NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of implantation of miniature lens systems for advanced age-related macular degeneration

Age-related macular degeneration is an eye disorder that affects older adults, leading to the gradual loss of central vision. This procedure involves removing the natural lens through a small cut at the front of the eye, and implanting an artificial lens system into the eye. The aim is to improve central vision.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) 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 IP overview was prepared in January 2016.

Procedure name

- Implantation of miniature lens systems for advanced age-related macular degeneration

Specialist societies

- Royal College of Ophthalmologists.

Description

Indications and current treatment

Age-related macular degeneration (AMD) is the commonest cause of irreversible blindness in industrialised countries. It usually occurs in older adults and is associated with degeneration of the macula – a small area at the centre of the retina responsible for central vision, and for appreciation of fine detail and colour.

There are 2 main types of AMD, the most common of which is atrophic or 'dry' macular degeneration. This dry form is characterised by thinning of the macular retina. It develops slowly, causing a gradual loss in central vision. The other type is neovascular or 'wet' AMD, which is characterised by the growth of new blood vessels behind the retina, causing retinal bleeding and scarring. The new vessels are described according to whether they can be seen clearly (classic) or poorly (occult) on fluorescein angiography. The onset and disease progression of wet AMD is much faster than in the dry form. Both types of AMD typically affect both eyes, although 1 eye may be affected before the other.

Optical aids such as magnifying glasses may help patients with dry or wet AMD, to read and do tasks needing fine-detail vision. For wet AMD there are several treatment options but most patients have repeated intravitreal injections of antivascular endothelial growth factor agents, with ongoing regular clinic review. There is currently no standard treatment for dry AMD.

What the procedure involves

The aim of an implantable miniature lens system is to magnify the image on the macula, or to optically move the image onto an undamaged part of the retina. Implantation of lens systems for advanced age-related macular degeneration (AMD) is usually done under local anaesthesia. The natural lens of the eye is removed through a small incision at the limbus (the area where the cornea meets the sclera) and the new lens system is inserted. Artificial lens systems consist of either a miniature telescope prosthesis implanted in the capsular bag of the natural lens, or 2 separate lenses, with 1 lens implanted in front of and 1 lens implanted behind the iris.

The implantation technique varies according to the system being used. Generally, if a telescope prosthesis is used, a larger limbal incision may be needed. Viscoelastic fluid is used during implantation to facilitate the insertion and is then removed by irrigation or aspiration. When a single miniature telescope prosthesis is used, images are magnified by the implanted lens system and focused on the macula. When a system of 2 separate lenses is used, the lenses are rotationally aligned to deflect a magnified image away from the most damaged part of the macular and towards a less damaged area. In both cases,

the contralateral eye is used for peripheral vision. After implantation, patients need visual rehabilitation.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to implantation of miniature lens systems for advanced age-related macular degeneration. The following databases were searched, covering the period from their start to 04.08.2015: 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). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

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	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. 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.
Patient	Patients with advanced age-related macular degeneration.
Intervention/test	Implantation of miniature lens systems.
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.

List of studies included in the IP overview

This IP overview is based on 314 patients (322 eyes) from 1 non-randomised comparative study[1-3] and 4 case series[4-7].

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.

Table 2 Summary of key efficacy and safety findings on implantation of miniature lens systems for advanced age-related macular degeneration

Study 1 IMT study group Hudson H (2006)[1], (2008)[2], Boyer (2015)[3]

Details

Study type	**Non-randomised comparative study (fellow eye controls)**
Country	USA
Recruitment period	Not stated
Study population and number	n=**217** patients with bilateral, end-stage AMD
Age and sex	Mean age (years): 75.6 (range 55–93); Male: 52.5% (114/217)
Patient selection criteria	Inclusion criteria: Age at least 55 years; moderate to profound bilateral BCDVA between 20/80 and 20/800 on ETDRS visual acuity chart (patients had to achieve at least a 5-letter improvement on chart with an external telescope in the eye scheduled for implantation) resulting from geographic atrophy or disciform scars associated with AMD and adequate peripheral field in contralateral eye. Exclusion criteria: Eyes with active choroidal neovascularization, and those that had therapy for choroidal neovascularization within 6 months, previous intraocular surgery, corneal surgery, endothelial cell count <1600 cells/mm2, an anterior chamber depth of 2.5 mm, with marked cognitive disorders were excluded.
Technique	Phacoemulsification is done and a 12 mm incision made to implant a fixed-focus telescopic prosthesis, ×2.2 or ×3 (IMT; VisionCare Ophthalmic Technologies) in 1 eye. 115 eyes received 2.2× device, 91 eyes received 3× device. The implant is inserted into the capsular bag and fixed in position and wound is sutured and a peripheral iredectomy is done. Post-operative education is given for 3–6 months.
Follow-up	**12 months[1], 2 years[2], 5 years[3]**
Conflict of interest/source of funding	VisionCare Opthalmic Technologies Inc, Saratoga CA.

Analysis

Follow-up issues: At 1 year, data on 192/206 patients was available for analysis. At 2 years of the 206 eyes with IMT implanted, 13 patients were lost to follow-up, 10 died during the study period, 1 patient did not return to 2-year visit, and 8 patients had the devices removed. Only 174 eyes were available for follow-up at 2 years. 63 patients (31 in group 1 and 32 in group 2) were available for follow-up at 60 months in IMT002-LTM.

Study design issues: For IMT002 (prospective study) and IMT002-LTM (an extension of IMT002 study) in 28 centres, fellow eye was used as control group. A total of 32 surgeons performed the procedure. Patients were not blinded to which eye was treated. Long-term visual acuity was measured at 18, 24 and 60 months. Quality of life was only assessed at 1 year using the National Eye Institute Visual function Questionnaire 25-item survey. Outcome measures were not compared with baseline data.

A retrospective subgroup analyses was done with stratification for age, group 1: 65–75 years (n=70) and group 2: >75 years (n=127). Of the 217 patients, 20 patients aged 55–65 were excluded from data analysis on age stratification due to small number of patients.

Study population issues: There was no difference in preoperative visual acuity measures between the 2× and 3× devices. 8 study eyes received an IOL during an unsuccessful telescope implantation procedure. 22 fellow eyes underwent intrastudy cataract extraction and IOL implantation.

Other issues: The authors comment that improvements in the fellow eye may be due to visual rehabilitation. The authors note that the implantation procedure is complex and careful patient selection with management of expectations is important.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **217**

Implantation success: 95% (206/217)

Visual acuity outcomes

	Implanted eye % (n)	**Fellow eye % (n)**	**p value**
Gain ≥3 lines in BCDVA at 1 year	66.7 (128/192)	12.5 (24/192)	p<0.0001
Gain ≥3 lines in in BCNVA at 1 year	67.7 (130/192)	33.3 (64/192)	p<0.0001
Mean BCDVA improvement	3.5 lines	0.8 lines	p<0.0001
Mean BCNVA improvement	3.2 lines	1.8 lines	p<0.0001
Gain ≥3 lines in near and distance BCVA at 1 year	53.1	10.4	
Gain ≥3 lines in in BCVA at 2 years[2]	59.5 (103/173)	10.3 (18/174)	p<0.0001
Loss ≥2 lines in BCDVA at 12 months*	2.1	8.9	p=0.005

**(actual numbers not given)*

Mean BCVA improved 3.6±1.9 lines and 2.8±2.3 lines from baseline in eyes with the 3× and 2.2× models respectively compared with 0.5 line gain in fellow eyes (p<0.0001).

Fellow eyes with intrastudy cataract surgery

The paired difference between the mean change in BCVA between telescope implanted eyes and the fellow eye that had cataract surgery with IOL placement was 2.7 and 3.2 lines respectively (p=0.0002).

