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Research Article

Intraocular Lenses in the Treatment of Macular Diseases Affecting the Fovea

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Abstract

Introduction: Age related macular degeneration is the leading cause of legal blindness in the developed world. Currently no treatments exist for the majority of patients that suffer from this disease with injections only available to slow the advanced form of the disease. Patients can be offered various external devices above and beyond corrective glasses, however these are cumbersome and often compliance is very low. Age related macular degeneration is just one of many diseases that affect the macula and the fovea, all these diseases often share the fact that the central visual field is severely diminished. Implantable telescopic devices have been designed hat can be placed within the eye itself with the function of magnifying images on the retina and deflecting the image produced away for the diseased macula and fovea.

Methodology: PUBMED searches were used to discover all of the published trials using these intraocular telescopic devices. OF the many terms searched and found it was discovered that there were 4 separate trials using different designed lenses and different treatment protocols. These 4 were compared and contrasted.

Results: All 4 trials showed improvement in patients' post-operative visual acuity when compared to before. Complications of either the procedure or the follow up of the patient were not reported in 3 of the trials, and in the remaining trial severe complications were extremely rare. 3 trials did report significant loss of peripheral vision after implantation. Certain trials placed more emphasis than others on pre implantation software analysis and post implant rehabilitation and it is likely that these components play as large a factor in the success of the treatments as the design of the intraocular telescopic device itself. The best results did appear to come when there had been the most extensive post-operative rehabilitation however due to the intensive nature of the program patient compliance and satisfaction with the scheme was low.

Conclusion: The post-operative visual acuity was improved in all patient groups up to a year after operation. The downside is that the degree of peripheral visual field loss and time consuming rehabilitation mean that patient satisfaction is not yet optimal. However given the elderly nature of these patients and their difficulty in preforming simple activities of daily living these significant improvements in visual acuity are extremely helpful with watching television or reading and thus improving quality of life.

Keywords: *Intra Ocular Lens (IOL); Macular Degeneration; Implantable Miniature Telescope (IMT); IOL-VIP; iolAMD; Intraocular Telescopic Device; Lipschitz Macular Implant (LMI)*

Abbreviations

ADL: Activities of Daily Living; AMD: Age-Related Macular Degeneration; BCVA: Best Corrected Visual Acuity; CDVA: Corrected Distance Visual Acuity; CNVA: Correct Near Visual Acuity; ETDRS: Early Treatment Diabetic Retinopathy Study; FE: Fellow Eye; IMT: Implantable Miniature Telescope; IOL: Intraocular Lens; LOGMAR: Logarithmic Minimum Angle of Resolution; LMI: Lipshitz Macular Implant; OCT: Ocular Coherence Tomography; OE: Operated Eye; PRL: Preferred Retinal Locus; SD: Standard Differentiation; VEGF: Vascular Endothelial Growth Factor

Introduction

Macular disease

There are various congenital or acquired conditions which lead to disease of the macula. This specific area of the retina is critical for central vision and depth perception and the human visual system is extremely dependent on the preservation of the fovea and the structures around it for maintaining sight. Diseases of the macula such as Age-related macular degeneration (AMD) are the most prominent in the developed world. AMD can be divided into two groups: the first with drusen formation between the Bruch's membrane and the retinal pigment epithelium (dry AMD), and the second with the presence of neovascularisation in addition to the drusen deposition (wet AMD). AMD is the leading cause of legal blindness in the developed world in older people and the incidence is rising in those above the age of 55 [1]. For the management of patients with dry AMD no medical treatment currently exists, with exception of the late stage geographical atrophy that is currently being evaluated for slowing down disease progression [2]. There are anti-VEGF therapies for when there is neovascularisation (aflibercept and ranibizumab among others). These therapies purely prevent the complications of bleeding and central scotoma establishment and vision stability associated with the disease process but don't assist with the progressive visual problems common to both types of AMD or macular disease.

Another prevalent disease of the macula and fovea is diabetic macular oedema. This is a disease which falls upon the more severe end of the spectrum of diabetic retinopathy and occurs when fluid leaking from damaged capillary beds resulting in ischaemia and in the severe state results in dysfunction within the macula. This causes a severe deterioration in central vision from vascular exudation and ischaemia at the fovea consequent progression capillary non-perfusion. Diabetic Macular oedema can be treated with anti-VEGF therapy and steroid implantation and treatments for this condition can include the use of laser photocoagulation and are only effective for slowing and stability of disease progression. A disease which can also present with a similar picture is retinal vein occlusion. The extent of visual loss following such an event is varied, however it is well documented that worse visual acuity immediately following the acute event is associated with progression to retinal ischemia [3] and significantly worse disease. This retinal ischemia often extends to the macula and fovea and is very often irreversible although depending on the site of the initial event there may still remain areas of healthy retina elsewhere.

