The Implantable Miniature Telescope for macular degeneration

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Purpose of review

The function is described of the Implantable Miniature Telescope, which is completing clinical development for bilateral end-stage macular degeneration, and 6-month results of the Phase II/III IMT002 prospective, multicenter study are presented. Multispecialty patient management and implications of the study's findings are discussed.

Recent findings

No medical treatments are currently available for bilateral end-stage age-related macular degeneration (atrophic or disciform scar age-related macular degeneration). The visual prosthetic device discussed in this update is implanted in the posterior chamber to reduce the impact of the scotomata on the patient's central vision. The goal of treatment is to improve the patient's ability to perform everyday activities and participate in roles and hobbies that impact their quality of life. Patients implanted with the device experienced clinically significant gains in visual acuity and quality of life at 6 months. In total, 89% gained two or more lines of best-corrected near or distance visual acuity. The device was generally safe and well tolerated. The surgical technique is important to minimize surgically related reduction in endothelial cell density.

Summary

This age-related macular degeneration visual prosthesis has been shown to improve visual acuity and quality of life for the bilateral end-stage age-related macular degeneration patient population that at present has no other acceptable options. Endothelial cell density from baseline to 6 and 12 months after device implantation was reduced due to trauma from the surgical procedure, but was compatible with a healthy cornea. Meticulous surgical technique and a comprehensive, multispecialty approach to preoperative and postoperative patient management are essential for successful outcomes.

Keywords

age-related macular degeneration, endothelial cell density, implantable miniature telescope, quality of life

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Abbreviations

AMD	age-related macular degeneration
ECD	endothelial cell density
IOL	intraocular lens

1040-8738

Introduction

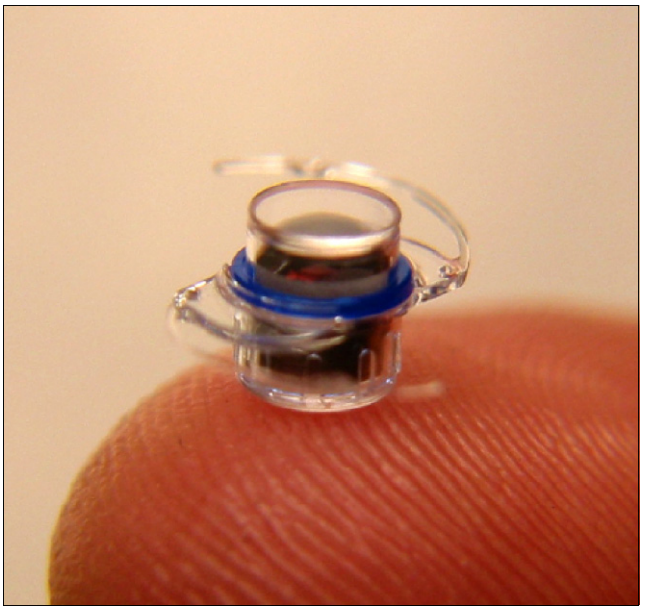
Advanced age-related macular degeneration (AMD) afflicts nearly 1.8 million persons in the United States and is the leading cause of severe vision loss in people over age 60 [1,2]. Advanced AMD is considered end-stage when choroidal neovascularization or geographic atrophy produces bilateral, untreatable macular scars causing central scotomata and moderate to profound visual impairment. This level of visual impairment limits ability to engage in daily activities that require detailed central vision. It is also associated with depression, increased dependency and accidents, and an overall decrease in the quality of life [3,4].

Although a number of treatments for exudative AMD are available or are being developed [5–7,8•], no medical treatments exist for end-stage AMD. Low vision devices, such as magnifying glasses or external telescopes, are currently the only option for patients with scotomata affecting vision. These devices are generally cumbersome, cosmetically unappealing, and provide a very restricted field of view (<10° for a 3× telescope) for static visual tasks. Furthermore, the vestibular ocular reflex conflict caused by the need to scan the visual field using head movement rather than natural eye movement may lead to nausea and intolerance of these devices [9].