Vision (BCDVA) gain stratified by age in implanted eye

	12 months	**24 months**	**36 months**	**48 months**	**60 months**
65 to ≤75 years (n)	**65**	**60**	**22**	**38**	**31**
Gain≥ 3 lines % (n)	66.2 (43)	61.7 (37)	50.0 (11)	57.9 (22)	58.1 (18)
Gain≥ 2 lines % (n)	80.0 (52)	75.0 (45)	68.2 (15)	68.4 (26)	67.7 (21)
Mean ±SD line change	3.6±2.1 lines	3.3±2.0 lines	2.4±2.8 lines	2.7±2.6 lines	2.7±2.7 lines
≥75 years (n)	**109**	**95**	**42**	**46**	**32**
Gain≥ 3 lines % (n)	66.1 (72)	57.9 (55)	57.1 (24)	41.3 (19)	37.5 (12)

Safety

Adverse events

	1 year % (n)	**2 years % (n)**	**60 months % (n)**
Aborted surgery (as a result of 7 posterior capsule rupture, 1 choroidal effusion, 2 choroidal haemorrhage, 1 zonular dehiscence-IOL was implanted)	5 (11/217)		
Device removal (2 surgical trauma resulting in condensation inside telescope, 2 removed during corneal transplant, 8 due to patient dissatisfaction) all replaced with conventional IOL.	3.9 (8/206)	5.8 (12/206)	-
Loss of 2 or more lines in BCDVA or BCNVA without a 2-line improvement in the other test distance	5.2 (10/192)	IMT 0.6 (1/173) versus fellow eye 7.5 (13/174) [p=0.0013]	6.7 (14/206)
Corneal decompensation at 1 year (both required device removal and corneal transplantation more than 1 year after initial surgery).	1 (2/206)	0	
Choroidal neovascularization (at 6 months, treated with focal laser photocoagulation through telescope without complications)	0.5 (1/206)	2 (4/206)	
Inflammatory deposits on device	21 (44/206)	25 (51/206)	
Pigment deposits on device	10 (20/206)	11 (23/206)	
Guttata	8 (16/206)	8 (16/206)	

Gain≥ 2 lines % (n)	79.8 (87)	74.7 (71)	73.8 (31)	63.0 (29)	59.4 (19)
Mean ±SD line change	3.4±2.2 lines	3.1±2.2 lines	3.0±1.8 lines	2.2±2.6 lines	2.1±2.9 lines
Overall patients (n)	**174**	**155**	**64**	**84**	**63**
Gain≥ 2 lines % (n)	NR	NR	NR	NR	62
Mean line change	NR	3.2 lines	NR	NR	2.4±2.69 lines

Vision loss (≥ 2 lines) stratified by age

	12 months	**24 months**	**36 months**	**48 months**	**60 months**
65 to ≤75 years (n)	**65**	**60**	**22**	**38**	**31**
Implanted eye					
% (n)	1.5 (1)	0	9.1 (2)	5.3 (2)	9.4 (3)
Fellow eye					
% (n)	6.2 (4)	5.0 (3)	9.1 (2)	10.5 (4)	16.1 (5)
≥75 years (n)	**109**	**95**	**42**	**46**	**32**
Implanted eye					
% (n)	1.8 (2)	2.1 (2)	0	4.3 (2)	9.4 (3)
Fellow eye					
% (n)	9.2 (10)	12.5 (12)	14.3 (6)	13.0 (6)	28.1 (9)

Quality of life and functional outcomes at 1 year (National Eye Institute Visual Function Questionnaire scores on scale of 0 [low] to 100 [maximum])

	Preoperative mean score (n=206)	**12-month mean score (n=192)**	**P value**
General health	63.2	58.7	0.03
General vision	35.4	50.3	<0.0001
Near activities	25.5	37.3	<0.0001
Distance activities	34.3	42.4	<0.0001
Colour vision	63.9	67.2	NS
Social functioning	49.3	58.3	<0.0001
Mental health	39.8	49.3	<0.0001
Role difficulties	37.4	44.8	0.0002
Dependency	37.2	48.3	<0.0001
Ocular pain	88.0	88.5	NS
Driving	2.1	1.9	NS
Peripheral vision	67.6	62.9	0.0009
Overall composite (excludes	43.9	50.3	<0.0001

Posterior synechiae	6 (13/206	7 (15/206)	
Increased intraocular pressure (IOP) within 7 days requiring treatment (no further details were given)	28 (57/206)		
Increased IOP beyond 7 days requiring treatment	3 (6/206)		
Corneal oedema within 30 days	7(14/20 6)		
Corneal oedema beyond 30 days (required grafts at 9 and 12 months)	1 (2/206)	4.3 (9/206)	
Iris prolapse	6 (12/206)	5 (11/206)	6 (12/206)
Iris incarceration			1 (3/206)
Iris damage			4 (9/206)
Iris trans illumination defects <21 days after surgery			3 (7/206)
Iris transillumination defects lasting >21 days			5 (11/206)
Iris atrophy < or > 7 days after surgery			6 (12/206)
Corneal abrasion	5(11/20 6)		
Iritis beyond 30 days after implant	4 (8/206)	6 (12/206)	6 (12/206)
Foreign body sensation	3 (7/206)		
Anterior chamber inflammation beyond 30 days	2.4%		
Device dislocation	1 (2/206)	1.4 (3/206)	
Sub-retinal haemorrhage	0	0	2.4 (5/206)
Vitreous haemorrhage < or > than 7 days after surgery			2 (4/206)
Vitreous in anterior chamber < or > than 7 days after surgery			4 (8/206)
Vitreous loss			4 (9/206)

There were no reports of endophthalmitis or hypopyon, retinal detachment, retinal tear or posterior capsular opacification.

Ocular complications and adverse events stratified by

general health)			

Gain in telescope eye BCVA was correlated with improvement in NEI-VFQ 25 scores.

In the subgroup analysis, both age groups showed clinically significant quality of life improvement from baseline in majority of the subscales. Quality of life gains were highest in group 1 for the subscales with significant changes in subscale scores and composite scores.

age group

At 60 months follow-up, patents in group 2 (>75 years of age) had the highest cumulative incidence of complications in 87% (13/15) categories listed. Only iris damage and iris prolapse occurred more frequently in group 1 (65-75 years of age) than group 2.

Group 2 reported more adverse events in 79% (11/14) events listed.

Endothelial cell density (ECD) and morphometry

Endothelial cell density was reduced by 20% below baseline at 3 months and 25% at 1 year (this exceeded the 17% end point defined in the study protocol). The mean cell loss from 1 to 2 years was 2.4%. There was no significant change in coefficient of variation or percentage of hexagonal endothelial cells 6 months to 2 years after surgery. Chronic loss was 3% per year.

ECD loss was les in group 1 than in group 2 (35% versus 40%) at 60 months.

The decrease in ECD was correlated with post-surgical odema ($p<0.0001$) suggesting that endothelial damage occurred during surgery, rather than during the postoperative period.

Abbreviations used: AMD, age-related macular degeneration; BCDVA, best-corrected distance visual acuity; BCNVA, best-corrected near visual acuity; BCVA, best-corrected visual acuity; ETDRS, early treatment of diabetic retinopathy study; IOL, intraocular lens; NEI-VFQ, National Eye Institute Visual Function Questionnaire; SD, standard deviation.

Study 4 Alio J (2004)

Details

Study type	**Case series**
Country	Spain
Recruitment period	not stated
Study population and number	n=**40 eyes (40 patients)** with dry-type AMD.
Age and sex	Mean age: 77.1 years (range 61–87); male: 42.5% (19/40)
Patient selection criteria	Inclusion criteria: age >60 years; stable form of AMD; BCVA in selected eye not better than 20/80 or worse than 20/200; BCVA 20/80 or worse in fellow eye. Exclusion criteria: other eye disease; neurological disorder; immunosuppressive disease; extreme sensitivity.
Technique	Intraocular miniaturised telescope with magnification of 3.0× (Vision Care Ophthalmic Technologies).
Follow-up	**12 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: 4 patients were lost to follow-up.