There are several other inherited diseases such as Stargardts's disease and Best's syndrome or acquired diseases such as macular hole and drug induced maculopathies that share the features of localized macular and foveal dysfunction of the aforementioned diseases.

These diseases all leave patients with a significantly reduced central visual field with such foveal dysfunction that simple activities of daily living such as reading and watching television become difficult. Patients that present for therapy at a very late stage of the disease must rely upon their ability to adapt to their loss of visual field and devices such as low vision aids, namely hand held magnifiers, external telescopes and headset closed circuit television that can assist people with their vision and activities of daily living [4]. The low vision aids are often not well tolerated due to the clumsy and obstructive nature of telescopes and headsets which leads to them often being discontinued by patients, or the nature of aging conditions such as arthritis limits the ability of patients to use devices comfortably. As a result of this inability to manage steadily deteriorating visual function, macular disease is among the leading causes of anxiety, depression and trauma in the older population [5].

With all these diseases it stands to reason that if the light rays that fall on the unhealthy macula could be diverted and an image magnified to land on a healthy part of retina then a patient could perceive better vision from a para-central visual field and ideally with the support of less cumbersome external ocular devices. As a result of this various intraocular lens systems have been developed to aid help patients better adapt to the loss of these valuable areas of retina.

Telescopic devices

When external telescopes were first used in this disease they were designed according to the Galilean model or astronomical model for telescopes (Figures 1 and 2). The astronomical telescope uses a plus lens (as the ocular lens) and an objective lens separated by the sum of their focal lengths. This produces parallel rays that form an in-focus magnification on the retina, but this is inverted and therefore

a prism is required to correct this (Figure 1). The Galilean model accounts for this by using a minus lens as the ocular lens and the distance between the ocular and objective lenses is set as the difference between the absolute value of their focal lengths; this produces an upright and in focus image (Figure 2). Both these images are formed at a point on the away from the fovea, this ensures that the image will be recorded from an area of the retina less likely to be damaged by macular disease.

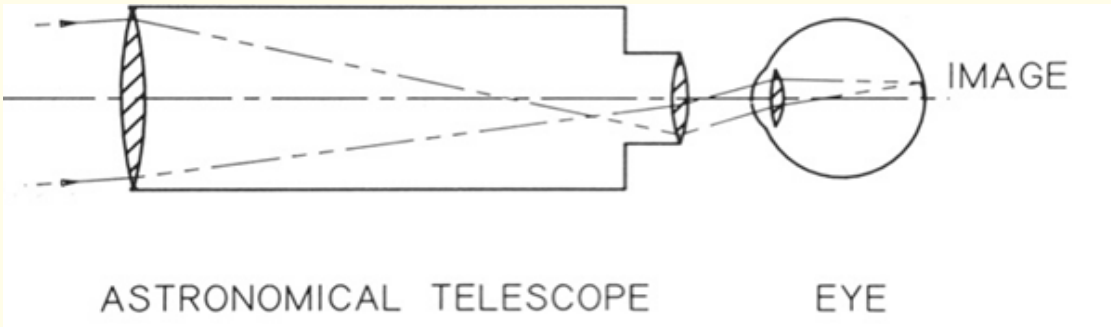

Figure 1: *Schematic representation of light rays passing through an astronomical telescope and the formation of an image on the retina [16].*

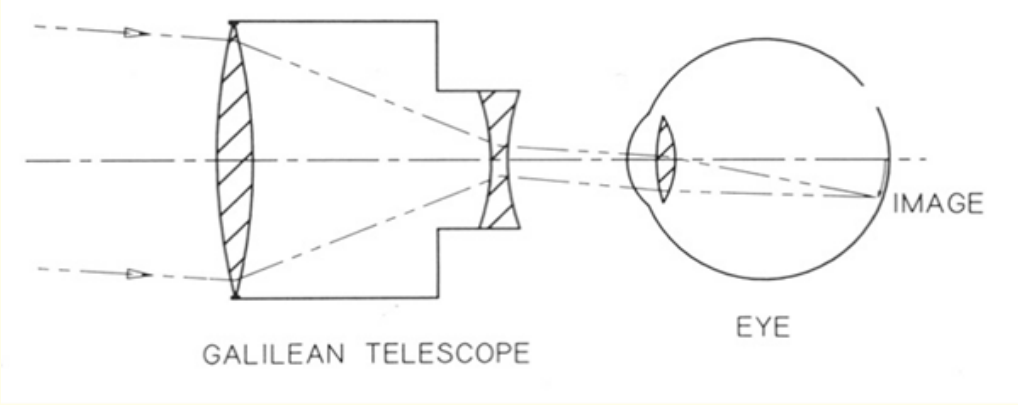

Figure 2: *Schematic representation of light rays passing through a Galilean telescope and the formation of an image on the retina [16].*

