

# **NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE**

## **INTERVENTIONAL PROCEDURES PROGRAMME**

### **Interventional procedure overview of arteriovenous crossing sheathotomy for branch retinal vein occlusion**

Branch retinal vein occlusion (BRVO) is a blockage in one of the branch retinal veins in the eye and is usually associated with high blood pressure. As a result of ageing and raised blood pressure, the artery wall can harden and thicken, which can compress the retinal vein with which it shares a common sheath. This causes obstruction to the flow of blood within the vein at this point, and may lead to complete blockage of the vein itself.

In an arteriovenous crossing sheathotomy, the artery and the vein are separated from each other using a very small blade to cut away the sheath that they share. The aim of the procedure is to improve blood flow in the vein, reduce surrounding swelling (oedema) and improve sight.

## **Introduction**

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

## **Date prepared**

This overview was prepared in September 2009.

## **Procedure name**

- Arteriovenous crossing sheathotomy for branch retinal vein occlusion
- Arteriovenous decompression surgery for branch retinal vein occlusion
- Arteriovenous limiting membrane surgery for branch retinal vein occlusion

## **Specialty societies**

- Royal College of Ophthalmology

## Description

### *Indications and current treatment*

Branch retinal vein occlusions typically occur at arteriovenous crossings.

At these locations the artery and vein share a common adventitial sheath. As a result of ageing and raised blood pressure, the artery wall hardens and thickens, leading to compression of the retinal vein. This causes obstruction to the flow of blood within the vein at this point, and may be associated with secondary thrombosis, macular oedema, and decreased visual acuity.

Usual management may include observation due to the variable natural history and progression of the condition. In patients with no improvement, common treatments include grid laser photocoagulation of the macula, or intravitreal injection of triamcinolone or an anti-vascular endothelial growth factor agent. More invasive surgical procedures may include pars plana vitrectomy alone (without sheathotomy).

### *What the procedure involves*

The principle behind the surgery is that by cutting the sheath surrounding the two vessels and physically separating them at the crossing site, venous drainage is restored.

In arteriovenous sheathotomy the overlying artery is separated from the vein with a microvitrectomy blade. A pars plana vitrectomy (surgical removal of the vitreous) is usually performed. An incision of the adventitial sheath is then made adjacent to the arteriovenous crossing and then extended along the membrane that holds the blood vessels in position, to the point of the crossing. At this juncture, the blade is used to separate adhesions holding the artery to the vein. The artery is then lifted away from the vein.

### *List of studies included in the overview*

This overview is based on 296 patients from two randomised controlled trials<sup>1,2</sup>, four non randomised controlled studies<sup>3, 4, 5, 6</sup> and one case series<sup>7</sup>.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

### *Efficacy*

An randomised controlled trial (RCT) of 40 patients reported that the mean improvement in best corrected visual acuity (BCVA) score was greater in the intravitreal injection group ( $12.2 \pm 12.3$ ) than in the sheathotomy group ( $4.4 \pm 8.9$ ) at 1-month follow-up ( $p = 0.026$ ). However, improvements in outcome

scores were not significantly different between the groups at any other follow-up time up to 6 months<sup>1</sup>. An RCT of 36 patients reported that both groups demonstrated significant improvement in BCVA from baseline. However, there was no statistically significant difference between the sheathotomy group ( $0.014 \pm 0.15$ ) and the vitrectomy alone group ( $0.08 \pm 0.18$ ) at 31-month follow-up ( $p = 0.25$ )<sup>2</sup>.

A non randomised controlled study of 68 patients reported no significant difference in mean BCVA between patients in the sheathotomy group ( $0.35 \pm 0.25$ ) and those who refused surgery ( $0.22 \pm 0.16$ ) at 6-week follow-up (measurement of significance not reported)<sup>3</sup>. In this study 60% (26/43) of patients in the sheathotomy group gained 2 or more lines of acuity compared to 20% (5/25) of patients in the no surgery group at 6-week follow-up (measurement of significance not reported).

A non randomised controlled study of 40 patients reported that the mean number of lines of BCVA gained in patients treated by sheathotomy (4.55 lines) was significantly greater than in patients in the control group (either no surgery or grid laser photocoagulation) (1.55 lines) at 14- to 19-month follow-up ( $p = 0.023$ ) (length of follow up inconsistent between the groups)<sup>4</sup>. A non randomised controlled study of 36 patients reported that there was no significant difference in the mean change in BCVA from baseline in the sheathotomy group ( $0.29 \pm 0.35$ ) and the vitrectomy alone group ( $0.30 \pm 0.22$ ) at 1-year follow-up ( $p = 0.71$ )<sup>5</sup>. A non randomised controlled study of 16 patients reported no significant difference in the mean change in BCVA from baseline in the sheathotomy group ( $0.30 \pm 0.28$ ) and the no surgery group ( $0.72 \pm 0.47$ ) at 3-year follow-up ( $p = 0.053$ )<sup>6</sup>.

A case series of 60 patients reported that mean BCVA improved significantly from  $0.71 \pm 0.16$  at baseline to  $0.25 \pm 0.16$  at 6-month follow-up ( $p < 0.0001$ )<sup>7</sup>.

A case series of 60 patients treated with sheathotomy for BRVO with macular oedema reported recurrence of macular oedema in 3% (2/60) of patients at 12- to 16-month follow-up<sup>7</sup>.

## **Safety**

### **Retinal damage**

A non randomised controlled study of 36 patients reported a peripheral retinal tear (successfully treated by laser coagulation and fluid –air exchange) in 5% (1/20) of patients in the sheathotomy group and no patient in the vitrectomy alone group (significance and length of follow-up not reported)<sup>5</sup>.

### **Haemorrhage**

In the sheathotomy group of an RCT of 36 patients 6% (1/18) had limited haemorrhage due to retinal vascular damage (controlled by high pressure perfusion) (length of follow-up not reported)<sup>2</sup>. Vitreous haemorrhage, which

resolved spontaneously, was reported in 19% (2/10) of patients in the sheathotomy group of a non randomised controlled study of 36 patients<sup>5</sup>.

### **Loss of BCVA**

A non randomised controlled study of 68 patients reported that 2% (1/43) of patients in the sheathotomy group and 36% (9/25) of patients in the no surgery group lost 2 or more lines of visual acuity at 6 weeks follow-up<sup>3</sup>.

### **Cataract**

An RCT of 40 patients reported that the mean increase in cataract grade was not significantly different between patients treated with sheathotomy or by intravitreal injection ( $p = 0.382$ ) (absolute figures and length of follow-up not reported)<sup>1</sup>. A non randomised controlled study of 40 patients reported cataract development in 15% (3/20) of patients in the sheathotomy group (length of follow-up not reported)<sup>4</sup>. A non randomised controlled study of 36 patients reported cataracts in 10% (2/20) of the sheathotomy group and 6% (1/16) of the vitrectomy alone group (measurement of significance and length of follow-up not reported)<sup>5</sup>. In a non randomised controlled study of 16 patients, cataracts developed in 7 out of 8 eyes in the sheathotomy group at a mean follow-up of 20.1 months<sup>6</sup>.

## **Literature review**

### ***Rapid review of literature***

The medical literature was searched to identify studies and reviews relevant to arteriovenous crossing sheathotomy for branch retinal vein occlusion. Searches were conducted of the following databases, covering the period from 1 January 2003 to 06 February 2009 and studies in the in original overview for this topic were also considered: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy).

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

**Table 1 Inclusion criteria for identification of relevant studies**

| Characteristic    | Criteria                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|-------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Publication type  | <p>Clinical studies were included. Emphasis was placed on identifying good quality studies.</p> <p>Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study.</p> <p>Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.</p> |
| Patient           | Patients with branch retinal vein occlusion.                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Intervention/test | Arteriovenous crossing sheathotomy.                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Outcome           | Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.                                                                                                                                                                                                                                                                                                                                                             |
| Language          | Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.                                                                                                                                                                                                                                                                                                                                  |

### ***Existing assessments of this procedure***

There were no published assessments from other organisations identified at the time of the literature search.