Study design issues: An additional 21 cases were recruited to the study but did not complete study protocol up to 12-month follow-up. These patients were excluded (7 had insufficient data for follow-up, 7 were implanted with previous model, 3 patients were implanted with an ×2.2 model rather than ×3).

The study narrative states that 40 eyes of 40 patients were included but distance visual acuity data is only presented for 35 eyes of 35 patients.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 40 eyes
Distance visual acuity

Mean line (ETDRS) in implanted eye:
• Preoperative = 10.2 (n = 35)
• 1 month postoperative = 8.1 (n = 29)
• 6 months postoperative = 6.4 (n = 28)
• 12 months postoperative = 6.8 (n = 23)

Mean Snellen equivalent in implanted eye:
• Preoperative = 20/209 (n = 35)
• 1 month postoperative = 20/129 (n = 29)
• 6 months postoperative = 20/87 (n = 28)
• 12 months postoperative = 20/96 (n = 23)

At 1 year, mean improvement for uncorrected distance visual acuity was 3.5 lines for implanted eye, and mean deterioration of fellow eye was 1.1 lines.

Mean uncorrected distance visual acuity at 1 year:
• Implanted eye = 0.6 logMAR
• Fellow eye = 0.9 logMAR, p=0.003

Near visual acuity

Mean line (ETDRS) in implanted eye:
• Preoperative = 9.5 (n = 32)
• 1 month postoperative = 8.3 (n = 23)
• 6 months postoperative = 5.0 (n = 18)
• 12 months postoperative = 5.1 (n = 16)

Mean Snellen equivalent in implanted eye:
• Preoperative = 180 (n = 32)
• 1 month postoperative = 134 (n = 23)
• 6 months postoperative = 63 (n = 18)
• 12 months postoperative = 65 (n = 16)

Mean uncorrected near visual acuity at 1 year:
• Baseline:0.8 logMAR (0.16±0.13, range 0.1 to o.5 in decimal values)
• Implanted eye at 1 year = 0.4 logMAR, baseline versus follow-up, p=0.003
• Fellow eye at 1 year = 0.5 logMAR, implanted eye versus feloow eye, p=not significant</td><td>Adverse events
<table><tr><th></th><th>% (n)</th></tr><tr><td>Device explantation (3 because of patient dissatisfaction, 2 due to bubbles inside telescope and 1 due to diplopia)</td><td>17 (6/36)</td></tr><tr><td>Hypopyon (treated with topical steroids)</td><td>11.1 (4/36)</td></tr><tr><td>Intraoperative iris damage</td><td>5.6 (2/36)</td></tr><tr><td>Intraoperative zonule rupture</td><td>2.8 (1/36)</td></tr><tr><td>Iris sphincter erosion 6 months postoperatively</td><td>2.8 (1/36)</td></tr><tr><td>Intraoperative vitrous bulge</td><td>2.8 (1/36)</td></tr><tr><td colspan="2">Transient complications</td></tr><tr><td>Corneal oedema</td><td>25 (9/36)</td></tr><tr><td>Fibrin at pupil</td><td>33.3 (12/36)</td></tr><tr><td>Synechias</td><td>19.4 (7/36)</td></tr><tr><td>Hyphema</td><td>11.1 (4/36)</td></tr><tr><td>Conjunctivitis</td><td>5.6 (2/36)</td></tr><tr><td>Uveitis</td><td>8.3 (3/36)</td></tr><tr><td>Cyclitic membrane</td><td>2.8 (1/36)</td></tr><tr><td colspan="2">Persistent complications</td></tr><tr><td>Persistent pupillary cyclitic membrane</td><td>2.8 (1/36)</td></tr><tr><td>Persistent synechias</td><td>5.6 (2/36)</td></tr><tr><td>Posterior capsular opacification</td><td>11.1 (4/36)</td></tr></table>
Mean endothelial cell loss at 12 months = 34.5% (calculated for 10 eyes)</td></tr>
<tr><td colspan="2">Abbreviations used: AMD, age-related ,macular degeneration; BCDVA, best-corrected distance visual acuity; BCNVA, best-corrected near visual acuity; BCVA, best-corrected visual acuity; ETDRS, early treatment of diabetic retinopathy study.</td></tr>
</table>

Study 5 Orzalesi N (2007)

Details

Study type	**Case series**
Country	Italy
Recruitment period	Not stated
Study population and number	n=**40 eyes (35 patients)** with a stable central scotoma due to macular disease.
Age and sex	Not stated
Patient selection criteria	Inclusion criteria: Patients with low vision 1.7 to 1.3 logMAR were included. Exclusion criteria: pseudophakic in both eyes; visual acuity >0.5 logMAR in fellow eye; no improvement in visual acuity using a simulator; corneal abnormalities; low endothelial cell count and/or shallow anterior chamber; experienced satisfactory improvement in visual performance after simply following preoperative visual training programme.
Technique	Intraocular lenses for visually impaired people (IOL-Vip system, Soleko, Pontecorvo Italy) consisting of 2 intraocular lenses (that act as a Gaililean telescope) implanted. A high negative power intraocular lens is implanted in the capsular bag with concomitant implantation of a high plus power anterior chamber intraocular lens (ACIOL) after phacoemulsification of the patient's own lenses. All patients underwent a laser peripheral iridotomy before placement of ACIOL. In addition every patient had a preoperative endothelial cell count.
Follow-up	**20 months (range 7–35)**
Conflict of interest/source of funding	Not stated.

Analysis

Study design issues: Consecutive cases, surgery performed at an ambulatory center. Extensive preoperative training and software programs were used to select the patients.

Study population issues: Patients had central scotomas and maculopathy.

Other issues: The authors note that the low optical magnifying power of the lens system allows maintenance of the peripheral visual field, thus making it suitable for monocular or binocular implantation.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 40 eyes
Visual acuity outcomes
The mean preoperative BCVA was 0.77 compared with 1.28 preoperatively.
Patients with very poor preoperative visual acuity (≤1.1 logMAR, n=28):
• Mean best reading magnification decreased from ×11.6 to ×3.5 (gain of ×8.1)
• Best reading distance increased from 2.66 cm to 8.21 cm (gain of 5.55 cm)

Patients with relatively good preoperative visual acuity (≤1.0 logMAR, n=12):
• Mean best reading magnification decreased from ×3 to ×1.3 (gain of ×1.7)
• Best reading distance increased from 8.87 cm to 21.46 cm (gain of 12.59 cm)

All patients experienced a gain in BCDVA.

The lens system was subjectively well tolerated and most patients retained or improved their mobility and orientation.</td><td>Adverse events
<table><tr><th></th><th>% (n)</th></tr><tr><td>Endothelial cell loss (procedure related) at end of follow-up</td><td>7%</td></tr><tr><td>Papillary block with increased intraocular pressure in first cases (managed by laser iridotomy). In all subsequent cases, preoperative iridotomy was performed.</td><td>n=3</td></tr><tr><td>Anterior capsule fibrosis and posterior capsule opacification 6 months after phacoemulsification (treated using Nd-YAG laser).</td><td>n=1</td></tr></table>There were no severe complications such as corneal oedema, iris and papillary changes, excess inflammation and/or sepsis, macular oedema, retinal detachment, glaucoma or intraocular lens displacement.</td></tr>
<tr><td colspan="2">Abbreviations used: AMD, age-related ,macular degeneration; BCDVA, best-corrected distance visual acuity; BCNVA, best-corrected near visual acuity; BCVA, best-corrected visual acuity; ETDRS, early treatment of diabetic retinopathy study.</td></tr>
</table>

Study 6 Amselem L (2008)

Details

Study type	**Case series**
Country	Spain
Recruitment period	Not stated
Study population and number	n=**13 eyes (10 patients)** with low vision and central scotoma due to severe macular degeneration.
Age and sex	Mean age 74.1 years; 60% (6/10) male
Patient selection criteria	Inclusion criteria: patients with unilateral or bilateral stable central visual acuity loss caused by myopic choroidal neovascularization and central scotoma due to untreatable end-stage AMRD determined by flourescien angiography, those phakic with evidence of cataract were included. Exclusion criteria: pseudophakic or phakic patients with pseudoexfoilation, with a history of intraocular surgery in 3 months before study were excluded.
Technique	Surgery performed under peribulbar anaesthesia in an outpatient setting. Intraocular lenses for visually impaired people (IOL-Vip system, Soleko, Pontecorvo Italy) consisting of 2 intraocular lenses (that act as a Gaililean telescope) implanted. A high negative power intraocular lens is implanted in the capsular bag with concomitant implantation of a high plus power anterior chamber intraocular lens (ACIOL) after phacoemulsification of the patient's own lens. All patients underwent a laser peripheral iridotomy before placement of ACIOL. In addition every patient had a preoperative endothelial cell count.
Follow-up	**12 months**
Conflict of interest/source of funding	Not stated.