Since then there has been extensive research in to this area which has led to the design of more sophisticated models as well as safer operating techniques. One of these is IOL-Vip system [6] which consists of two intraocular lenses (IOL) arranged as a high minus power bi-concave IOL in the capsular bag and a high plus power biconvex IOL in the anterior chamber. This recreates the Galilean arrangement and gives a magnification of 1.3x and an upright image. The lenses are inserted during lens extraction surgery which are often well tolerated.

Another device similar to this is the iolAMD, which also uses a Galilean design. Like the IOL-VIP it has a high-minus lens in the anterior chamber but the difference is that high plus lens is placed in the ciliary sulcus. This arrangement allows free rotation of the anterior IOL relative to the posterior IOL, which means that the path of light can be adjusted, if necessary, through rotation or replacement of the anterior IOL. This allows for modification in the event of worsening progression of the disease [7].

The implantable miniature telescope (IMT) (IMT; VisionCare Ophthalmic Technologies, Saratoga, CA) is an injectable, fixed focus optical device. It is designed as a compound micro-optical system comprised of anteriorly and posteriorly positioned wide-angle micro-optics

housed in a quartz cylinder [8]. This design allows for a 20 - 24° forward field to be projected onto 55° of the retina, which significantly reduces the peripheral visual field [9]. This means that the IMT can only be implanted into one eye and the other has to be used for peripheral vision.

In 1997 Lipshitz [10] designed the implantable Miniature telescope (IMT) with the aim of creating a lens which produced a magnified image upon the retina. The IMT is the most widely researched and used of the lenses we have looked at in this review however due to its design it could only ever be implanted into one eye since it would so severely disrupt the patient's peripheral visual field that the other eye would need to remain unoperated to perceive the peripheral field. In 2008 Lipschitz created another model known as the Lipschitz Macular Implant (LMI) (Optolight visual technology). The LMI uses 2 IOLs in a Cassegrain telescopic formation. The system magnifies light that comes through the centre of the optic 2.5x but also allows peripheral light through and maintains peripheral vision. Hence the patient will have a magnified central field but still be oriented due to preservation of peripheral vision (Figure 3). In this regard the LMI is superior to its predecessor [11]. The rehabilitation and training required for patients with the LMI is shorter than for those with the IMT and BCVA was improved to a greater degree in them as well.

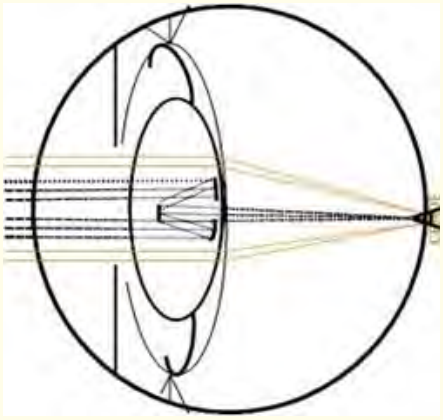

Figure 3: *LMI showing magnification of central image with preservation of peripheral vision [11].*

Most of the modern IOL trials require extensive patient pre-assessment with software use to best assess degree of visual function and postoperative prognosis as well as targeted rehabilitation strategies.

Although all the trials that are currently active only look at the uses of these implantable devices in AMD there is the belief that this technology could one day be used in many different macular pathologies such as diabetic maculopathy, Stargardt disease, macular hole, solar retinitis, Usher syndrome and toxoplasmosis as well as any other macular pathology resulting in end stage atrophy around and involving the fovea. Our aim was review the current literature currently available on the use of these intraocular lenses for macular disease and observe their outcomes and complications.

Methodology

We used PUBMED searches in order to find the literature. In our initial search we used the headings <intraocular lens AND telescopic AND macular degeneration>; this yielded 9 articles of which 3 were concerning the IMT, 2 concerned the iol-AMD and 1 was about the LMI. The remaining 3 articles were not relevant to this review. Of the 2 articles which discussed the iol-AMD, both used the same data set and so this was what we used in or results section later. The article referencing the LMI was also the only one we could find on this lens and so it was used for our results [11]. However once we entered the search specifically <implantable miniature telescope> we found another 17 papers linked to the IMT, and while they all largely contained similar data, the most in depth and long term study was written by Boyer and

was subsequently the one we used for our assessment of the IMT [9]. We tried broader searches to look for IOL use for macular disease and were unsuccessful till we tried <intraocular implant AND macular disease> which led us to 48 search results of which one was the IOL-VIP study which was the only paper we could find that assessed the use of these devices in patients with diseases other than AMD [6] and so we used this data set for our analysis. On searching specifically for <IOL-VIP> we found no further papers.