### ***Related NICE guidance***

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

#### **Interventional procedures**

- Arteriovenous crossing sheathotomy for branch retinal vein occlusion. NICE interventional procedures guidance 72 (2004). Review in progress (this overview). Available from [www.nice.org.uk/IPG72](http://www.nice.org.uk/IPG72)

#### **Technology appraisals**

- None

#### **Clinical guidelines**

- None

#### **Public health guidance**

- None

**Table 2 Summary of key efficacy and safety findings on arteriovenous crossing sheathotomy for branch retinal vein occlusion**

| Abbreviations used: BCVA ,best corrected visual acuity; BRVO, branch retinal vein occlusion; IOP, intraocular pressure; NS, not significant;                                                                                                                                                                                                                                                                 |  |                                                                                                                                                                                                                                                                            |                      |                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                     |                                                                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| Study details                                                                                                                                                                                                                                                                                                                                                                                                |  | Key efficacy findings                                                                                                                                                                                                                                                      |                      | Key safety findings                                                                                                                                                                                                                                                                                                                                                                     | Comments                                                                                                            |                                                                                            |
| Chung E J (2008) <sup>1</sup>                                                                                                                                                                                                                                                                                                                                                                                |  | <b>Visual acuity</b>                                                                                                                                                                                                                                                       |                      | <b>Complications</b>                                                                                                                                                                                                                                                                                                                                                                    | Prospective study                                                                                                   |                                                                                            |
| <b>RCT (blinded assessment)</b>                                                                                                                                                                                                                                                                                                                                                                              |  | Evaluated using the early treatment diabetic retinopathy study visual acuity charts with correction for individual refractive error.                                                                                                                                       |                      | Elevated IOP >21mmHG was reported in 25 (5/20) of patients in the intravitreal injection group and 10% (2/20) of the sheathotomy group (length of follow-up not reported). At 1-month follow-up the mean IOP was significantly higher in the intravitreal injection group (p = 0.029) (absolute figures not reported), however this was no longer significant at other follow-up times. | No loss to follow up reported.                                                                                      |                                                                                            |
| Republic of Korea                                                                                                                                                                                                                                                                                                                                                                                            |  | Baseline<br>(n = 40)                                                                                                                                                                                                                                                       | 6 months<br>(n = 40) | p =                                                                                                                                                                                                                                                                                                                                                                                     | All procedures undertaken by the same retinal specialist and evaluations undertaken by the same blinded specialist. |                                                                                            |
| Study period: 2005 to 2006                                                                                                                                                                                                                                                                                                                                                                                   |  | Sheathotomy                                                                                                                                                                                                                                                                | 26.9 ± 14.0          | 38.4 ± 15.3                                                                                                                                                                                                                                                                                                                                                                             | <0.001                                                                                                              | Power calculation on 20% chance of detecting 35% improvement in BCVA and macular thickness |
|                                                                                                                                                                                                                                                                                                                                                                                                              |  | Intravitreal injection                                                                                                                                                                                                                                                     | 24.9 ± 14.6          | 38.4 ± 13.6                                                                                                                                                                                                                                                                                                                                                                             | 0.002                                                                                                               |                                                                                            |
| Study population: patients with Macular oedema secondary to BRVO Age: 58 years (mean) Sex: 68% females                                                                                                                                                                                                                                                                                                       |  | Changes from baseline were significant at 1-month, 3-month, and 6-month follow-up for the intravitreal group, but only significant at 3- and 6-month follow-up in the sheathotomy group.                                                                                   |                      | The mean increase in cataract grade was not statistically significant between the groups (p = 0.382). Significant cataract progression (increase of 2 or more grades in cataract score) was reported in 35% (7/20) of patients in the sheathotomy group, and 40% (8/20) of patients in the intravitreal injection group.                                                                |                                                                                                                     |                                                                                            |
| <b>n=40 (20 sheathotomy, 20 intravitreal injection)</b>                                                                                                                                                                                                                                                                                                                                                      |  | At 1-month follow-up there was a significantly greater improvement in score in the intravitreal injection group (12.2 ± 12.3) than in the sheathotomy group (4.4 ± 8.9) (p = 0.026). At all other follow-up times the differences between the groups were not significant. |                      | No serious vision-threatening complications such as infectious endophthalmitis, vitreous haemorrhage, sclera perforation, or retinal detachment were reported in either study group.                                                                                                                                                                                                    |                                                                                                                     |                                                                                            |
| Inclusion criteria: recent onset BRVO <6 months, best corrected early treatment diabetic retinopathy study score ≤40 letter, intra-retinal haemorrhage involving the foveal centres, generalised breakdown of the inner blood-retina barrier or diffuse thickening of the retina. No previous intraocular surgery, grid laser photocoagulation, history of glaucoma, or comorbidity affecting visual acuity. |  | <b>Eye characteristics</b>                                                                                                                                                                                                                                                 |                      |                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                     |                                                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                              |  | Total macular volume (mm <sup>3</sup> ), mean ± standard deviation                                                                                                                                                                                                         |                      |                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                     |                                                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                              |  | Baseline<br>(n = 40)                                                                                                                                                                                                                                                       | 6 months<br>(n = 40) | p =                                                                                                                                                                                                                                                                                                                                                                                     | No significant differences between groups in baseline clinical or demographic characteristics.                      |                                                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                              |  | Sheathotomy                                                                                                                                                                                                                                                                | 9.6 ± 1.1            | 7.9 ± 1.3                                                                                                                                                                                                                                                                                                                                                                               | <0.001                                                                                                              |                                                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                              |  | Intravitreal injection                                                                                                                                                                                                                                                     | 10.3 ± 2.2           | 8.3 ± 1.5                                                                                                                                                                                                                                                                                                                                                                               | 0.002                                                                                                               |                                                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                              |  | (p = 0.595 between groups)                                                                                                                                                                                                                                                 |                      |                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                     |                                                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                              |  | Foveal thickness (µm), mean ± standard deviation                                                                                                                                                                                                                           |                      |                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                     |                                                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                              |  | Baseline<br>(n = 40)                                                                                                                                                                                                                                                       | 6 months<br>(n = 40) | p =                                                                                                                                                                                                                                                                                                                                                                                     | Authors state that intravitreal injection usually carried out under topical anaesthesia.                            |                                                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                              |  | Sheathotomy                                                                                                                                                                                                                                                                | 395 ± 115.8          | 244.8 ± 121.2                                                                                                                                                                                                                                                                                                                                                                           | <0.001                                                                                                              |                                                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                              |  | Intravitreal injection                                                                                                                                                                                                                                                     | 212.6 ± 61.1         | 281.4 ± 123.4                                                                                                                                                                                                                                                                                                                                                                           | 0.001                                                                                                               |                                                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                              |  | (p = 0.669 between groups)                                                                                                                                                                                                                                                 |                      | Patients included have recent onset disease which may have resolved spontaneously.                                                                                                                                                                                                                                                                                                      |                                                                                                                     |                                                                                            |
| <b>Follow-up:6 months (median)</b>                                                                                                                                                                                                                                                                                                                                                                           |  |                                                                                                                                                                                                                                                                            |                      |                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                     |                                                                                            |
| Conflict of interest: None                                                                                                                                                                                                                                                                                                                                                                                   |  |                                                                                                                                                                                                                                                                            |                      |                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                     |                                                                                            |