Analysis

Follow-up issues: Postoperative follow-up visits done at 1 day, 1 week, and 1, 3, 6 and 1 year.

Study design issues: Prospective case series. The cornea-anterior chamber depth and intraocular lens-endothelium distance (AC IOL distance) and AC IOL-PC IOL distance was evaluated by high frequency ultrasound biomicroscopy and optical coherence tomography (OCT). Endothelial cell count was measured at 12 and 18 months.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 13 eyes
Visual acuity
The mean BCVA was 1.37±0.34 logMAR preoperatively and 0.68±0.19 logMAR at 1-year follow-up (p<0.001).

Refraction
There was no statistically significant difference between the theoretically calculated and clinically evaluated residual refraction (p=0.17).

Magnification
The mean best corrected magnification was ×1.35±0.07; the difference between eyes with the long axial length and eyes with short axial length was not significant. The mean best corrected ‘clinical gain’ was 44%.

Anterior chamber depth and intraocular lens-endothelium distance
The mean ACD in 8 hyperopic eyes was 3.38 mm and the mean AC IOL endothelium distance was 1.91 mm; the mean ACD in 5 myopic eyes was 4.36 mm and the mean AC IOL-endothelium distance was 3.02 mm. At 18 months, a mean ACD of 2.23 mm in hyperopic eyes and 3.18 mm in myopic eyes was seen.

IOL was well tolerated in both monocular and binocular procedures.</td><td><table><tr><th>Adverse events</th><th>% (n)</th></tr><tr><td>Intraocular hypertension (24±3 mmHg) and mild sectorial corneal odema in immediate postoperative period (resolved with administration of topical steroids)</td><td>40 (4/10)</td></tr><tr><td>Ocular pain due to mild corneal epithelial trauma (resolved with no complications)</td><td>20 (2/10)</td></tr><tr><td>Posterior capsule opacification (had a Nd-YAG laser capsulotomy with good results)</td><td>30 (3/10)</td></tr><tr><td>Diplopia</td><td>0</td></tr><tr><td>Explantation/replacement</td><td>0</td></tr><tr><td>Mechanical trauma to intraocular structures</td><td>0</td></tr></table>
Endothelial cell count (EDC)
The mean EDC was 2675±244 cells/mm2 preoperatively and 2378±270 cells/mm2 at 12 months follow-up, a mean cell loss of 11.1%. At 18 months, EDC was 2264±250 cells/mm2 with a mean cell loss of 5.2% from 12 to 18 months. There were no cases of endothelial decompensation.</td></tr>
<tr><td colspan="2">Abbreviations used: AMD, age-related ,macular degeneration; BCDVA, best-corrected distance visual acuity; BCNVA, best-corrected near visual acuity; BCVA, best-corrected visual acuity; ETDRS, early treatment of diabetic retinopathy study; IOL, intraocular lenses.</td></tr>
</table>

Study 7 Agarwal A (2008)

Details

Study type	**Case series**
Country	India
Recruitment period	June-Dec 2006
Study population and number	n=**6 eyes (6 patients)** with bilateral macular pathology and visual acuity worse than 20/200 4 eyes had AMD, 1 eye each had myopic macular degeneration or macular dystrophy.
Age and sex	Age not stated; Male: 83.3% (5/6)
Patient selection criteria	Inclusion criteria: patients with bilateral macular pathology; with distance or near visual acuity less than 20/200; cataract with nuclear sclerosis grade less than 2; no other ocular or systemic disease; vision improved when tested with ×2.5 external telescope.
Technique	Conventional coaxial phacoemulsification was performed. Lipshitz macular implant (Optolight Vision Technology), a modified conventional IOL that follows the Cassegrain telescope configuration, using 2 miniature mirrors was implanted in the capsular bag. This magnifies image on retina using a mirror telescope (×2.5). All patients placed on routine postoperative regimen of topical antibiotic steroid combination for 6 weeks.
Follow-up	**6 months**
Conflict of interest/source of funding	Not stated.

Analysis

Study design issues: Prospective pilot study, all surgeries performed by the same surgeon. Quality of life measured using a questionnaire.

Other issues: The authors suggest that this implant can be used bilaterally because it provides enlarged central and normal peripheral vision.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **6 eyes**

Visual acuity outcomes

The operated eyes gained a mean 3.66±1.88 lines in distance acuity at 6 months (the fellow eyes lost a mean 1.41 lines) and the mean increase in the ETDRS score for near acuity was 50.83±9.15 logMAR.

	Preoperative	**1 month**	**6 months**
Mean BCDVA in implanted eye (logMAR)	1.47	0.96	0.94 (p=0.014)
Mean BCNVA in implanted eye (ETDRS score, logMAR)	24.16	68.33	75.00 (p=0.014)

A good central fundus view was possible around the mirrors in all eyes. Fundus fluroscein angiography showed good visibility of the retina up to the mid periphery.

Quality of life at 6 months

Quality-of-life questionnaire showed that the ability to read large print, count money and move independently was improved after surgery in most patients. The ability to read watches or clocks, dial the telephone and use a computer keyboard improved moderately in most patients. The ability to read small print improved slightly in most patients.

Mean quality-of-life score (mean ±SD):

- Preoperatively = 11.16±1.72
- Postoperatively = 4.5±0.83, p=0.014

Safety

Adverse events

	% (n)
Intraoperative complications	0
Lost lines at 1 week as a result of slight postoperative inflammatory reaction. This improved after 1 month.	1
Postoperative cystoid macular oedema that spontaneously resolved.	1
Shadowing of images that occluded the unoperated eye; both patients adapted within 3 months of surgery.	2

All patients reported slight glare, especially in bright sunlight and while night driving in the postoperative period but this improved by 6 months.

Mean change in endothelial count in operated eye = –5.79±4.07% cells/mm^2.

Abbreviations used: AMD, age-related ,macular degeneration; BCDVA, best-corrected distance visual acuity; BCNVA, best-corrected near visual acuity; ETDRS, early treatment of diabetic retinopathy study.

Efficacy

Visual acuity

Mean change in best corrected distance visual acuity – gain in 3 or more lines

In a non-randomised comparative study of 217 patients with age-related macular degeneration (AMD) comparing vision in an eye with an implanted telescope lens system with fellow eye as control, 67% (128/192) of implanted eyes gained 3 or more lines in best-corrected distance visual acuity (BCDVA) compared with 13% (24/192) of fellow eyes at 1-year follow-up ($p<0.0001$)[1]. At 2-year follow-up, 60% (103/173) of implanted eyes had gained 3 or more lines in BCDVA compared with 10% (18/174) of fellow eyes ($p<0.0001$)[2]. Mean BCDVA improved by 3.5 lines in implanted eyes compared with 0.8 lines in fellow eyes ($p<0.0001$)[1]. At 5-year follow-up, the mean BCDVA improvement from baseline (±standard deviation) was 2.4(±2.69) lines in all patients (n=76). The subgroup analysis in which patients were stratified by age showed that the improvement was 2.7(±2.7) lines in those aged 65–75 years and 2.1(±2.9)2 lines in those aged over 75 years[3].