To conduct our analysis we inserted the tables showing pre and post-operative parameters of vision from the 4 studies listed above and then we compared and contrasted the improvements and complications between the devices using what similar parameters they did use and converting some units of measurements to make them more comparable.

Results

IMT

The largest trial on IOLs looked at the results from the IMT in 217 patients over the course of 5 years. The trial looked at the improvement in best corrected visual acuity in implanted eyes and at significant complications.

Table 1 compares the improvement in best corrected visual acuity (BCVA) between 2 separate age groups using lines on an Early Treatment Diabetic Retinopathy Study chart (EDTRS) as a marker for visual acuity. It shows that the in the 65 - 75 age group the improvement was more marked at all times during the 60 month follow up and the most significant retention of vision was also in this group. A BCVA increase of three lines was seen in both ages' groups at 24 months. The study also showed that the best gain in visual acuity was in the first 12 months however in both age groups the number of patients that showed the significant improvement of 2 or 3 lines decreased at every year over the 5 years. This may suggest that the IOL implant would fail as time progressed or it was suggesting that the disease was advancing and the initial gains reported were being lost. It also does appear that significant numbers were lost to follow up over the 5 years, the implications of this on the data trend is difficult to assess.

	12 months	24 months	36 months	48 months	60 months
Age 65 to < 75 years (group 1)					
n	65	60	22	38	31
Gain ≥ 3 lines	43 (66.2%)	37 (61.7%)	11 (50.0%)	22 (57.9%)	18 (58.1%)
Gain ≥ 2 lines	52 (80.0%)	45 (75.0%)	15 (68.2%)	26 (68.4%)	21 (67.7%)
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
Age ≥ 75 years (group 2)					
n	109	95	42	46	32
Gain ≥ 3 lines	72 (66.1%)	55 (57.9%)	24 (57.1%)	19 (41.3%)	12 (37.5%)
Gain ≥ 2 lines	87 (79.8%)	71 (74.7%)	31 (73.8%)	29 (63.0%)	19 (59.4%)
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

Table 1: *Best-corrected distance visual acuity in patients implanted with the IMT, stratified by age group [9]. The table shows as time progresses the initial post-operative improvement in visual acuity declines, also large numbers of patients appear lost to follow.*

Ocular complications were defined as events directly related to the procedure occurring in the operative phase or the immediate post-operative phase, defined as 3 months after the operation; the details of which can be seen in table 2 [9]. There were more ocular complications in the older age group with only iris prolapse and iris damage occurring at a higher percentage in group 1 [9].

Anything occurring after this period of time was referred to as an adverse event and details of these can be seen in table 3 [9]. In the younger age group there were a total of 17 adverse events, but no reports of endophthalmitis, retinal detachment or retinal tear. The >75 group reported noticeably more adverse effects [9].

Significant ocular complications	Age 65 to < 75 years (group 1; n = 70)		Age ≥ 75 years (group 2; n = 127)	
	n	%	n	%
Aborted surgery	0	0.0	5	3.9
Choroidal detachment	0	0.0	2	1.6
Choroidal hemorrhage	0	0.0	1	0.8
Corneal edema ≤30 days after surgery	3	4.3	10	7.9
Iris atrophy ≤7 days after surgery	1	1.4	3	2.4
Iris damage	4	5.7	5	3.9
Iris incarceration	1	1.4	2	1.6
Iris prolapse	6	8.6	6	4.7
Iris transillumination defects ≤21 days after surgery	0	0.0	7	5.5
Phthisis	0	0.0	1	0.8
Posterior capsular rupture	1	1.4	6	4.7
Vitreous hemorrhage ≤7 days after surgery	0	0.0	1	0.8
Vitreous in anterior chamber ≤7 days after surgery	0	0.0	3	2.4
Vitreous loss	0	0.0	3	2.4
Vitreous loss – vitrectomy required	1	1.4	5	3.9

Table 2: *Significant ocular complications in patients implanted with the IMT [9].*