| Abbreviations used: BCVA ,best corrected visual acuity; BRVO, branch retinal vein occlusion; IOP, intraocular pressure; NS, not significant;                                                                                                                                  |                                                                                                                                                     |                      |                     |                                                                                             |                                                                                                                                                                                                  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|---------------------|---------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Study details                                                                                                                                                                                                                                                                 | Key efficacy findings                                                                                                                               |                      |                     | Key safety findings                                                                         | Comments                                                                                                                                                                                         |
| Kumagai K (2007) <sup>2</sup>                                                                                                                                                                                                                                                 | <b>Visual acuity</b>                                                                                                                                |                      |                     | <b>Complications</b>                                                                        | 4 of 40 patients initially enrolled were excluded from analysis as they had less than 12 months follow up                                                                                        |
| <b>RCT (non blinded assessment)</b>                                                                                                                                                                                                                                           | Mean logMAR ± standard deviation. Positive numbers represent poor vision, score of 0 is desirable                                                   |                      |                     | No patients in either group developed severe intraoperative or postoperative complications. |                                                                                                                                                                                                  |
| Japan                                                                                                                                                                                                                                                                         |                                                                                                                                                     | Sheathotomy (n = 18) | vitrectomy (n = 18) | p =                                                                                         | One patient 6% (1/18) in the sheathotomy group had limited haemorrhage due to retinal vascular damage during arteriovenous crossing dissection, which was controlled by high pressure perfusion. |
|                                                                                                                                                                                                                                                                               | Baseline                                                                                                                                            | 0.53 ± 0.29          | 0.52 ± 0.45         | 0.94                                                                                        |                                                                                                                                                                                                  |
|                                                                                                                                                                                                                                                                               | 3 months                                                                                                                                            | 0.25 ± 0.35          | 0.24 ± 0.29         | 0.88                                                                                        |                                                                                                                                                                                                  |
|                                                                                                                                                                                                                                                                               | 12 months                                                                                                                                           | 0.061± 0.15          | 0.15 ± 0.28         | 0.24                                                                                        |                                                                                                                                                                                                  |
|                                                                                                                                                                                                                                                                               | Final follow up                                                                                                                                     | 0.014 ± 0.15         | 0.08 ± 0.18         | 0.25                                                                                        |                                                                                                                                                                                                  |
| Study period: 2001 to 2003                                                                                                                                                                                                                                                    | Both groups showed significant improvement over baseline at 3, 6, and 12 months.                                                                    |                      |                     |                                                                                             | No significant differences between groups in baseline clinical or demographic characteristics.                                                                                                   |
|                                                                                                                                                                                                                                                                               | Subgroup analysis of patients with symptoms for more than or for less than 4 weeks indicated no significant difference in terms of visual outcomes. |                      |                     |                                                                                             |                                                                                                                                                                                                  |
| Study population: patients with macular oedema secondary to BRVO Age: 62 years (mean) Sex: 58% females                                                                                                                                                                        | <b>Eye characteristics</b>                                                                                                                          |                      |                     |                                                                                             | Authors state that visual acuity outcome assessment was done unblinded to treatment group                                                                                                        |
|                                                                                                                                                                                                                                                                               | Mean foveal thickness (µm) ± standard deviation                                                                                                     |                      |                     |                                                                                             |                                                                                                                                                                                                  |
|                                                                                                                                                                                                                                                                               |                                                                                                                                                     | Sheathotomy (n = 18) | vitrectomy (n = 18) | p =                                                                                         |                                                                                                                                                                                                  |
|                                                                                                                                                                                                                                                                               | Baseline                                                                                                                                            | 484 ± 147            | 429 ± 204           | 0.94                                                                                        |                                                                                                                                                                                                  |
|                                                                                                                                                                                                                                                                               | 1 week                                                                                                                                              | 380 ± 140            | 334 ± 139           | NS                                                                                          |                                                                                                                                                                                                  |
|                                                                                                                                                                                                                                                                               | 12 months                                                                                                                                           | 258 ± 90             | 252 ± 105           | NS                                                                                          |                                                                                                                                                                                                  |
|                                                                                                                                                                                                                                                                               | Both groups showed significant improvement over baseline at 1 week , 6 months, and 12 months, but not at 1 or 3 months.                             |                      |                     |                                                                                             |                                                                                                                                                                                                  |
| Inclusion criteria: recent onset BRVO <8 weeks, macular oedema and haemorrhage involving the second branch of the central retinal vein, no sign of macular traction, thickening of the centre of the macula no previous grid laser photocoagulation, or vitreous haemorrhage. |                                                                                                                                                     |                      |                     |                                                                                             |                                                                                                                                                                                                  |
| Technique: Sheathotomy following pars plana vitrectomy vs vitrectomy alone. Posterior capsule removed after surgery to prevent postoperative opacification. No corticosteroids injected in either study group.                                                                |                                                                                                                                                     |                      |                     |                                                                                             |                                                                                                                                                                                                  |
| <b>Follow-up: 31 months (mean)</b>                                                                                                                                                                                                                                            |                                                                                                                                                     |                      |                     |                                                                                             |                                                                                                                                                                                                  |
| Conflict of interest: None                                                                                                                                                                                                                                                    |                                                                                                                                                     |                      |                     |                                                                                             |                                                                                                                                                                                                  |

| Abbreviations used: BCVA ,best corrected visual acuity; BRVO, branch retinal vein occlusion; IOP, intraocular pressure; NS, not significant;                                            |  |                                                                                                                                                                                                                                                             |                               |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Study details                                                                                                                                                                           |  | Key efficacy findings                                                                                                                                                                                                                                       |                               | Key safety findings                                                                                                                                           | Comments                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Mester U (2002) <sup>3</sup>                                                                                                                                                            |  | Visual acuity                                                                                                                                                                                                                                               |                               | Complications<br><br>2% (1/43) of patients in the sheathotomy group and 36% (9/25) of patients in the no surgery group lost 2 or more lines of visual acuity. | Study included in table 2 of IP 222<br><br>Prospective follow up. No loss reported.<br><br>Surgical technique varies within the patient cohort, with later patients having more of the limiting internal membrane removed. Subgroup analysis suggested that this may have a significant independent therapeutic benefit.<br><br>Patient selection was by preference for surgery those with comparable BRVO who refused this surgical intervention served as a control group.<br><br>Visual acuity examiner was not masked to the treatment groups.<br><br>The best functional improvement was observed in eyes with a short duration of BRVO.<br><br>3 patients in the sheathotomy group with persistent large capillary nonperfusion received laser treatment |
| Non randomised controlled study                                                                                                                                                         |  | Sheathotomy (n = 43)      No surgery (n = 25)                                                                                                                                                                                                               |                               |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Germany                                                                                                                                                                                 |  | Baseline BCVA                                                                                                                                                                                                                                               | 0.16 ± 0.12      0.23 ± 0.12  |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|                                                                                                                                                                                         |  | 6-week follow-up                                                                                                                                                                                                                                            | 0.35 ± 0.25      0.22 ± 0.16  |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Study period: August 1999–April 2001                                                                                                                                                    |  | Gained at least two lines of visual acuity                                                                                                                                                                                                                  | 60% (26/43)      20% (5/25)   |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|                                                                                                                                                                                         |  | Gained four lines or more of visual acuity                                                                                                                                                                                                                  | 28% (12/43)      Not reported |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Study population: patients with macular oedema secondary to BRVO                                                                                                                        |  | (measurement of significance not reported).                                                                                                                                                                                                                 |                               |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Age: 66 years (mean) Sex: not reported                                                                                                                                                  |  | (details of the visual acuity assessment scale not reported)                                                                                                                                                                                                |                               |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| n=68 (43 sheathotomy and vitrectomy, 25 no surgery)                                                                                                                                     |  | Incomplete occlusion of the branch retinal vein was seen on angiography in all patients with improvement of >4 lines in the sheathotomy group. In this group a significantly greater improvement in BCVA was reported in patients <65 years old (p = 0.04). |                               |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Inclusion criteria: BRVO with macular oedema and extensive haemorrhage BCVA 20/50 or less, duration of symptoms <3 months, no functional improvement to medical therapy.                |  |                                                                                                                                                                                                                                                             |                               |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Technique: Sheathotomy with a vitreous scissors to dissect the internal limiting membrane and separate the overlying artery from the vein following pars plana vitrectomy Vs no surgery |  |                                                                                                                                                                                                                                                             |                               |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Both groups also received isovolemic hemodilution therapy over 10 days                                                                                                                  |  |                                                                                                                                                                                                                                                             |                               |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Follow-up: 6 weeks (mean)                                                                                                                                                               |  |                                                                                                                                                                                                                                                             |                               |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Conflict of interest: None                                                                                                                                                              |  |                                                                                                                                                                                                                                                             |                               |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| IP overview: arteriovenous crossing sheathotomy for branch retinal vein occlusion                                                                                                       |  |                                                                                                                                                                                                                                                             |                               | Page 8 of 23                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