In a case series of 40 eyes (40 patients) implanted with a telescope lens system, mean uncorrected distance visual acuity (UCDVA) improved from baseline 0.9 logMAR to 0.6 logMAR in the implanted eye at 1-year follow-up. There were statistically significant differences between the implanted and fellow control eye (0.6 logMAR versus 0.9 logMAR, $p=0.003$)[4].

In a case series of 40 eyes (35 patients) implanted with an intraocular lens system, all patients showed an improvement of visual acuity. The mean preoperative best-corrected visual acuity (BCVA) was 0.77 compared with 1.28 preoperatively[5].

In a case series of 13 eyes (10 patients) implanted with an intraocular lens system, the mean BCVA was 1.37(±0.34) logMAR preoperatively and 0.68± 0.19 logMAR at 1-year follow-up ($p<0.001$)[6].

In a case series of 6 eyes (6 patients) implanted with an intraocular telescopic lens, the mean gain in distance acuity was 3.66(±1.88) lines. The BCDVA had improved significantly at 6-month follow-up ($p=0.014$)[7].

Mean change in best corrected near visual acuity (BCNVA)-gain in 3 or more lines

In the non-randomised comparative study of 217 patients with AMD comparing vision in an eye with an implanted telescope lens system with fellow eye as control, 68% (130/192) of implanted eyes gained 3 or more lines in best-corrected near visual acuity compared with 33% (64/192) of fellow eyes at 1-year

follow-up (p<0.0001)[1]. Mean BCNVA improved by 3.2 lines in implanted eyes compared with 1.8 lines in fellow eyes (p<0.0001)[1].

In the case series of 40 eyes (40 patients) implanted with a telescope lens system, mean UCNVA improved from baseline 0.8 logMAR to 0.4 logMAR in the implanted eye (p=0.003) at 1-year follow-up. There was no statistically significant differences between the implanted and fellow control eye (0.4 logMAR versus 0.5 logMAR; p value not significant)[2].

In the case series of 6 eyes (6 patients) implanted with an intraocular telescopic lens, the mean increase in the early treatment diabetic retinopathy study (ETDRS) score for near acuity was 50.83±9.15 logMAR. BCNVA improved significantly (p=0.014)[7].

Change in quality of life

In the non-randomised comparative study of 217 patients, self-reported quality-of-life scores (assessed using the National Eye Institute's visual functioning questionnaire 25 item scores [NEI-VFQ-25]) improved by more than 7 points from baseline (p<0.01) on 7 of 8 relevant subscales (vision specific subscales and psychosocial vision targeted subscales), at 1-year follow-up. Overall, the mean NEI-VFQ-25 composite score improved significantly by 6.1±14.4 points from baseline (p<0.0001). In the subgroup analysis for age stratification, both age groups (65–75 years, and over 75 years) showed clinically significant improvement in quality of life from baseline in most subscales but it was higher in those aged 65–75 years (5-point change in individual subscale scores or composite scores is considered as clinically significant)[1].

In a case series of 6 eyes (6 patients) implanted with an intraocular telescopic lens, the mean quality-of-life score significantly improved from baseline 11.16±1.72 to 4.5±0.83 (p=0.014) at 6-month follow-up[7].

Safety

Aborted surgery

Surgery was stopped in 5% (11/217) of patients because of complications such as posterior capsule rupture in 7 patients, choroidal effusion in 1 patient, choroidal haemorrhage in 2 patients and zonular dehiscence in 1 patient in a non-randomised comparative study of 217 patients[1].

Device explantation

Device explantation was reported in 6% (12/206) of patients in the non-randomised comparative study of 217 patients at 2-year follow-up. Two were removed because of surgical trauma resulting in condensation inside the telescope, 2 were removed during corneal transplantation, and 8 were removed

because of patient dissatisfaction. All devices were replaced with a conventional intraocular lens[2].

Device explantation was reported in 17% (6/36) of patients in a case series of 40 eyes (40 patients) implanted with an intraocular miniature lens. Three were removed because of patient dissatisfaction, 2 because of condensation in the telescope and 1 because of diplopia. All devices were replaced with a conventional intraocular lens[4].

Corneal decompensation

Corneal decompensation was reported in 1% (2/206) of patients in the non-randomised comparative study of 217 patients at 1-year follow-up. Both needed device removal and corneal transplantation more than 1 year after initial surgery[1].

Choroidal neovascularization

Choroidal neovascularization after telescope implantation was reported in 2% (4/206) of patients in the non-randomised comparative study of 217 patients at 2-year follow-up. One patient had successful treatment with focal laser photocoagulation through the telescope without complications. Details about management of the neovascularization in other 3 patients were not reported[1].

Increased intraocular pressure

Increased intraocular pressure (IOP) within 7 days needing treatment was reported in 28% (57/206) of patients in the non-randomised comparative study of 217 patients. Increased IOP beyond 7 days needing treatment was reported in 3% (6/206) of patients in the same study. No further details were reported[1].

Intraocular hypertension (24±3 mm Hg) and mild sectorial corneal oedema in immediate postoperative period (resolved with administration of topical steroids) was reported in 40% (4/10) of patients in a case series of 10 patients (13 eyes)[6].

Hypopyon

Hypopyon (treated with topical steroids) was reported in11% (4/36) of patients in a case series of 40 patients (40 eyes). No further details were reported[4].

Posterior capsule opacification

Posterior capsule opacification (treated successfully with a Nd-YAG laser capsulotomy) was reported in 30% (3/10) of patients in a case series of 10 patients (13 eyes)[6].

Deposits on device

Inflammatory deposits on the device were reported in 25% (51/206) of implanted eyes and pigment deposits on the device were reported in 11% (23/206) of implanted eyes in the non-randomised comparative study of 217 patients. No further details were reported[1].

Loss of 3 or more lines of BCVA

Loss of 3 or more lines of BCVA occurred in less than 1% (1/173) of implanted eyes compared with 8% (13/174) of fellow control eyes (p=0.0013) in the non-randomised comparative study of 217 patients. No further details were given[2].

Vision loss of 2 or more lines

In the non-randomised comparative study of 217 patients with AMD comparing an implanted telescope lens system with fellow eye controls, the loss of 2 or more lines in BCDVA was significantly less in implanted eyes compared with fellow eyes (2% compared with 9%; p=0.005) at 1-year follow-up[1]. In the subgroup analysis for age stratification, 3 patients (9%) in each group (65–75 years, and over 75 years) had lost more than 2 lines of BCDVA at 60-month follow-up. Both groups had greater vision loss in the fellow eyes (65–75 years, 16% [n=5]; compared with 28% [n=9] in those over 75 years)[5].

Other ocular adverse events

Ocular adverse events were reported in the non-randomised comparative study of 217 patients up to 60 months after the procedure, including: iris prolapse in 6% (12/206) of patients, iris incarceration in 1% (3/206), iris damage in 4% (9/206), iris transillumination defects lasting more than 21 days in 5% (11/206), iritis lasting more than 30 days in 6% (12/206), iris atrophy more than 7 days after surgery in 6% (12/206), guttata in 8% (16/206) of patients and posterior synechiae in 7% (15/206) of patients were reported in the non-randomised comparative study of 217 patients at 2-year follow-up. No further details were reported[1].

Transient complications reported in a case series of 40 patients included corneal oedema in 25% (9/36) of patients, fibrin at the pupil in 33% (12/36), synechiae in 19% (7/36), hyphema in 11% (4/36), conjunctivitis in 6% (2/36), uveitis in 8% (3/36) and cyclitic membrane in 3% (1/36). Persistent complications included pupillary cyclitic membrane in 1 eye, synechias in 2 eyes and posterior capsular opacification in 4 eyes[4].

