Retinopathy

Laser treatment still has a pivotal role in retinal disease

Guest Editor:
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The article by Shah et al (2011; summarised alongside) discusses the role of laser treatment in the management of retinal vascular diseases, in particular considering its role following the advent of anti-vascular endothelial growth factor (VEGF) therapy.

Laser therapy has long been established as an effective treatment for both proliferative diabetic retinopathy (PDR) and diabetic macular oedema (DMO), and from the 1970s onwards it was also used to treat choroidal neovascularisation in age-related macular degeneration (AMD). Its role in treating branch and central retinal vein occlusion was established in the 1980s and 1990s, respectively.

Laser photocoagulation for PDR and DMO is thought to improve oxygenation of the inner retina by reducing the production of proangiogenic cytokines such as VEGF. Laser may also act directly by shutting down leaking microaneurysms and improving the function of the retinal pigment epithelium.

Several studies have shown conclusively that laser reduces the risk of visual loss in PDR and DMO. In June 2010, the Diabetic Retinopathy Clinical Research Network (2010) published results of a multicentre, randomised, controlled trial of 854 eyes with DMO and compared the effectiveness of laser, intravitreal triamcinolone (IVTA) and intravitreal ranibizumab (an anti-VEGF agent). They reported a nine-letter improvement in best corrected visual acuity over 12 months in people treated with anti-VEGF therapy, either alone or in combination with laser treatment.

These results have widely led to a change in practice when treating DMO. Anti-VEGF injections are fast-acting and have fewer side-effects than laser and IVTA. Monthly treatments are given until retinal thickness no longer improves and can be resumed if oedema recurs or worsens. However, laser therapy still has a role in people unable to tolerate or comply with monthly injections and perhaps in those with cardiovascular disease, as anti-VEGF agents may confer a small risk of arterial thromboembolic events (Wong et al, 2007).

Exudative AMD was treated with laser or photodynamic therapy before the results of large trials in 2006 showed that intravitreal ranibizumab was a superior treatment (Rosenfeld et al, 2006). Focal laser can still be used for extrafoveal choroidal neovascularisation to avoid the treatment burden and risks of multiple injections. Sector or panretinal photocoagulation is still essential to avoid the neovascular complications of retinal vein occlusion.

The authors of the present article conclude that although there has been a substantial decrease in the use of laser over recent years, it continues to serve an important role in the management of retinal disease, in particular in DMO and vein occlusions that respond poorly to anti-VEGF therapy.

Diabetic Retinopathy Clinical Research Network (2010) Randomized trial evaluating ranibizumab plus prompt or deferred laser or triamcinolone plus prompt laser for diabetic macular edema. *Ophthalmology* **117**: 1064–77

Rosenfeld PJ, Brown DM, Heier JS et l (2006) Ranibizumab for neovascular age-related macular degeneration. *N Engl J Med* **355**: 1419–31

Wong TY, Liew G, Mitchell P (2007) Clinical update: new treatments for age-related macular degeneration. *Lancet* **370**: 204–6

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ACTA OPHTHALMOLOGICA

Diabetic retinopathy screening optimised by set of risk factors

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓

1 Complications of diabetic retinopathy (DR) can be reduced if the lesions are detected early by fundus photography.

2 As people with average or slow disease progression may undergo superfluous examinations, the authors sought to identify risk factor variables that could be entered into a decision model to optimise screening intervals.

3 Data from 5365 people with diabetes who had undergone 23 324 eye examinations were used.

4 The overall risk of requiring treatment for DR was affected by retinopathy grade and HbA_{1c}; risk was also affected by disease duration in T1D and by increasing age at diagnosis in T2D.

5 The authors concluded that a subset of risk factors should be used to optimise screening intervals for DR.

Mehlsen J, Erlandsen M, Poulsen PL, Bek T (2011) Indentification of independent risk factors for the development of diabetic retinopathy requiring treatment. *Acta Ophthalmol* **89**: 515–21

AMERICAN JOURNAL OF OPHTHALMOLOGY

Anti-VEGF and laser therapies are effective in DR

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓

1 Laser therapy has been the mainstay treatment for proliferative diabetic retinopathy (PDR) and diabetic macular oedema (DMO); new technologies include anti-vascular endothelial growth factor (anti-VEGF) therapy.

2 In this perspective, the authors consider laser management of retinal and neovascular diseases, and compare the effectiveness of laser therapy with anti-VEGF therapy.

3 Scatter panretinal photocoagulation is widely used for PDR and after venous occlusive events.

4 Focal/grid laser therapy has a role in DMO and can be used in combination with anti-VEGF therapy; this is also useful for people unwilling to receive injections.

5 Photodynamic therapy may be useful for the treatment of central serous chorioretinopathy and idiopathic polypoidal choroidal vasculopathy; it has largely been replaced by anti-VEGF therapy for age-related macular degeneration.

6 Anti-VEGF therapy is effective in preventing vision loss and improving vision, neovascular age-related macular degeneration and retinal vein occlusions; in DMO, anti-VEGF therapy seems to provide superior visual acuity results as well as being faster acting and potentially safer that focal/grid laser therapy.