| Abbreviations used: BCVA ,best corrected visual acuity; BRVO, branch retinal vein occlusion; IOP, intraocular pressure; NS, not significant;                                                 |  |                                                                                                                                                                                                                                                                       |                  |           |                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |              |
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| Study details                                                                                                                                                                                |  | Key efficacy findings                                                                                                                                                                                                                                                 |                  |           | Key safety findings                                                                                                                            | Comments                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |              |
| Mason III J (2004) <sup>4</sup>                                                                                                                                                              |  | Visual acuity                                                                                                                                                                                                                                                         |                  |           | Complications<br><br>In the sheathotomy group, nuclear sclerotic cataract developed in 15% (3/20) of patients (follow up period not reported). | Study included in table 2 of IP 222<br><br>Prospective study, All patients completed 12 months of follow-up. Three patients did not return for final follow-up (2 controls and 1 surgery).<br><br>Consecutive case accrual.<br><br>Patients were given the choice whether they had sheathotomy surgery or join the control group.<br><br>Patients in the control group were allowed to elect laser treatment. Ten patients received laser treatment, making comparison to other studies difficult.<br><br>Visual acuity outcome assessed using a number of different analyses.<br><br>Authors note that groups were similar in respect to baseline characteristics. |              |
| Non randomised controlled study                                                                                                                                                              |  | Group mean score                                                                                                                                                                                                                                                      |                  |           |                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |              |
| USA                                                                                                                                                                                          |  | Sheathotomy (n = 20)                                                                                                                                                                                                                                                  | Control (n = 20) | p =       |                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |              |
| Study period: June 1999 – June 2002                                                                                                                                                          |  | Baseline BCVA                                                                                                                                                                                                                                                         | 20/250           | 20/180    |                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Not reported |
|                                                                                                                                                                                              |  | Final follow up                                                                                                                                                                                                                                                       | 20/63            | 20/125    |                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0.02         |
|                                                                                                                                                                                              |  | Mean number of lines of visual acuity gained.                                                                                                                                                                                                                         | 4.55             | 1.55      |                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 0.023        |
| Study population: patients with macular oedema secondary to BRVO Age: not reported, Sex: 65% Female                                                                                          |  | Gained six lines or more of visual acuity.                                                                                                                                                                                                                            | 40% (8/20)       | 5% (1/20) |                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Not reported |
| n=40 (20 sheathotomy and vitrectomy, 20 no surgery or grid laser photocoagulation)                                                                                                           |  | Baseline foveal ischaemia or foveal haemorrhage were not associated with a worse visual outcome at 12-month follow-up. However patients with primary open angle glaucoma at baseline were more likely to have BCVA 20/200 or worse at 12-month follow-up (p = 0.003). |                  |           |                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |              |
| Inclusion criteria: BRVO with macular oedema BCVA less than or equal to 20/70, patients with and extensive haemorrhage were not excluded.                                                    |  |                                                                                                                                                                                                                                                                       |                  |           |                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |              |
| Technique: Sheathotomy with a modified microvitreoretinal blade to separate the overlying artery from the vein following pars plana vitrectomy Vs no surgery or grid laser photocoagulation. |  |                                                                                                                                                                                                                                                                       |                  |           |                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |              |
| Follow-up: 14 to 19 months (group means)                                                                                                                                                     |  |                                                                                                                                                                                                                                                                       |                  |           |                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |              |
| Conflict of interest: Supported by a grant                                                                                                                                                   |  |                                                                                                                                                                                                                                                                       |                  |           |                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |              |

| Abbreviations used: BCVA ,best corrected visual acuity; BRVO, branch retinal vein occlusion; IOP, intraocular pressure; NS, not significant;                                                                                                                                                                                                                                                |  |                                                                                                                                                                                                                                      |                      |                    |                         |                                                                                 |                        |                                                                                                                                                                                      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|--------------------|-------------------------|---------------------------------------------------------------------------------|------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Study details                                                                                                                                                                                                                                                                                                                                                                               |  | Key efficacy findings                                                                                                                                                                                                                |                      |                    | Key safety findings     |                                                                                 | Comments               |                                                                                                                                                                                      |
| Yamamoto S (2004) <sup>5</sup>                                                                                                                                                                                                                                                                                                                                                              |  | <b>Visual acuity</b>                                                                                                                                                                                                                 |                      |                    | <b>Complications</b>    |                                                                                 | Prospective follow-up. |                                                                                                                                                                                      |
| <b>Non randomised controlled study</b>                                                                                                                                                                                                                                                                                                                                                      |  | BCVA evaluated using the early treatment diabetic retinopathy study visual acuity charts.                                                                                                                                            |                      |                    | Outcome                 | Sheathotomy                                                                     | Vitrectomy             | Loss to follow-up not reported – assumed none.                                                                                                                                       |
| Japan                                                                                                                                                                                                                                                                                                                                                                                       |  | Mean score (logMAR) ± standard deviation                                                                                                                                                                                             |                      |                    | Peripheral retinal tear | 5% (1/20)                                                                       | 0% (0/16)              |                                                                                                                                                                                      |
| Study period: 2000 to 2003                                                                                                                                                                                                                                                                                                                                                                  |  |                                                                                                                                                                                                                                      | Sheathotomy (n = 20) | vitectomy (n = 16) | p =                     | Treated successfully with endolaser retinal coagulation and fluid air exchange) |                        | Advential sheathotomy was performed in patients with a compression of the occluded vein by an overlying artery at an arteriovenous crossing when not covered with dense haemorrhage. |
| Study population: patients with macular oedema secondary to BRVO Age: 61 years (mean) Sex: 28% females                                                                                                                                                                                                                                                                                      |  | Baseline                                                                                                                                                                                                                             | 0.53 ± 0.35          | 0.62 ± 0.37        | 0.44                    | Vitreous haemorrhage (resolved spontaneously)                                   | 10% (2/20)             |                                                                                                                                                                                      |
|                                                                                                                                                                                                                                                                                                                                                                                             |  | 12 months                                                                                                                                                                                                                            | 0.25 ± 0.28          | 0.32 ± 0.31        | 0.54                    |                                                                                 |                        | Surgical method for each patient was selected preoperatively by two surgeons.                                                                                                        |
|                                                                                                                                                                                                                                                                                                                                                                                             |  | Change from baseline was statistically significant in both groups (p = 0.008 and 0.001 respectively)                                                                                                                                 |                      |                    |                         |                                                                                 |                        |                                                                                                                                                                                      |
|                                                                                                                                                                                                                                                                                                                                                                                             |  | Improvement in BCVA (logMAR)                                                                                                                                                                                                         | 0.29 ± 0.35          | 0.30 ± 0.22        | 0.71                    | Cataract (measurement of significance and follow-up not reported).              |                        | Authors state that a larger randomised study is necessary to evaluate the efficacy of sheathotomy.                                                                                   |
| <b>n=36 (20 sheathotomy and vitrectomy, 16 vitrectomy alone)</b>                                                                                                                                                                                                                                                                                                                            |  | <b>Eye characteristics</b>                                                                                                                                                                                                           |                      |                    |                         |                                                                                 |                        |                                                                                                                                                                                      |
| Inclusion criteria: BRVO with macular oedema not otherwise described.                                                                                                                                                                                                                                                                                                                       |  | Mean foveal thickness (µm) ± standard deviation                                                                                                                                                                                      |                      |                    |                         |                                                                                 |                        |                                                                                                                                                                                      |
|                                                                                                                                                                                                                                                                                                                                                                                             |  |                                                                                                                                                                                                                                      | Sheathotomy (n = 20) | vitectomy (n = 16) | p =                     |                                                                                 |                        |                                                                                                                                                                                      |
|                                                                                                                                                                                                                                                                                                                                                                                             |  | Baseline                                                                                                                                                                                                                             | 626.8 ± 189.2        | 559.5 ± 157.6      | 0.27                    |                                                                                 |                        |                                                                                                                                                                                      |
| Technique: under local anaesthesia, sheathotomy with a modified microvitrectoretinal blade to separate the overlying artery from the vein following pars plana vitrectomy vs vitrectomy alone. Simultaneous phacoemulsification for cataracts and intraocular lens implantation in 10 eyes in the sheathotomy group and 13 eyes in the vitrectomy alone group (not significantly different) |  | 12 months                                                                                                                                                                                                                            | 255.2 ± 137.2        | 193.6 ± 113.9      | 0.07                    |                                                                                 |                        |                                                                                                                                                                                      |
|                                                                                                                                                                                                                                                                                                                                                                                             |  | Difference in foveal retinal thickness was not significantly different at any time point.                                                                                                                                            |                      |                    |                         |                                                                                 |                        |                                                                                                                                                                                      |
|                                                                                                                                                                                                                                                                                                                                                                                             |  | Fluorescein angiography showed re-perfusion of the occluded vein in 50% (10/20) eyes in the sheathotomy group and 13% (2/16) of eyes in the vitrectomy alone group at 6-months follow-up (measurement of significance not reported). |                      |                    |                         |                                                                                 |                        |                                                                                                                                                                                      |
| <b>Follow-up: 12 months (median)</b>                                                                                                                                                                                                                                                                                                                                                        |  |                                                                                                                                                                                                                                      |                      |                    |                         |                                                                                 |                        |                                                                                                                                                                                      |
| Conflict of interest: None                                                                                                                                                                                                                                                                                                                                                                  |  |                                                                                                                                                                                                                                      |                      |                    |                         |                                                                                 |                        |                                                                                                                                                                                      |