In addition, other complications reported include ocular pain due to mild corneal epithelial trauma (20% [2/10]) patients[6], corneal abrasion in 5% (11/206) of patients, foreign body sensation in 3% (7/206), anterior chamber inflammation lasting beyond 30 days in 2.4% (actual numbers not reported), device dislocation in 1% (3/206), sub-retinal haemorrhage in 2% (5/206), vitreous haemorrhage more than 7 days after surgery in 2% (4/206), vitreous in the anterior chamber more than 7 days after surgery in 4% (8/206) and vitreous loss in 4% (9/206)[1].

Endothelial cell density (ECD) loss

Endothelial cell density was reduced by 20% below baseline at 3-month follow-up and by 25% at 1 year, compared with fellow eye controls, in the non-randomised comparative study of 217 patients with AMD implanted with a telescope lens system. The mean cell loss from 1 year to 2 years was 2%. In the subgroup analysis for age, ECD loss was less in those aged between 65 and 75 years than in those over 75 years (35% compared with 40%) at 60-month follow-up. The decrease in ECD was correlated with post-surgical odema ($p<0.0001$), suggesting that endothelial damage occurred during surgery, rather than during the postoperative period. Chronic loss was 3% per year[1-3].

Validity and generalisability of the studies

- There are several different systems available and the safety and efficacy may differ between them.
- Visual acuity outcomes reported in the literature vary in nature, and direct comparisons of reported efficacy between studies are made more difficult by this factor.
- None of the studies included randomised controls. The non-randomised comparative study used fellow eyes as the control group, but patients were not masked as to which eye had been treated[1-3].
- Most of the studies are small with limited follow-up.
- Three studies included only patients older than 70 years[1-3,4.6]. The remaining 2 studies did not specify an age limit in the inclusion criteria[5, 7].

Existing assessments of this procedure

The Australia and New Zealand Horizon Scanning Network published a summary on implantable miniature telescopes for macular degeneration in August 2007[6]. The report concluded that the procedure gave patients a significant improvement in their vision as reported to the Food and Drug Administration (FDA). There were, however, serious safety concerns and lack of data for the patients who did not benefit from the device implantation. Further evidence is required to fully assess whether the implantable miniature telescope will be worthy of clinical use.

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

- Implantation of miniature lens systems for advanced age-related macular degeneration. NICE interventional procedure guidance 272 (2008). Available from: www.nice.org.uk/guidance/IPG272
- Epiretinal brachytherapy for wet age-related macular degeneration. NICE interventional procedure guidance 415 (2011). Available from: www.nice.org.uk/guidance/IPG415
- Macular translocation with 360° retinotomy for wet age-related macular degeneration. NICE interventional procedure guidance 340 (2010). Available from: www.nice.org.uk/guidance/IPG340
- Limited macular translocation for wet age-related macular degeneration. NICE interventional procedure guidance 339 (2010). Available from: www.nice.org.uk/guidance/IPG339
- Radiotherapy for age-related macular degeneration. NICE interventional procedure guidance 49 (2004). Available from: www.nice.org.uk/guidance/IPG49
- Transpupillary thermotherapy for age-related macular degeneration. NICE interventional procedure guidance 58 (2004). Available from: www.nice.org.uk/guidance/IPG58

Technology appraisals

- Aflibercept solution for injection for treating wet age-related macular degeneration. NICE technology appraisal guidance 294 (2013). Available from: www.nice.org.uk/guidance/TA294
- Ranibizumab and pegaptanib for age-related macular degeneration. NICE technology appraisal guidance 155 (2008). Available from: www.nice.org.uk/guidance/TA155
- Guidance on the use of photodynamic therapy for age-related macular degeneration. NICE technology appraisal guidance 68 (2003). Available from: www.nice.org.uk/guidance/TA68

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 is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. 2 Specialist Advisor Questionnaires for implantation of miniature lens systems for advanced age-related macular degeneration were submitted and can be found on the NICE website .

Patient commentators' opinions

NICE's Public Involvement Programme sent xxx questionnaires to xxx NHS trusts for distribution to patients who had the procedure (or their carers). NICE received xxx completed questionnaires.

Section to be inserted if there is no patient commentary

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Section to be inserted if patient commentators raised no new issues

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers.

Section to be inserted if patient commentators raised new issues

The patient commentators raised the following issues about the safety/efficacy of the procedure, which did not feature in the published evidence or the opinions of specialist advisers, and which the Committee considered to be particularly relevant:

- [insert additional efficacy and safety issues raised by patient commentators and highlighted by IPAC, add extra rows as necessary].
- [Last item in list].

Issues for consideration by IPAC

- The Implantable Minitaure Telescope is US FDA approved for monocular implantation in the capsular bag in patients with bilateral central scotomas associated with end stage age related macular degeneration, and visually significant cataract.
- NCT02227498: ARGUS II Retinal Prosthesis System Dry AMD Feasibility Study Protocol (Bionic eye treatment). Study type: Interventional, single group assignment; population: patients with severe age-related macular degeneration (AMD) n=5; primary outcomes: vision function, adverse events;, UK; study start date: October 2014, completion date March 2018; Location: Manchester Royal Eye Hospital (at Manchester Vision Regeneration (MVR) Laboratory at the National Institute for Health Research / Wellcome Trust Manchester Clinical Research Facility).

References

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2. Hudson HL, Stulting RD et al (2008). Implantable telescope for end-stage age-related macular degeneration: long-term visual acuity and safety outcomes. American Journal of Ophthalmology 146 (5) 664-673.
3. Boyer D, Freund KB et al (2015). Long-term (60-month) results for the implantable miniature telescope: efficacy and safety outcomes stratified by age in patients with end-stage age-related macular degeneration. Clinical Ophthalmology 9 1099-1107.
4. Alio JL, Mulet EM, Ruiz-Moreno JM et al. (2004) Intraocular telescopic lens evaluation in patients with age-related macular degeneration. Journal of Cataract and Refractive Surgery 30: 1177–89.
5. Orzalesi N, Pierrottet CO, Zenoni S et al. (2007) The IOL-Vip system. A double intraocular implant for visual rehabilitation of patients with macular disease. Ophthalmology 114: 860–5.
6. Amselem L, Diaz-Llopis M et al (2008). Clinical magnification and residual refraction after implantation of a double intraocular lens system in patients with macular degeneration. J Cataract Refract Surgery. 38:1571-1577.
7. Agarwal A, Lipshitz I, Jacob S et al. (2008) Mirror telescopic intraocular lens for age-related macular degeneration. Design and preliminary clinical results of the Lipshitz macular implant. Journal of Cataract and Refractive Surgery 34: 87–94.
8. Adelaide Health Technology Assessment on behalf of National Horizon Scanning Unit (HealthPACT and MSAC), ‘Implantable miniature telescope for macular degeneration. Horizon Scanning Technology Prioritising Summary’ [online]. Available from: www.horizonscanning.gov.au

Appendix A: Additional papers on implantation of miniature lens systems for advanced age-related macular degeneration