The Implantable Miniature Telescope visual prosthesis

The AMD visual prosthetic device used in the prospective, multicenter IMT002 study (Implantable Miniature Telescope (IMT) by Dr Isaac Lipshitz, VisionCare Ophthalmic Technologies, Saratoga, California, USA), was developed to reduce visual impairment due to bilateral end-stage AMD [10]. The prosthesis incorporates multiple ultra-precision, wide-angle micro-optics that function as a fixed-focus telephoto system together with the cornea (Fig. 1). The device's glass cylinder housing the micro-optics is 4.4 mm long and 3.6 mm in

Figure 1 The Implantable Miniature Telescope



A quartz wide-angle micro-optic is seen through the front window and anterior aspect of the device cylinder. A blue polymethylmethacrylate light restrictor encircles the cylinder anterior to the carrier plate.

diameter. Positioned in the capsular bag, the device protrudes through the pupil by 0.1–0.5 mm and allows for a clearance of about 2.5 mm from the anterior window of the device to the corneal endothelium. The rigid haptic loops are 13.5 mm in diameter. The prosthesis projects an enlarged image of the patient's central visual field onto the retina (55°, versus focused on the 5° macula), thus reducing the size of the scotoma relative to the objects in the central field of vision. The implanted eye sees a 20–24° wide field of view due to the enlarged image projection (2.2 or 3 times retinal image enlargement depending on device model).

Importance of comprehensive patient management

To realize the benefits of this visual prosthesis, the patient must be managed both preoperatively and postoperatively by a team of specialists, rather than an individual practitioner. Leading the team approach, the retina specialist generally determines whether the patient is a candidate for implantation based on retinal pathology and refers selected patients to an anterior segment surgeon for further evaluation. This surgeon determines whether the patient meets certain anterior segment criteria for lens extraction and implantation of the visual prosthesis. These criteria include zonular stability, preoperative endothelial cell density (ECD), and other surgical requirements. After the anterior segment surgeon fulfils his or her role on the team by completing the implantation, the retina specialist refers the patient to a visual rehabilitation program led by a visual rehabilitation specialist.

Through this comprehensive approach, the patient learns to fully use this new visual status in activities of daily living, including those necessary for self-care, community and social integration, hobbies and reading. The importance of this multidisciplinary approach for patient management cannot be overlooked, as it is a requirement for comprehensive patient management and successful outcome. Each practitioner in the team utilizes his or her expertise to the fullest and refers patients out for activities beyond that expertise. In this way, appropriate patients are selected, patient expectations are managed, and success with the device is maximized.

Implantation

Implantation of the AMD visual prosthesis follows lens extraction by phacoemulsification. Special care must be taken during the unique implantation procedure because of the dimensions of the prosthesis and the need to avoid damage to ocular structures. The device is secured in the capsular bag with a nonstandard, large-incision technique. The implantation procedure includes a 10 to 12 mm scleral or limbal incision to accommodate the dimensions of the device and reduce the risk of surgical trauma to the cornea by contact during insertion. A large 7 mm capsulorrhexis allows for easier implantation of the device into the capsular bag. Dispersive and cohesive ocular viscoelastic devices are required to create space between ocular structures, maintain the anterior chamber, and to coat the device and cornea for maximum protection of the endothelium. A downward angulation with posterior pressure is required while attempting to insert the device through the anterior chamber and into the bag. Proper wound construction is also important to allow good wound alignment and to reduce the amount of surgically induced astigmatism. Wound closure usually requires from 6 to 8 sutures.

Phase II/III study

A prospective, multicenter clinical trial of this prosthetic device was conducted in patients with central vision loss associated with untreatable advanced AMD with bilateral macular scars (end-stage AMD). This report presents the 6-month efficacy and preliminary 12-month safety results. Patients with active choroidal neovascularization (CNV) or treatment of CNV in the preceding 6 months, history of intraocular or corneal surgery in the study eye, endothelial cell density less than 1600 cells/mm^2, anterior chamber depth <2.5 mm, nar-

row angle, and pathology that compromised peripheral vision were excluded.

Thirty-two anterior segment surgeons performed the surgical procedures. Patients enrolled and scheduled for surgery numbered 217, and 206 were successfully implanted with the device. Participating patients had a mean age of 76 years and stable disease.

After lens extraction by phacoemulsification techniques, the prosthesis was implanted in the capsular bag of one eye to improve central vision. The other eye was not implanted to provide peripheral vision for orientation and mobility. Patients who were implanted underwent six visual rehabilitation visits postoperatively to learn how to use their new visual status in activities of daily living. Retina specialists, anterior segment surgeons, optometrists, and visual rehabilitation therapists were involved in preoperative and postoperative assessment and care.