Significant adverse events	Age 65 to < 75 years (group 1; n = 70)		Age ≥ 75 years (group 2; n = 127)	
	n	%	n	%
Choroidal neovascularization	0	0.0	4	3.1
Corneal edema >30 days after surgery	4	5.7	9	7.1
Corneal transplant (subset of persistent vision-impairing corneal edema)	2	2.9	2	1.6
Decrease >2 lines BCDVA in telescope-implanted eye	4	5.7	10	7.9
Device failure	0	0.0	2	1.6
Endophthalmitis	0	0.0	0	0.0
Iris atrophy >7 days after surgery	2	2.9	6	4.7
Iritis >30 days after surgery	7	10.0	5	3.9
Persistent unresolved corneal edema (subset of corneal edema >30 days after surgery)	3	4.3	6	4.7
Persistent vision-impairing corneal edema (subset of persistent unresolved corneal edema)	3	4.3	4	3.1
Retinal detachment	0	0.0	0	0.0
Retinal tear	0	0.0	0	0.0
Subretinal hemorrhage	0	0.0	5	3.9
Telescope dislocation	0	0.0	3	2.4
Telescope removal	1	1.4	10	7.9
Vitreous hemorrhage >7 days after surgery	1	1.4	2	1.6
Vitreous in anterior chamber >7 days after surgery	1	1.4	4	3.1

Table 3: *Significant adverse events in patients implanted with the IMT [9].*

BCDVA: Best Corrected Distance Visual Acuity.

iolAMD

With the regards to the iolAMD there has been no stratification based on age or gender in any of the published data. Also very few complications have been reported, 1 patient had an error in the placement of the IOLs but this was corrected in a subsequent surgery. A precautionary intraoperative peripheral iridectomy was performed in 9 eyes [7]. The lack of any significant adverse effects is likely linked to the small sample size.

Preoperative simulation was carried out using a handheld extraocular magnifier with a built-in prism (IOL-VIP system, Soleko SPA). The corrected distance visual acuity (CDVA) was recorded with the simulator in place and the results were cross-checked against the location of the preferred retinal locus (PRL) as determined by microperimetry testing [7]. Microperimetry will be further explored in the 'future designs' segment of this review. This is how implantation location and lens selection were better tailored to each individual patient.

The surgical technique used was complicated and has been extensively described by Qureshi., *et al* [7].

The mean CDVA increased 67% overall from baseline at the final postoperative review, and the mean corrected near visual acuity (CNVA) improved more than 50%. The increase in mean CDVA exceeded the increase predicted by preoperative simulation and the level of acuity expected with a theoretical ×1.25 to ×1.3 magnification [7]. The full trial data from all 18 eyes can be seen in table 4.

Eye	**Spherical Equivalent (D)**		**Cylinder (D)**		**Corrected Distance Visual Acuity**				
			Near (Decimalized Snellen Equivalent)		**Distance (Decimalized Snellen)**				
	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Simulated	**Postop**
1	−2.25	−4.50	−0.50	0.00	< 0.080	0.125	0.040	0.060	0.060
2	1.00	−3.50	−1.00	−1.00	0.125	0.220	0.100	0.125	0.125
3	1.15	−3.00	−0.75	−2.00	0.125	0.250	0.125	0.160	0.250
4	−2.00	−3.00	0.00	0.00	< 0.080	0.180	0.040	0.050	0.063
5	−4.25	−6.00	−1.50	−2.00	< 0.080	0.080	0.100	0.200	0.080
6	1.00	0.00	0.00	−1.75	< 0.080	0.220	0.100	0.200	0.320
7	−1.00	1.50	−2.00	−2.25	0.250	0.180	0.200	0.200	0.400
8	0.00	−3.00	0.00	0.00	< 0.080	< 0.080	0.050	0.050	0.010
9	0.75	3.00	−1.25	−2.00	0.090	0.125	0.060	0.080	0.100
10	0.00	0.00	−0.25	−2.00	< 0.080	0.090	0.080	0.130	0.130
11	−0.75	1.00	−1.25	−1.75	0.250	0.250	0.160	0.320	0.250
12	0.40	0.00	−0.75	0.00	< 0.080	0.180	0.010	0.063	0.100
13	0.75	1.00	−0.50	0.00	0.125	0.180	0.063	0.080	0.160
14	0.25	−3.25	−0.50	−1.25	0.180	0.400	0.250	0.500	0.400
15	7.50	1.50	−1.00	−1.25	0.220	0.500	0.250	0.400	0.320
16	0.00	−2.50	−1.00	−2.00	0.125	0.180	0.125	0.125	0.160
17	−0.50	−4.00	0.00	−1.00	0.330	0.330	0.250	0.400	0.400
18	−3.85	−3.75	−0.75	−1.50	< 0.080	0.180	0.200	0.250	0.320
All (mean)	−0.10	−1.58	−0.72	−1.21	< 0.140	0.210	0.120	0.190	0.200