The following table outlines the studies that are considered potentially relevant to the IP 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
Bansal AS, Baker P et al (2011). An implantable visual prosthetic for end-stage macular degeneration. Expert Review of Ophthalmology.6 (2) (pp 141-145)	Implantable Miniature Telescope™ prosthesis	The visual prosthetic is implanted into the lens capsule after cataract extraction to improve vision by reducing the size of the patient's central scotoma in the implanted eye. Peripheral vision is maintained through the fellow eye. Results from a large multicentre clinical trial demonstrated that the visual prosthetic provided a >two-line improvement in visual acuity in over 90% of patients with an accompanying improvement in quality of life.	Review
Brown GC, Brown MM et al (2011). Comparative effectiveness and cost-effectiveness of the implantable miniature telescope. Ophthalmology 118 (9) 1834-1843.	Preference-based comparative effectiveness (human value gain) and the cost-utility (cost-effectiveness) of a telescope prosthesis (implantable miniature telescope) for AMD. Published, evidence-based data from the IMT002 Study Group clinical trial. Ophthalmic utilities were obtained from a validated cohort of >1000 patients with ocular diseases.	The mean, discounted QALY gain associated with use of the telescope prosthesis over 12 years was 0.7577. When the QALY loss of 0.0004 attributable to the adverse events was factored into the model, the final QALY gain was 0.7573. This resulted in a 12.5% quality of life gain for the average patient during the 12 years of the model. The average cost-utility versus no therapy for use of the telescope prosthesis was $14389/QALY. The incremental cost-utility referent to control fellow eyes was $14063/QALY, whereas the incremental cost-utility referent to fellow eyes that underwent intra-study cataract surgery was $11805/QALY	Paper assesses cost effectiveness of IMT for AMD.
Waisbren EC. and Brown MM (2009). Implantable telescope for end-stage age-related macular degeneration: Long-term visual acuity and safety outcomes - Commentary. Evidence-Based			commentary

Ophthalmology.10 (3) (pp 135-137).			
Farid, M (2013). Transscleral suturing of the implantable miniature telescope. Journal of Cataract & Refractive Surgery 39 (7) 979-983.		A technique is described for transscleral suturing of the implantable miniature telescope device for end-stage age-related macular degeneration. It provides stabilization and centration of the implantable miniature telescope device in the case of capsule rupture or severe zonular dialysis	Describes technique.
Garcia-Feijoo J, Duran-Poveda S, Cuina-Sardina R et al. (2001) Ultrasound biomicroscopy of an implantable miniaturized telescope. Archives of Ophthalmology 119: 1544–5.	n = 2	Both patients had subjective visual improvement. In one patient, one of the haptics was placed in the sulcus rather than the capsular bag and so the telescope was not optimally positioned. One of the most important preoperative factors should be the depth of the anterior chamber.	Larger studies are included.
Garfinkel RA, Berinstein DM, Frantz R (2006) Treatment of choroidal neovascularization through the implantable miniature telescope. American Journal of Ophthalmology 141: 766–7.	n = 1	At 6-month follow-up, the patient had retinal haemorrhage with an area of subretinal fluid temporal to the macular atrophy. The patient underwent focal laser photocoagulation through the telescope without complication.	Case report. Safety event reported in table 2.
Joondeph BC (2014). Antivascular endothelial growth factor injection technique for recurrent exudative macular degeneration in a telescope-implanted eye. Retinal cases & brief reports 1-3.	n=1 Case report Management of a patient with neovascular age-related macular degeneration and an implantable miniature telescope.	The patient developed recurrent choroidal neovascularisation after telescope implantation and was successfully managed with a series of antivascular endothelial growth factor injections and serial ocular coherence tomography imaging and taking into consideration the unique geometric dimensions of the telescope.	Larger studies included in table 2.
Kaskaloglu M, Uretmen O, Yagci A (2001) Medium-term results of implantable miniaturized telescopes in eyes with age-related macular degeneration. Journal of Cataract and Refractive Surgery 27: 1751–5.	Case series n=3 patients with bilateral dry-type AMD and grade 1 nuclear sclerosis. Intraocular miniaturised telescope with magnification of 3.0x implanted. Follow-up-18 months.	Visual acuity improved in all 3 at 18 months follow-up. Patients complained about the narrow field of view. Case 1 developed mild anterior segment inflammation 2 and 6 months postoperatively that resolved with topical steroids and cycloplegics.	Larger studies included in table 2.
Lane SS, Kuppermann BD et al (2004). A prospective multicenter trial to evaluate the safety and effectiveness			Larger studies included in table 2.

of the implantable miniature telescope. Am J Opthalmol 137:993-1001.			
Morrow T (2010). Telescope placed in eye improves central vision. Managed Care 19 (12) 47-48.			General review on IMT.
Primo SA (2010). Implantable miniature telescope: lessons learned. [Review] [9 refs]. Optometry (St Louis, (2) 86-93.	Implantable Miniature Telescope (IMT) retrospective review of 2 patients to determine patients level of functional success and satisfaction.	Four years after implantation, 1 patient continued to use the telescope prosthesis eye for all visual activities; the other patient did not perceive any benefit from the device and continued to primarily use the fellow nonimplanted eye. The benefit of the telescopic prosthesis was most likely accounted for by the level of visual acuity in both eyes postimplantation and eye dominance. Optometrists can aid the multidisciplinary team by preoperatively determining which eye, if implanted, offers the optimal potential functional benefit for appropriate candidates.	Review
Singer MA, Amir N et al (2012). Improving quality of life in patients with end-stage age-related macular degeneration: focus miniature ocular implants. Clinical Ophthalmology 6 33-39.	Four new devices the Implantable Miniature Telescope (IMT, VisionCare Ophthalmic Technologies), Intraocular Lens for Visually Impaired People (IOL-VIP, IOL-VIP System), and Lipschitz Mirror Implant (LMI, Optolight Vision Technology) are implanted into the anterior segment while the Argus II (Second Sight Medical Products) is implanted into the posterior segment.	The IMT is the only device that has been shown to increase the patient quality of life (measured by VFQ score) by seven points at 6 months compared to baseline. It is the only FDA-approved device in the US while the Argus has been approved in Europe. Each of these prosthetics has potential benefits for patients.	Review
Singer MA, del Cid MR et al (2010). Pars plana posterior capsulotomy in a patient with a telescope prosthesis for age-related macular degeneration. Archives of Ophthalmology 128 (8) 1065-1067.	Case report n=1 A pars plana capsulotomy using a 25-gauge vitrector was performed to remove posterior capsule opacification a patient with a telescope prosthesis for end-stage AMD.	The development of visually significant PCO in patients with a telescope prosthesis is a rare occurrence that poses a unique treatment dilemma. Given the risks of damaging the device with Nd:YAG laser, a method for pars plana capsulotomy using a 25-gauge vitrectomy instrument was determined and successfully performed to remove PCO in a telescope-implanted eye.	Safety event already reported in table 2.
Tabernero J, Qureshi MA et al (2015). An			Design and development

aspheric intraocular telescope for age-related macular degeneration patients. Biomedical Optics Express 6 (3) 1010-1020.			of an intraocular telescope for AMD.

Appendix B: Related NICE guidance for implantation of miniature lens systems for advanced age-related macular degeneration

Guidance	Recommendations
Interventional procedures	**Implantation of miniature lens systems for advanced age-related macular degeneration. NICE interventional procedure guidance 272 (2008)** 1.1 Evidence on the efficacy of implantation of miniature lens systems for advanced age-related macular degeneration (AMD) shows that the procedure can improve both vision and quality of life in the short term. Short-term safety data are available for limited numbers of patients. There is currently insufficient long-term evidence on both efficacy and safety. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to undertake implantation of miniature lens systems for advanced AMD should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the need to adapt to having a lens system implanted into one eye, the risk of early complications and the uncertainties about long-term efficacy and safety. They should provide clear information. In addition, the use of the Institute's information for patients ('Understanding NICE guidance') is recommended. • Audit and review clinical outcomes of all patients having implantation of miniature lens systems for advanced AMD (see section 3.1). 1.3 Patient selection is crucial and should include detailed assessment to predict the patient's ability to process visual stimuli following the operation. 1.4 Further publication of safety and efficacy outcomes would be useful, specifically with regard to longer term follow-up. The Institute may review the procedure upon publication of further evidence. **Epiretinal brachytherapy for wet age-related macular degeneration. NICE interventional procedure guidance 415 (2011)** 1.1 Current evidence on the efficacy of epiretinal brachytherapy for wet age-related macular degeneration (AMD) is inadequate and limited to small numbers of patients. With regard to safety, vitrectomy has well-recognised complications and there is a possibility of subsequent radiation retinopathy. Therefore this procedure should only be used in the context of research. Research studies should address whether epiretinal brachytherapy reduces the progression of wet AMD and whether it can reduce the number of injections of antivascular endothelial growth factor agents (anti-VEGF) required. Long-term outcomes should be reported.