| Abbreviations used: BCVA ,best corrected visual acuity; BRVO, branch retinal vein occlusion; IOP, intraocular pressure; NS, not significant;                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                               |                     |                    |     |          |             |             |       |           |             |             |       |                      |             |             |       |                                                                                                                                                                                                                                                   |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|--------------------|-----|----------|-------------|-------------|-------|-----------|-------------|-------------|-------|----------------------|-------------|-------------|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Study details                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Key efficacy findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                    | Key safety findings                                                                                                                                                                                                                                                                                                                                                                                                                           |                     |                    |     |          |             |             |       |           |             |             |       |                      |             |             |       |                                                                                                                                                                                                                                                   |
| <p>Oh I D (2008)<sup>6</sup></p> <p><b>Non randomised controlled study</b></p> <p>Republic of Korea</p> <p>Study period: 2000 to 2003</p> <p>Study population: patients with macular oedema secondary to BRVO Age: 62 years (mean) Sex: 50% females, Duration of symptoms = 15.8 weeks (mean).</p> <p><b>n=16 (8 sheathotomy and vitrectomy, 8 no surgery)</b></p> <p>Inclusion criteria: BRVO with macular oedema , BCVA 20/100 or less</p> <p>Technique: Sheathotomy with a modified microvitrectoretinal blade to separate the overlying artery from the vein following pars plana vitrectomy. Removal of the internal limiting membrane in all patients vs no surgery</p> <p><b>Follow-up: 3 years (minimum)</b></p> <p>Conflict of interest: Not reported</p> | <p><b>Visual acuity</b></p> <p>BCVA.</p> <p>Mean score ± standard deviation</p> <table> <tr> <th></th><th>Sheathotomy (n = 8)</th><th>No surgery (n = 8)</th><th>p =</th></tr> <tr> <td>Baseline</td><td>1.10 ± 0.34</td><td>1.15 ± 0.43</td><td>0.814</td></tr> <tr> <td>36 months</td><td>0.80 ± 0.36</td><td>0.43 ± 0.39</td><td>0.066</td></tr> <tr> <td>Change from baseline</td><td>0.30 ± 0.28</td><td>0.72 ± 0.47</td><td>0.053</td></tr> </table> <p>Change from baseline was statistically significant in both groups (p = 0.018 and 0.003 respectively)</p> <p><b>Surgical characteristics</b></p> <p>Surgical decompression of the arteriovenous crossing site was achieved in all patients in the sheathotomy group.</p> <p>Foveal thickness and oedema reduced in the Sheathotomy group but this was not reflected in improved acuity.</p> |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                               | Sheathotomy (n = 8) | No surgery (n = 8) | p = | Baseline | 1.10 ± 0.34 | 1.15 ± 0.43 | 0.814 | 36 months | 0.80 ± 0.36 | 0.43 ± 0.39 | 0.066 | Change from baseline | 0.30 ± 0.28 | 0.72 ± 0.47 | 0.053 | <p><b>Complications</b></p> <p>Cataracts developed in 7 out of 8 eyes in the sheathotomy group. They were treated by phacoemulsification and intraocular lens implantation at a mean of 20.1-month follow-up after this sheathotomy procedure</p> |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Sheathotomy (n = 8)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | No surgery (n = 8) | p =                                                                                                                                                                                                                                                                                                                                                                                                                                           |                     |                    |     |          |             |             |       |           |             |             |       |                      |             |             |       |                                                                                                                                                                                                                                                   |
| Baseline                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 1.10 ± 0.34                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 1.15 ± 0.43        | 0.814                                                                                                                                                                                                                                                                                                                                                                                                                                         |                     |                    |     |          |             |             |       |           |             |             |       |                      |             |             |       |                                                                                                                                                                                                                                                   |
| 36 months                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 0.80 ± 0.36                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 0.43 ± 0.39        | 0.066                                                                                                                                                                                                                                                                                                                                                                                                                                         |                     |                    |     |          |             |             |       |           |             |             |       |                      |             |             |       |                                                                                                                                                                                                                                                   |
| Change from baseline                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 0.30 ± 0.28                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 0.72 ± 0.47        | 0.053                                                                                                                                                                                                                                                                                                                                                                                                                                         |                     |                    |     |          |             |             |       |           |             |             |       |                      |             |             |       |                                                                                                                                                                                                                                                   |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                    | <p>Prospective follow-up, loss not reported.</p> <p>Criteria used to allocate patients to different groups are not described</p> <p>Consecutive case accrual.</p> <p>Patient selection criteria for sheathotomy or no surgery not reported.</p> <p>One surgeon undertook all procedures.</p> <p>There were no statistically significant differences between the two groups in terms of baseline clinical and demographic characteristics.</p> |                     |                    |     |          |             |             |       |           |             |             |       |                      |             |             |       |                                                                                                                                                                                                                                                   |