Table 4: *Preoperative and postoperative parameters in patients implanted with the Iol-AMD [7]. The table shows the spherical equivalent and cylinder as well as near and distance visual acuity post operatively as compared to before. The table shows worsening of sphere and cylinder post operatively but significant improvement in visual acuity on average.*

IOL-VIP

Patients selected for the IOL-VIP trial were also assessed using the same IOL-VIP software as mentioned above which was designed by the authors of this trial. The software can be downloaded online and details of it can be found in the paper [6]. The software also recorded the ADLs that the patients would aim to recover to assess whether the IOL-Vip procedure will meet their needs, hence reducing the development of unrealistic expectations [6]. The aim of this was also to find the PRL. What was also added to this trial was that all patients underwent 2-week preoperative training (12 30-minute training sessions) and a 3-month postoperative rehabilitation program (5 30-minute training sessions per week for 12 weeks) aimed at training and consolidating the PRL [6]. This was the most prescriptive post implantation rehabilitation and although necessary to help improve the efficacy of the intervention the intensive and long nature of this therapy was very difficult for patients considering their advanced age [6].

Trials looking at the IOL-VIP system did state whether the eyes that were being followed belonged to a male or female patient and their age although there was no direct comparison between these subgroups within the trial. The trial however did specifically show whether the affected eyes suffered from AMD or other diseases, such as Stargardt's disease, so comparisons could be made on those accounts, albeit minimally. The study looked at 40 eyes of 35 patients.

No complications of surgery or follow up have been reported to date [6].

Follow up of patients with this procedure and IOL design has shown improvement in postoperative best corrected visual acuity (BCVA), mean reading distance and reading magnification. However the downside remains a degree of peripheral visual loss.

Table 5 shows the postoperative improvements in pre-operative and postoperative BCVA [6].

Eye	Age	Gender	Diagnosis	Preoperative BCVA (logMAR)	Postoperative BCVA (logMAR)
1	65	M	AMD	e	0.7
2	79	M	AMD	1.3	1
3	75	F	AMD	1.7	1
4	78	M	AMD	1.7	1
5	70	F	AMD	1	0.7
6	68	M	AMD	1.1	1
7	68	F	AMD	1.3	0.7
8	70	F	AMD	1.7	1
9	70	M	AMD	1.7	1
10	67	M	AMD	1.3	0.7
11	86	F	AMD	1.7	1
12	65	F	AMD	1.7	1
13	57	M	Stargardt disease	1.7	1
14	78	F	AMD	1.7	1
15	80	F	AMD	1.1	0.7
16	76	F	AMD	1.3	0.8
17	82	M	Macular hole	0.7	0.4
18	63	F	Angioid streaks	1.7	0.8
19	82	M	AMD	1.7	1.1

20	81	F	AMD	1.1	0.7
21	73	F	AMD	1	0.6
22	73	F	AMD	1.7	1
23	82	M	Myopia	1.1	0.4
24	74	F	AMD	1.7	1.1
25	59	F	Myopia	1.7	1.3
26	86	F	AMD	1.7	0.8
27	78	F	AMD	1.7	0.8
28	67	M	AMD	1.3	0.7
29	78	M	Myopia	0.7	0.4
30	69	M	Myopia	1	0.5
31	72	F	AMD	0.7	0.4
32	72	F	AMD	0.7	0.4
33	68	F	AMD	1.3	0.8
34	68	F	AMD	1	0.7
35	75	M	AMD	0.8	0.5
36	75	M	AMD	1	0.5
37	73	M	AMD	1.1	0.7
38	73	M	AMD	0.8	0.5
39	78	M	AMD	0.8	0.5
40	78	M	AMD	1.1	0.7

Table 5: *Demographics of the 35 Patients (40 Eyes) and Preoperative and Postoperative Best-Corrected Visual Acuity (BCVA) Measured by Means of Early Treatment Diabetic Retinopathy Study Charts, after 2 weeks' and 3 Months' Rehabilitation Programs, Respectively in patients implanted with the IOL-VIP [6].*

LMI

The Lipshitz macular implant is the newest of the IOL designs and as such has the smallest sample size with which to draw any conclusions. There was no stratification of age or gender. Follow up of these patients at 6 months showed there were no intraoperative complications as well as significant improvements in distance BCVA and near BCVA as well as normal fundus and IOL position on various imaging modalities [11] (Table 6).

Preoperative assessment of the patients involved a detailed examination including near and distance visual acuity with and without an external telescope, slitlamp examination, tonometry, pachymetry, specular microscopy, fundus examination, and fundus fluorescein angiography [11]. This did not include the microperimetry or the software use of some of the other trials.

