procedures.
- The possible initial undertreatment of some eyes with proliferative retinopathy. The follow-up study will show whether this is limited to the initial stages and whether outcome is affected.

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