| Abbreviations used: BCVA ,best corrected visual acuity; BRVO, branch retinal vein occlusion; IOP, intraocular pressure; NS, not significant;                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                     |                   |                   |     |      |             |             |         |  |                   |                   |     |           |          |          |         |                                                                |                                                                                                                                                                                                                                                                  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|-------------------|-------------------|-----|------|-------------|-------------|---------|--|-------------------|-------------------|-----|-----------|----------|----------|---------|----------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Study details                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Key efficacy findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Key safety findings | Comments          |                   |     |      |             |             |         |  |                   |                   |     |           |          |          |         |                                                                |                                                                                                                                                                                                                                                                  |
| <p>Shimura M (2008)<sup>7</sup></p> <p><b>Case series</b></p> <p>Japan</p> <p>Study period: 2004 to 2006</p> <p>Study population: patients with macular oedema secondary to BRVO Age: 63 years (mean) Sex: 47% females, Duration of symptoms = 29 days (mean).</p> <p><b>n=60</b></p> <p>Inclusion criteria: BRVO with macular oedema , BCVA &lt;0.3, foveal thickness &gt;400 µm, history of cataract surgery without complications &gt; 3 months before this procedure, no medical therapy, grid laser photocoagulation, no other previous ocular surgery, no diabetes, ocular inflammation, trauma, or vitreoretinal disease.</p> <p>Technique: Sheathotomy under local anaesthesia with a micro sheathotomy knife to separate the overlying artery from the vein following pars plana vitrectomy.</p> <p><b>Follow-up: 6 months (median)</b></p> <p>Conflict of interest: study supported by grant</p> | <p><b>Visual acuity</b></p> <p>Mean score ± standard deviation</p> <table> <tr> <td></td><td>Baseline (n = 60)</td><td>6 months (n = 60)</td><td>p =</td></tr> <tr> <td>BCVA</td><td>0.71 ± 0.16</td><td>0.25 ± 0.16</td><td>&lt;0.0001</td></tr> </table> <p>Level of interleukin-6 and baseline BCVA were independent predictors of improvement in visual acuity (p &lt; 0.001 for both)</p> <p><b>Eye characteristics</b></p> <p>Mean foveal thickness (µm) ± standard deviation</p> <table> <tr> <td></td><td>Baseline (n = 60)</td><td>6 months (n = 60)</td><td>p =</td></tr> <tr> <td>Thickness</td><td>586 ± 85</td><td>289 ± 64</td><td>&lt;0.0001</td></tr> </table> <p>Level of interleukin-6 was an independent predictor of improvement in foveal thickness (p &lt; 0.001)</p> <p><b>Macular oedema</b></p> <p>Recurrence of macular oedema occurred in 3% (2/60) of patients at 12 and 16 months respectively.</p> |                     | Baseline (n = 60) | 6 months (n = 60) | p = | BCVA | 0.71 ± 0.16 | 0.25 ± 0.16 | <0.0001 |  | Baseline (n = 60) | 6 months (n = 60) | p = | Thickness | 586 ± 85 | 289 ± 64 | <0.0001 | <p><b>Complications</b></p> <p>No safety outcomes reported</p> | <p>Prospective follow-up</p> <p>Consecutive case accrual.</p> <p>6% (4/64) of patients initially treated were excluded from analysis due to repeat vitrectomy for retinal detachment after pars plana vitrectomy (not stated whether sheathotomy performed).</p> |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Baseline (n = 60)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 6 months (n = 60)   | p =               |                   |     |      |             |             |         |  |                   |                   |     |           |          |          |         |                                                                |                                                                                                                                                                                                                                                                  |
| BCVA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0.71 ± 0.16                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0.25 ± 0.16         | <0.0001           |                   |     |      |             |             |         |  |                   |                   |     |           |          |          |         |                                                                |                                                                                                                                                                                                                                                                  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Baseline (n = 60)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 6 months (n = 60)   | p =               |                   |     |      |             |             |         |  |                   |                   |     |           |          |          |         |                                                                |                                                                                                                                                                                                                                                                  |
| Thickness                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 586 ± 85                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 289 ± 64            | <0.0001           |                   |     |      |             |             |         |  |                   |                   |     |           |          |          |         |                                                                |                                                                                                                                                                                                                                                                  |

## ***Validity and generalisability of the studies***

- Some studies included cataract surgery during the index procedure. It is difficult to differentiate whether visual acuity improved as a result of this or the sheathotomy.
- Very small study sizes, particularly in controlled studies.
- The comparator varied between studies. Some used no surgery (often patient self selection) and some pars plana vitrectomy without sheathotomy.
- Different metrics have been used to report visual acuity outcomes across the studies, making comparison of results difficult.

## **Specialist Advisers' opinions**

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr B Aylward (Royal College of Ophthalmologists), Mr A G Caswell (Royal College of Ophthalmologists), Mr T Williamson (Royal College of Ophthalmologists).

- All three Specialist Advisers considered this procedure to be novel and of uncertain safety and efficacy.
- The main comparators are observation, intravitreal injections (such as triamcinolone), vitrectomy alone, or laser photocoagulation.
- The key efficacy outcomes by which to evaluate this procedure include improved blood flow (on fluorescein angiography), resolution of macular oedema and/or reduced macular thickness, and improvement in BCVA.
- Reported or observed adverse events relating to this procedure may include haemorrhage from vein or artery, vitreous haemorrhage, retinal detachment, cataract development, and recurrent BRVO.
- Additional theoretical adverse event may include endophthalmitis and/or ophthalmitis, or glaucoma.
- There is a risk of the procedure worsening vision.
- The occluded vein re-canalises spontaneously in some cases.

- The procedure may be combined with other interventions.
- Extensive training is not required; the procedure uses an established surgical technique.
- The impact of this procedure on the NHS if found to be safe and efficacious would likely be minor.
- Randomised controlled trials are the only way forward for assessing this technique effectively. One trial is currently ongoing (details Korean RCT Arteriovenous Crossing Sheathotomy Versus Intravitreal Triamcinolone Acetonide Injection expected completion Aug 2007).

## **Patient Commentators' opinions**

NICE's Patient and Public Involvement Programme was unable to obtain patient commentary for this procedure.

## **Issues for consideration by IPAC**

- Non English language studies were excluded from this overview.
- Two of the studies (Mester [2002], and Mason III [2004]) were included in table 2 of the overview for interventional procedures guidance 222 (the original overview for this procedure).

## References

- 1 Chung EJ, Lee H, and Koh HJ. (2008) Arteriovenous crossing sheathotomy versus intravitreal triamcinolone acetonide injection for treatment of macular edema associated with branch retinal vein occlusion. *Graefes Archive for Clinical & Experimental Ophthalmology* 246: 967–974.
- 2 Kumagai K, Furukawa M, Ogino N et al. (2007) Long-term outcomes of vitrectomy with or without arteriovenous sheathotomy in branch retinal vein occlusion. *Retina* 27: 49–54.
- 3 Mester U and Dillinger P. (2002) Vitrectomy with arteriovenous decompression and internal limiting membrane dissection in branch retinal vein occlusion. *Retina* 22: 740–746.
- 4 Mason J, III, Feist R, White M, Jr. et al. (2004) Sheathotomy to decompress branch retinal vein occlusion: a matched control study. *Ophthalmology* 111: 540–545.
- 5 Yamamoto S, Saito W, Yagi F et al. (2004) Vitrectomy with or without arteriovenous adventitial sheathotomy for macular edema associated with branch retinal vein occlusion. *American Journal of Ophthalmology* 138: 907–914.
- 6 Oh IK, Kim S, Oh J et al. (2008) Long-term visual outcome of arteriovenous adventitial sheathotomy on branch retinal vein occlusion induced macular edema. *Korean Journal of Ophthalmology* 22: 1–5.
- 7 Shimura M, Nakazawa T, Yasuda K et al. (2008) Visual prognosis and vitreous cytokine levels after arteriovenous sheathotomy in branch retinal vein occlusion associated with macular oedema. *Acta Ophthalmologica* 86: 377–384.