Postoperative assessment involved follow-up visits at 1 day, 1 week, and 1 and 6 months. Slitlamp examination, noncontact tonometry, anterior segment optical coherence tomography (AS-OCT), specular microscopy, and fundus evaluation were performed at each visit. The near and distance BCVAs were also measured at all visits [11]. There was no recorded postoperative rehabilitation program.

	Distance Acuity (logMAR)								Near Acuity (ETDRS Score, LogMAR)							
	Pre-op		1 month Post-op		6 months Post-op		Lines Gained or Lost		Pre-op		1 month Post-op		6 months Post-op		**Change in score**	
Case	**OE**	**FE**	**OE**	**FE**	**OE**	**FE**	**OE**	**FE**	**OE**	**FE**	**OE**	**FE**	**OE**	**FE**	**OE**	**FE**
1	0.6	0.6	0.78	0.6	0.48	0.6	1.5	0.0	37	55	77	55	87	37	50	-18
2	2.0	0.6	0.8	0.6	1.0	0.78	6.0	-1.5	7	67	55	67	55	67	48	0
3	1.3	1.0	1.0	1.0	1.0	1.18	3.0	-1.5	7	37	67	37	72	37	65	0
4	1.45	0.78	1.0	1.0	1.0	1.18	2.5	-4.0	37	87	77	77	87	67	50	-20
5	1.45	1.3	1.18	1.3	1.18	1.45	3.0	-1.5	35	82	67	82	72	72	37	-10
6	2.0	2.0	1.0	2.0	1.0	2.0	6.0	0.0	22	55	67	55	77	52	55	0
Mean	1.47	1.05	0.96	1.08	0.94	1.2	3.66	-1.41	24.2	63.8	68.3	62.2	75	55.3	50.8	-8.00
SD	0.52	0.54	0.15	0.52	0.24	0.5	1.88	1.46	14.4	18.7	8.16	16.6	11.9	15.7	9.15	9.38

Table 6: *Changes in distance and near visual acuities in operated and fellow eyes of those patients implanted with the LMI. Patients were followed up at 1 month and 6 months postoperatively and shows improvement in lines gained and logMAR scale up to 6 months [11].*

Discussion

Summary of the trials

Directly comparing each of the trials is challenging since each study used different parameters to monitor success, followed up patients for differing lengths of time and used different measuring tools in their experiments (e.g. LogMAR vs snellen vs lines gained). Also some of the studies assessed changes in near BCVA while others did not. However it was possible to create a table of the mean changes in distance BCVA in each study, first converting all values approximately to LogMAR and then working out what changes in 'lines read' this would signify on an ETDRS chart. Since the trials ran for different lengths the collation of data below is only valid for patients within 12 months of the procedure. The IMT trial followed patients for 60 months and showed the fluctuation in results with that but since no other trial has yet published data to that extent of follow up data recorded at those intervals could not be compared to any of the others.

Since each row on the ETDRS chart is spaced via a value of 0.1 log unit and higher lines constitute a higher value as well as increased size of characters to read, a reduction of 0.1 logMAR between pre-op and post op recordings would denote a line gained; hence with regards to the IOL-VIP, since the reduction is 0.52, this would translate into the patient being able to read 5 more lines. The IMT trial measured specifically 'lines gained' during reading so these values didn't have to be calculated they could just be inserted directly. This can all be seen in table 7.

IOL Model	**Mean Distance BCVA (LogMAR)**		**Mean Lines gained (post-op)**
	Pre-op	Post-op	
IOL-VIP	1.28	0.77	5.2
Iol-AMD	0.92	0.7	2.1
LMI	1.47	0.94	5.1
IMT			3.6

Table 7: *Collation of the mean distance BCVA of the IMT, IOL-VIP and iol-AMD, pre operatively and post operatively, as well as the conversions into 'lines gained'. Also the mean 'lines gained' for the IMT.*

So as can be seen from the above table each trial improved, on average, the distance BCVA of their patient cohort within the first year of surgery. Comparatively the IOL-VIP and LMI showed the greatest improvement with their groups, however it should be noted that the patients in the Iol-AMD group had the best initial BCVA so there was less scope for improvement. In addition to this the mean BCVA of the patients post op in this group was lower than any of the others, indicating the patients had the best vision post op of all the groups. Therefore even though the improvement in terms of 'lines gained' may not be as spectacular as the IOL-VIP and LMI it doesn't mean that the Iol-AMD is an inferior device. The IMT appears to be within the middle, in terms of improvement, however the trial did show that as time progressed the 'lines gained' did decrease and it would be interesting to see if this same pattern between the lenses is observed if all the patients were followed up for 60 months.