7 Although the success of anti-VEGF therapy has decreased the use of laser therapies, it was concluded that laser therapy still has a pivotal role, such as in PDR and for the treatment of venous occlusion, and provides an alternative treatment in some cases of DMO.

Shah AM, Bressler NM, Jampol LM (2011) Does laser still have a role in the management of retinal vascular and neovascular diseases? *Am J Ophthalmol* **152**: 332–9

INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE

Serum lipids linked with CSMO in people with diabetes

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓

1 Diabetic retinopathy (DR) is a common complication of diabetes; diabetic macular oedema (DMO) can occur with DR, and clinically significant macular oedema (CSMO) is a major cause of vision loss.

2 As the role of lipids in the pathogenesis of DR and DMO is unknown, 500 adults with diabetes were prospectively recruited from eye clinics.

3 The presence of DR, DMO and CSMO were determined, and fasting total cholesterol, triglyceride, HDL-cholesterol, non-HDL-cholesterol and LDL-cholesterol were assessed.

4 In total, 321 participants (65.2%) had any DR, comprising 149 (33.0%) with DMO and 68 (15.1%) with CSMO.

5 After adjustments, those with higher total-, LDL- and non-HDL-cholesterol were more likely to have CSMO; serum lipids were not related to DR or DMO without CSMO.

6 It was concluded that serum lipids are independently linked with CSMO.

Benarous R, Sasongko MB, Qureshi S et al (2011) Differential association of serum lipids with diabetic retinopathy and diabetic macular oedema. *Invest Ophthalmol Vis Sci* **52**: 7464–9

BRITISH JOURNAL OF OPHTHALMOLOGY

Retinopathy can occur before diabetes diagnosis

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓

1 Although studies have demonstrated retinal changes at diagnosis of T2D, similar retinopathy may be observed preceding clinical recognition of diabetes.

2 A total of 295 people with T2D from the Diabetes Audit and Research in Tayside, Scotland, population-based register were included in this study.

3 Retinopathy was graded, and date of first diagnosis of diabetes ascertained from the register.

4 Of the participants, 14.68% (95% confidence interval [CI], 12.48–16.88%) had retinopathy at diagnosis.

5 The onset of detectable retinopathy was concluded to occur 5.77 years (95% CI, 4.6–7 years) before diagnosis.

Ellis JD, Zvandasara T, Leese G et al (2011) Clues to duration of undiagnosed disease from retinopathy and maculopathy at diagnosis in type 2 diabetes. *Br J Ophthalmol* **95**: 1229–33

INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE

Genes linked with DN and T2D are not linked with DR

Readability	✓✓✓
Applicability to practice	✓✓
WOW! factor	✓

1 As there is evidence that diabetic retinopathy (DR) shares risk factors with diabetic nephrology (DN) and macrovascular complications of T2D, genes associated with DN, T2D and vascular disease may be linked with DR.

2 Participants with T2D enrolled in the Candidate gene Association Resource (CARe) underwent fundus photography and genotyping of single nucelotide polymorphisms (SNPs) in 2000 candidate genes.

3 Of the 39 genes associated with DR, DN or T2D, only three SNPs in the P-selectin gene (*SELP*) were significantly linked with DR ($P<0.05$).

4 The authors found little evidence of a major DR gene; however, genetic variants associated with DR, such as those in *SELP*, should be studied further.

Sobrin L, Green T, Sim X et al (2011) Candidate gene association study for diabetic retinopathy in persons with type 2 diabetes: the Candidate gene Association Resource (CARe). *Invest Ophthalmol Vis Sci* **52**: 7593–602

INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE

Dexamethasone-cyclodextrin eye drops improve DMO

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓

1 Treatment of diabetic macular oedema (DMO) includes intravitreal injections or intravitreal implantation of corticosteroids and/or anti-vascular endothelial growth factor agents.

2 As with any surgical approach these procedures are at risk of complications.

3 The authors have developed a new approach for ocular pharmacology; microparticulate 1.5% dexamethasone-cyclodextrin eye drops have been shown to effectively deliver the drug in animal studies, and a modified form has shown excellent penetrance in the anterior section of the eye in humans.

4 This study reports the first clinical trial of 1.5% dexamethasone-cyclodextrin eye drops for the topical treatment of DMO in 19 patients.

5 Eye drops were administered three or six times daily for 4 weeks and then observed for 4 weeks without treatment; measures included visual acuity, intraocular pressure and optical coherence tomography to measure central macular thickness, recorded at baseline, week 4 and week 8.

6 At week 4, 63% of eyes (12/19) showed a central macular thickness decrease of more than 10% and 74% of eyes (14/19) showed an improvement in visual acuity (log of the minimal angle of resolution) by more than 0.1.

7 As no adverse effects were reported, it was concluded that topical dexamethasone-cyclodextrin eye drops decrease central macular thickness and improve visual acuity in DMO.

Tanito M, Hara K, Takai Y et al (2011) Topical dexamethasone-cyclodextrin microparticle eye drops for diabetic macular oedema. *Invest Ophthalmol Vis Sci* **52**: 7944–8

> *"As no adverse effects were reported, it was concluded that topical dexamethasone-cyclodextrin eye drops decrease central macular thickness and improve visual acuity in diabetic macular oedema."*