## Appendix A: Additional papers on arteriovenous crossing sheathotomy for branch retinal vein occlusion

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

| Article                                                                                                                                                                                                                                                                                                            | Number of patients/follow-up                 | Direction of conclusions                                                                                                                                                                                                                                                                                      | Reasons for non-inclusion in table 2   |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| Avci, R, Inan, U. U., and Kaderli, B.(2008)<br>Evaluation of arteriovenous crossing sheathotomy for decompression of branch retinal vein occlusion.<br>Eye 22 (1) 120–127                                                                                                                                          | n = 21 (11 sheathotomy)<br><br>FU = 9 months | Arteriovenous sheathotomy for decompression of BRVO in patients who have vision loss due to macular oedema was safe and effective for anatomical and functional improvement and resulted in significantly better visual outcomes than a matched control group of laser-treated eyes                           | Larger studies are included in table 2 |
| Cahill MT, Fekrat S. (2002) Arteriovenous sheathotomy for branch retinal vein occlusion. Ophthalmology Clinics of North America 15(4): 417–423.                                                                                                                                                                    | n = 27<br><br>FU = 12 months                 | 5 eyes retinal break (requiring a scleral buckle in one eye)                                                                                                                                                                                                                                                  | Larger studies are included in table 2 |
| Crafoord, S., Karlsson, N., and Ia, Cour M.(2008) Sheathotomy in complicated cases of branch retinal vein occlusion. Acta Ophthalmologica 86 (2) 146–150                                                                                                                                                           | n = 12<br><br>FU = 20 months                 | Microsurgical treatment with sheathotomy of BRVO is a technically feasible procedure with few complications. Postoperative increased reperfusion could explain the resolution of macular haemorrhage, oedema and ischaemia, and may improve visual function in patients with this common vascular eye disease | Larger studies are included in table 2 |
| Charbonnel, J., Glacet-Bernard, A., Korobelnik, J. F., et al (2004) Management of branch retinal vein occlusion with vitrectomy and arteriovenous adventitial sheathotomy, the possible role of surgical posterior vitreous detachment. Graefes Archive for Clinical & Experimental Ophthalmology 242 (3) 223–228. | n = 13<br><br>FU = 7 months                  | Vitrectomy with sheathotomy seems to be of benefit in the management of BRVO, particularly in eyes with no previous posterior vitreous detachment, and the main postoperative feature was the decrease in macular edema                                                                                       | Larger studies are included in table 2 |

|                                                                                                                                                                                                                                                                          |                                  |                                                                                                                                                                                                                                                          |                                               |
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| <p>Feltgen, N., Herrmann, J., Agostini, H et al (2006) Arterio-venous dissection after isovolaemic haemodilution in branch retinal vein occlusion: a non-randomised prospective study. Graefes Archive for Clinical &amp; Experimental Ophthalmology 244 (7) 829–835</p> | <p>n = 35</p> <p>FU = 1 year</p> | <p>Patients with BRVO may benefit from sheathotomy compared with a historical control group. Visual improvement was found irrespective of the successful dissection of vessels. The cataract formation rate and additional surgery was a shortcoming</p> | <p>Larger studies are included in table 2</p> |
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|                                                                                                                                                                                                                                                           |                                               |                                                                                                                                                                                                                                                                                                                |                                        |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| Han DP. (2003)<br>Arteriovenous crossing dissection without separation of the retina vessels for treatment of branch retinal vein occlusion. Retina 23(2):145–151.                                                                                        | n = 20<br><br>FU= 10.5 months                 | At final follow-up (5–15 months) 16 patients (80%) had improvement of two or more lines, remained unchanged in 2 patients (10%) and had worsened by at least two lines in 2 eyes (10%)                                                                                                                         | Larger studies are included in table 2 |
| Horio, N. and Horiguchi, M.(2005)<br>Effect of arteriovenous sheathotomy on retinal blood flow and macular edema in patients with branch retinal vein occlusion. American Journal of Ophthalmology 139 (4) 739–740.                                       | n = 6<br><br>FU = 6 months                    | Arteriovenous sheathotomy led to a transient improvement of the retinal blood flow and was effective in reducing macular oedema. It is not clear whether the transient effect of sheathotomy affects the long-term visual acuity and macular oedema                                                            | Larger studies are included in table 2 |
| Figuerola MS, Torres R, Alvarez MT.(2004)<br>Comparative study of vitrectomy with and without vein decompression for branch retinal vein occlusion: A pilot study. European Journal of Ophthalmology Vol 14(1) 40–47.                                     | n = 35 (15 sheathotomy)<br><br>FU = 18 months | Decompression was achieved in 11/15 (73%) patients.                                                                                                                                                                                                                                                            | Larger studies are included in table 2 |
| Fujii, G. Y., De Juan E Jr, and Humayun, M. S. (2003)<br>Improvements after sheathotomy for branch retinal vein occlusion documented by optical coherence tomography and scanning laser ophthalmoscope. Ophthalmic Surgery, Lasers & Imaging 34 (1) 49–52 | n = 1<br><br>FU = 6 months                    | This case indicates optical coherence tomography can detect an early positive effect of sheathotomy surgery on macular oedema, and scanning laser ophthalmoscope can document associated improvement in fixation stability                                                                                     | Larger studies are included in table 2 |
| Khokhar, A. R. and Shaikh, Z. A.(2006)<br>Sheathotomy for treatment of branch retinal vein occlusion. Journal of the Liaquat University of Medical and Health Sciences 5 (3) 102–105                                                                      | n = 20<br><br>FU = 10.5 months                | A surgically important adhesion between the retinal artery and vein at proximal AV crossings was encountered in all eyes undergoing AV sheathotomy. Cataract formation was a frequent complication. Visual improvement may occur after vitrectomy and AV sheathotomy without separation of the retinal vessels | Larger studies are included in table 2 |

|                                                                                                                                                                                                                                               |                                |                                                                                                                                                                                                                                                                          |                                        |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| Kube, T., Feltgen, N., Pache, M. et al (2005) Angiographic findings in arteriovenous dissection (sheathotomy) for decompression of branch retinal vein occlusion. Graefes Archive for Clinical & Experimental Ophthalmology 243 (4) 334–338   | n = 22<br><br>FU = 1 year      | Sheathotomy for decompression of BRVO leads to a significant decrease of AVP and may ameliorate retinal perfusion in the affected branch                                                                                                                                 | Larger studies are included in table 2 |
| Lakhanpal, R. R., Javaheri, M., Ruiz-Garcia, H.,(2005) Transvitreal limited arteriovenous-crossing manipulation without vitrectomy for complicated branch retinal vein occlusion using 25-gauge instrumentation. Retina 25 (3) 272–280        | n = 12<br><br>FU = 20 weeks    | Sheathotomy without vitrectomy may achieve outcomes comparable with those of arteriovenous adventitial sheathotomy for complicated BRVO                                                                                                                                  | Larger studies are included in table 2 |
| Le Rouic JF, Bejjani RA, Rumen F, et al. (2001) Adventitial sheathotomy for decompression of recent onset branch retinal vein occlusion. Graefes Archive for Clinical & Experimental Ophthalmology 239(10):747–751.                           | n = 3<br><br>FU = not reported | Sheathotomy did not lead to a significant visual improvement in our patients.                                                                                                                                                                                            | Larger studies are included in table 2 |
| Liang, X. L., Chen, H. Y., Huang, Y. S (2007) Pars plana vitrectomy and internal limiting membrane peeling for macular oedema secondary to retinal vein occlusion: a pilot study. Annals of the Academy of Medicine, Singapore 36 (4) 293–297 | n = 11<br><br>FU =13.5 months  | Pars plana vitrectomy and sheathotomy rapidly reduced the macular oedema caused by retinal vein occlusion, with improvement in BCVA                                                                                                                                      | Larger studies are included in table 2 |
| Lu, L., Li, Y., Yi, C et al (2003) Preliminary clinical observation of arteriovenous sheathotomy for treatment of branch retinal vein occlusion. Yen Ko Hsueh Pao [Eye Science] 19 (1) 33–38.                                                 | n = 6<br><br>FU = 20 months    | Anatomic and functional improvement of retina can be achieved in patients with BRVO through sheathotomy. However, the capillary nonperfusion and microaneurysm may follow this surgical procedure in some cases that need further treatment with laser photocoagulation. | Larger studies are included in table 2 |