With regards to complications during surgery or after only the IMT reported that these occurred and that is all but certainly due to its significantly larger sample size. Therefore it would be best to assume that the other systems would follow a similar profile if more patients were followed up rather than assume that there would be no complications even if 200 patients are followed. However this is purely an assumption and it is an area of future work for the other three lenses to be implanted into vastly more patients in order to get a true measure of the possible complications and their prevalence.

The studies each used complicated and different surgical techniques all of which can be read in more detail in the relevant studies. It would go beyond the scope of this review to describe each surgical procedure in detail.

With regards to pre and post-operative assessment each trial did it slightly differently. The IOL-VIP and iol-AMD performed very similar pre-operative assessments using software as well as microperimetry and the IOL-VIP established a very intensive post-operative rehabilitation program. This could be the reason that the 'lines gained' were the greatest in the IOl-VIP subgroup. Therefore it would mean that the pre and post-operative involvement with the patient may be equally as important as the individual design of the telescopic devices. It would be interesting to see if the results of the other lenses would improve should they use pre-operative software and post-operative rehabilitation. It is another area of future research to devise a less intensive and shorter rehabilitation program that maintains a similar efficacy.

Better Patient selection

Each successive design of IOL, while more sophisticated than the last, have always been met by the same issues, relevant patient selection using simulation tools, complex surgery, intensive visual rehabilitation after implantation and loss of peripheral vision. In order for this treatment to be more widely used it will be necessary to reduce these side effects.

A technology already used in the diagnosis of macular degeneration is fundus autofluorescence (FAF), which is a non-invasive imaging technique that detects fluorophores, naturally occurring molecules that absorb and emit light of specified wavelengths [12]. Examples of fluorophores include lipofuscin, drusen and rhodopsin, to name a few. A fundus camera is used to take a picture of the retina and areas high in any of the above mentioned fluorophores will become apparent. With regard to AMD it is the drusen that are most significant since this imaging modality will be able to spot areas of disease that are already clinically apparent as well as areas that are not yet visible on other modalities but will likely be the next clinically apparent area [13]. Therefore with the use of this technology before implantation of any IOL system it can better be ascertained which areas of the retina are most diseased and which may develop disease in the future. Subsequently a lens system specific to each patient's retina could be designed in order to produce an image over the healthiest part of retina and which will have the longest interval before the disease spreads to that location.

Microperimetry is the process whereby a fundus camera and an autotracking device are used to map a patient's area of retinal sensitivity. This can be used to ascertain which areas of the retina are the most diseased and which are the healthiest, during a functional exercise. The test can define a location known as the preferred retinal locus (PRL) which is defined as the area of the retina on which an image falls during tracking an object movements. Microperimetry can be used to establish how well the eye is able to fixate an image in this location

[14]. The charm of microperimetry is that it allows to differentiate between areas of disease that have lost function and those areas which appear diseased but there is no clinical manifestation [15]. While autofluorescence and other imaging such as OCT will demonstrate location and progression of disease microperimetry can decipher where it is relevant. Therefore, where before lenses would be designed that avoided producing an image over areas that demonstrated macular disease, now they could be designed to only avoid areas where there is functional loss. This could minimize the amount of peripheral vision that would be lost after implantation and it could reduce the length of the intensive post implantation visual rehabilitation.

Conclusion

In summary there is still a long way to go before there is an acceptable treatment of macular disease using intraocular lens to magnify and deflect images to healthier parts of the retina. All the trials, despite their varying methods of assessment, showed improvement in the BCVA of implanted eyes and this was maintained in follow up with very few significant complications reported. However the improvement comes at the cost of peripheral vision in most cases (with the exception of the LMI) and it wasn't reported how significant this might have been on the patient's life. That said the majority of patients were happy to be able to read books and recognize faces more easily. It should also be noted that no trial returned vision to the level before the advent of macular disease in these patients and the IOLs should only be seen as a method to improve quality of life in sufferers of the disease as it progresses. It should be noted that the IOL design is not likely the sole determinant of the success of the therapy and that the nature and extent of pre-operative assessment and post-operative rehabilitation plays a very important role in the efficacy of these treatments.

Further research and investigation needs to be done to determine the best patient group that would be suited to a specific magnification lens from pre-operative work up. The design and optical effect of deflection from an implant that can provide adequate alternative central vision without compromising peripheral vision also needs to be optimized to produce superior outcomes in large randomized clinical trials and this would eventually lead to custom surgery for individual patients so as to best improve the quality of life of sufferers from this disease. In addition much more research is required for their efficacy in other macular diseases to slow down the rate of progression and therefore maintain the existing vision for patients.

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There is no financial interest in writing and publishing this article.

Conflict of Interest

No conflict of interest exists in the publication of this article.

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Volume 7 Issue 6 August 2017