	Macular translocation with 360° retinotomy for wet age-related macular degeneration. NICE interventional procedure guidance 340 (2010) 1.1 Current evidence on macular translocation with 360° retinotomy for wet age-related macular degeneration (AMD) shows that this procedure is efficacious in only a proportion of patients and that there is a potential for serious adverse events. Therefore the procedure should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to undertake macular translocation with 360° retinotomy for wet AMD should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients and their carers understand the uncertainty about the procedure's safety and efficacy and provide them with clear information about both this procedure and alternative treatments (see section 2.5.1). In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended. • Audit and review clinical outcomes of all patients having macular translocation with 360° retinotomy for wet AMD (see section 3.1). **Limited macular translocation for wet age-related macular degeneration. NICE interventional procedure guidance 339 (2010)** 1.1 Current evidence on limited macular translocation for wet age-related macular degeneration (AMD) shows that this procedure is efficacious in only a proportion of patients and that there is a potential for serious adverse events. Therefore the procedure should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to undertake limited macular translocation for wet AMD should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients and their carers understand the uncertainty about the procedure's safety and efficacy and provide them with clear information about both this procedure and alternative treatments (see section 2.5.1). In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended. • Audit and review clinical outcomes of all patients having limited macular translocation for wet AMD (see section 3.1). **Radiotherapy for age-related macular degeneration. NICE interventional procedure guidance 49 (2004)** 1.1 Current evidence shows radiotherapy for age-related macular degeneration to have little efficacy. There are also concerns about its safety. It is suitable for use only within good quality research studies approved by a research ethics committee, specifying the dose of radiation used and with explicit patient consent. Publication of safety and efficacy outcomes will be useful in reducing the current uncertainty. The Institute is not undertaking further investigation at present.

	Transpupillary thermotherapy for age-related macular degeneration. NICE interventional procedure guidance 58 (2004) 1.1 Current evidence on the safety and efficacy of transpupillary thermotherapy for age-related macular degeneration does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research. 1.2 Clinicians wishing to undertake transpupillary thermotherapy for age-related macular degeneration should take the following action. • Inform the clinical governance leads in their Trusts. • 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. • Audit and review clinical outcomes of all patients having transpupillary thermotherapy for age-related macular degeneration. 1.3 Publication of safety and efficacy outcomes will be useful in reducing the current uncertainty. The Institute may review the procedure upon publication of further evidence.

Technology appraisals	**Guidance on the use of photodynamic therapy for age-related macular degeneration. NICE technology appraisal guidance 68 (2003)** 1.1 Photodynamic therapy (PDT) is recommended for the treatment of wet age-related macular degeneration for individuals who have a confirmed diagnosis of **classic with no occult** subfoveal choroidal neovascularisation (CNV) (that is, whose lesions are composed of classic CNV with no evidence of an occult component) and best-corrected visual acuity 6/60 or better. PDT should be carried out only by retinal specialists with expertise in the use of this technology. 1.2 PDT is not recommended for the treatment of people with **predominantly classic** subfoveal CNV (that is, 50% or more of the entire area of the lesion is classic CNV but some occult CNV is present) associated with wet age-related macular degeneration, except as part of ongoing or new clinical studies that are designed to generate robust and relevant outcome data, including data on optimum treatment regimens, long-term outcomes, quality of life and costs. 1.3 The use of PDT in **occult** CNV associated with wet age-related macular degeneration was not considered because the photosensitising agent (verteporfin) was not licensed for this indication when this appraisal began. No recommendation is made with regard to the use of this technology in people with this form of the condition. 1.4 Patients currently receiving treatment with PDT could experience loss of well-being if their treatment is discontinued at a time they did not anticipate. Because of this, all NHS patients who have begun a course of treatment with PDT at the date of publication of this guidance should have the option of continuing to receive treatment until their clinical condition indicates that it is appropriate to stop. **Ranibizumab and pegaptanib for age-related macular degeneration. NICE technology appraisal guidance 155 (2008)** 1.1Ranibizumab, within its marketing authorisation, is recommended as an option for the treatment of wet age-related macular degeneration if: • all of the following circumstances apply in the eye to be treated: o the best-corrected visual acuity is between 6/12 and 6/96 o there is no permanent structural damage to the central fovea o the lesion size is less than or equal to 12 disc areas in greatest linear dimension o there is evidence of recent presumed disease progression (blood vessel growth, as indicated by fluorescein angiography, or recent visual acuity changes) and • the manufacturer provides ranibizumab with the discount agreed in the patient access scheme (as revised in 2012). 1.2 It is recommended that treatment with ranibizumab should be continued only in people who maintain adequate response to therapy. Criteria for discontinuation should include persistent deterioration in visual acuity and identification of anatomical changes in the retina that

	indicate inadequate response to therapy. It is recommended that a national protocol specifying criteria for discontinuation is developed. 1.3 Pegaptanib is not recommended for the treatment of wet age-related macular degeneration. 1.4 People who are currently receiving pegaptanib for any lesion type should have the option to continue therapy until they and their clinicians consider it appropriate to stop. **Aflibercept solution for injection for treating wet age related macular degeneration. NICE technology appraisal guidance 294 (2013)** 1.1 Aflibercept solution for injection is recommended as an option for treating wet age-related macular degeneration only if: • it is used in accordance with the recommendations for ranibizumab in NICE technology appraisal guidance 155 (re-issued in May 2012) and • the manufacturer provides aflibercept solution for injection with the discount agreed in the patient access scheme. 1.2 People currently receiving aflibercept solution for injection whose disease does not meet the criteria in 1.1 should be able to continue treatment until they and their clinician consider it appropriate to stop.

Appendix C: Literature search for implantation of miniature lens systems for advanced age-related macular degeneration

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	28/01/2016	Issue 1 of 12, January 2016
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	28/01/2016	Issue 12 of 12, December 2015
HTA database (Cochrane Library)	28/01/2016	Issue 4 of 4, October 2015
MEDLINE (Ovid)	28/01/2016	1946 to January Week 3 2016
MEDLINE In-Process (Ovid)	28/01/2016	January 27, 2016
EMBASE (Ovid)	28/01/2016	1974 to 2016 Week 04
PubMed	28/01/2016	n/a
JournalTOCS	28/01/2016	n/a

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

1	Macular Degeneration/
2	Wet Macular Degeneration/
3	((macul* or retin*) adj4 (degener* or disease*)).tw.
4	(age adj4 relat* adj4 macul*).tw.
5	(dystroph* adj4 macul*).tw.
6	maculopath*.tw.
7	(ARMD or AMD).tw.
8	or/1-7
9	(implant* adj4 telescop*).tw.
10	((prosthe* or precision) adj4 telescop*).tw.
11	((optical or visual or telescop*) adj4 prosthe* adj4 device*).tw.
12	(miniatur* adj4 telescop*).tw.
13	(miniatur* adj4 ocular adj4 (implant* or system*)).tw.

14 (intraocular adj4 (magnif* or len*) adj4 (implant* or system)).tw.

15 (IOL-VIP or "IOL VIP").tw.

16 (galilean adj4 telescop*).tw.

17 IMT.tw.

18 Lens Implantation, Intraocular/

19 Miniaturization/

20 ((Lipshitz or Lipschitz) adj4 (mirror* or macular*) adj4 (implant* or system*)).tw.

21 LMI.tw.

22 or/9-21

23 8 and 22

24 animals/ not humans/

25 23 not 24

26 limit 25 to ed=20080130-20160131