|                                                                                                                                                                                                         |                             |                                                                                                                                                                               |                                                                                                     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|
| Opremcak EM, Bruce RA (1999). Surgical decompression of branch retinal vein occlusion via arteriovenous crossing sheathotomy: a prospective review of 15 cases. Retina 19(1): 1–5                       | n = 15<br><br>FU = 5 months | At final follow up 10 patients (67%) had improvement of an average of four lines<br><br>Three patients (20%) had worse acuity                                                 | Larger studies are included in table 2                                                              |
| Osteroh MD, Charels S. (1988) Surgical decompression of branch retinal vein occlusions. Archives of Ophthalmologists 106: 1569–71                                                                       | n = 1<br><br>FU = 8 months  | Not available                                                                                                                                                                 | Larger studies are included in table 2                                                              |
| Shah GK. Adventitial sheathotomy for treatment of macular edema associated with branch retinal vein occlusion. Current Opinion in Ophthalmology 2000; 11(3): 171–4.                                     | n = 5<br><br>FU = 6.5 years | Arteriovenous adventitial sheathotomy may be beneficial for select patients                                                                                                   | Larger studies are included in table 2                                                              |
| Sohn, J. H. and Song, S. J. (2006) Arteriovenous sheathotomy for persistent macular edema in branch retinal vein occlusion. Korean Journal of Ophthalmology 20 (4) 210–214                              | n = 22<br><br>FU = 3 months | Vitrectomy with AV sheathotomy can be one treatment option for the patients with recurrent macular edema in BRVO                                                              | Larger studies are included in table 2<br><br>Studies with longer follow up are included in table 2 |
| Wrigstad, A. and Algvere, P. (2005) Arteriovenous adventitial sheathotomy for branch retinal vein occlusion: report of a case with longterm follow-up. Acta Ophthalmologica Scandinavica 84 (5) 699–702 | n = 1<br><br>FU = 59 months | Adventitial sheathotomy may improve vision in selected cases of BRVO. Further studies are necessary to determine the role of sheathotomy in the management of cases with BRVO | Larger studies are included in table 2                                                              |

## Appendix B: Related NICE guidance for arteriovenous crossing sheathotomy for branch retinal vein occlusion

| Guidance                  | Recommendations                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|---------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Interventional procedures | <p><b>Arteriovenous crossing sheathotomy for branch retinal vein occlusion NICE interventional procedures guidance 72 (2004).</b></p> <p>(Current guidance).</p> <p>1.1 Current evidence on the safety and efficacy of arteriovenous sheathotomy for branch retinal vein occlusion does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research.</p> <p>1.2 Clinicians wishing to undertake arteriovenous sheathotomy for branch retinal vein occlusion should take the following actions:</p> <ul style="list-style-type: none"> <li>• Inform the clinical governance leads in their Trusts.</li> <li>• Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. Use of the Institute's Information for the Public is recommended.</li> <li>• Audit and review clinical outcomes of all patients having arteriovenous sheathotomy for branch retinal vein occlusion.</li> </ul> <p>1.3 Further research will be useful in reducing the current uncertainty. Controlled trials clearly defining patient selection, the timing of treatment and the combination of other treatment modalities used would be particularly helpful. The Institute may review the procedure upon publication of further evidence.</p> |

## Appendix C: Literature search for arteriovenous crossing sheathotomy for branch retinal vein occlusion

| Database                                                                    | Date searched | Version/files                                                                                                                            | No. retrieved |
|-----------------------------------------------------------------------------|---------------|------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)           | 06/02/09      | Issue 1, 2009                                                                                                                            | 0             |
| Database of Abstracts of Reviews of Effects – DARE (CRD website)            | 06/02/09      | N/A                                                                                                                                      | 3             |
| HTA database (CRD website)                                                  | 06/02/09      | N/A                                                                                                                                      | 2             |
| Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library) | 06/02/09      | Issue 1, 2009                                                                                                                            | 77            |
| MEDLINE (Ovid)                                                              | 06/02/09      | 1950 to January Week 4 2009                                                                                                              | 223           |
| MEDLINE In-Process (Ovid)                                                   | 06/02/09      | February 05, 2009                                                                                                                        | 4             |
| EMBASE (Ovid)                                                               | 06/02/09      | 1980 to 2009 Week 05                                                                                                                     | 258           |
| CINAHL (NLH Search 2.0)                                                     | 06/02/09      | 1981 to present                                                                                                                          | 5             |
| BLIC (Dialog DataStar)                                                      | 06/02/09      | 1993 to date                                                                                                                             | 0             |
| National Research Register (NRR) Archive                                    | 06/02/09      | Visual Outcome Following Arteriovenous Crossing Decompression Sheathotomy in Branch Retinal Vein Occlusion: A Pilot Study Completed 2001 |               |
| UK Clinical Research Network (UKCRN) Portfolio Database                     | 06/02/09      | Nothing found                                                                                                                            |               |
| Current Controlled Trials metaRegister of Controlled Trials - mRCT          | 06/02/09      | Sheathotomy vs. Intravitreal Triamcinolone for Branch Retinal Vein Occlusion Completed 2007                                              |               |
| Clinicaltrials.gov                                                          | 06/02/09      |                                                                                                                                          |               |

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

|   |                                                                            |
|---|----------------------------------------------------------------------------|
| 1 | Decompression, Surgical/ (5609)                                            |
| 2 | Ophthalmologic Surgical Procedures/ (6098)                                 |
| 3 | ((Ophthalm* or Eye*) adj3 (Surg* or Procedure* or Decompress*)).tw. (7790) |
| 4 | (Arteriovenous* adj3 (Sheathotom* or Dissect*)).tw. (66)                   |
| 5 | or/1-4 (18345)                                                             |
| 6 | Retinal Vein Occlusion/ (1979)                                             |
| 7 | (Retinal* adj3 Vein* adj3 Occlusion*).tw. (1994)                           |
| 8 | BRVO.tw. (213)                                                             |

|    |                                   |
|----|-----------------------------------|
| 9  | Macular Edema/ (2324)             |
| 10 | (Macular* adj3 Edema*).tw. (3174) |
| 11 | or/6-10 (6093)                    |
| 12 | 5 and 11 (365)                    |
| 13 | Animals/ (4293014)                |
| 14 | Humans/ (10456700)                |
| 15 | 13 not (13 and 14) (3224702)      |
| 16 | 12 not 15 (362)                   |
| 17 | 2003*.ed. (844606)                |
| 18 | 2004*.ed. (795730)                |
| 19 | 2005*.ed. (598673)                |
| 20 | 2006*.ed. (636007)                |
| 21 | 2007*.ed. (707223)                |
| 22 | 2008*.ed. (719436)                |
| 23 | 2009*.ed. (46980)                 |
| 24 | or/17-23 (4348655)                |
| 25 | 16 and 24 (223)                   |