Visual and functional results

Patients made important visual gains with their implanted eyes and reported improved function and quality of life. At 6 months, 89% (178/201) of eyes achieved a 2-line or more improvement in mean distance or near best corrected visual acuity (BCVA), surpassing the protocol's primary efficacy end point of 50%. A total of 68% (136/201) and 56% (113/201) achieved a 2-line or 3-line or more improvement in both distance and near BCVA, respectively. Overall, 98% of patients had improved or stable (less than a 1-line change) distance BCVA (BCDVA). Only 3% of patients were classified as profoundly impaired (less than 20/400 BCDVA) at 6 months, compared to 32% at baseline. Significant improvements in quality of life were also recorded. NEI 25-item Visual Function Questionnaire scores for vision-specific subscales covering General Vision, Near Activities, and Distance Activities, and all of the vision-targeted psychosocial domains of Dependency, Social Functioning, Mental Health, and Role Difficulties, improved to both statistically and clinically meaningful levels (range of 7–17 points). The mean overall composite score increased 7 points from baseline ($P < 0.0001$).

Corneal health results

Mean corneal ECD decreased from 2492 (±354) cells/mm^2 preoperatively to 1994 (±592) cells/mm^2 at 3 months, 1936 (±1160) at 6 months, and preliminary data indicate 1870 (±1184) cells/mm^2 at 12 months postoperatively. This represents a 20%, 22% and 25% loss from baseline levels at 3, 6 and 12 months, respectively. Stabilization of mean ECD after 3 months was seen after the 3 to 6 month period, with only marginal declines in ECD between postoperative visits thereafter. ECD reduction was correlated with postoperative day 1 edema that was +2 or greater in severity, indicating that the cell loss was due to trauma sustained at the time of surgery. At 6 months, there were no significant retinal complications.

Implications of results

The visual acuity and quality of life outcomes are meaningful for these patients with end-stage AMD. The ability to recognize friends, see the news, and be more independent is invaluable. However, new surgical procedures are invariably accompanied by a learning curve through which surgeons learn to perform a particular procedure with minimal complications, for example, minimizing the loss of endothelial cells during cataract extraction. After phacoemulsification performed by experienced surgeons, endothelial cell loss ranged from 4% to 15% [11,12], while phaco performed by a resident showed an endothelial cell loss of 11.6% [13]. Another study showed endothelial cell loss ranging from 16.5% to 19.4% after phaco of grade 3 cataracts by experienced surgeons [14]. Clearly, surgical experience, as well as many other variables, affects cell loss, and the numbers given above should not be viewed in absolute terms. Overwhelming evidence also exists for improved phacoemulsification results with practice.

Mastery of the learning curve is also important for preventing endothelial cell loss during implantation of this AMD visual prosthesis. Successful implantation requires considerably more skill, time and intensity than intraocular lens (IOL) implantation. The device is large – the anterior-window-to-posterior-window length is 4.4 mm – and has unique geometric properties. It must be carefully implanted while avoiding corneal touch to minimize endothelial cell loss. However, while implantation may be a challenging procedure, it can be mastered by an anterior segment surgeon following the recommended techniques. Surgeons participating in the Phase II/III study generally had greater cell loss in their first three cases, which suggests that the rate of endothelial cell loss decreases with surgical experience.

In addition to surgical experience, the preoperative ECD and corneal health is critical to a safe prosthesis implantation procedure. Patients in the Phase II/III study had mean ECD of almost 2500 cells/mm^2 before implantation, greater than the 1600 cells/mm^2 minimum inclusion criterion, and mean ECD was over 1850 cells/mm^2 12 months postoperatively.

Product labeling for the Artisan phakic intraocular lens specifies a minimal preoperative endothelial cell density

for implantation of that IOL. For persons over the age of 45, 2000 cells/mm^2 are required so that at least 1000 cells/mm^2 remain at age 75. This is based on the continual loss of endothelial cells of 1.8% per year after lens implantation seen in the 3-year clinical study of the Artisan phakic IOL implanted in 232 eyes.

Other investigators also identified preoperative cell count as the critical factor determining corneal failure after a certain number of years [15,16]. These investigators examined the percent cell loss per year after a surgical procedure. In the study by Panton and associates, eyes with counts greater than 1000 cells/mm^2 before implantation of anterior chamber lenses had a 1.5% per year rate of decompensation, while eyes with lower cell counts had a 57% rate [16]. Thus, corneal decompensation depended highly on presurgery ECD.

Although mean ECD in the IMT002 Phase II/III study were in acceptable ranges 12 months postoperatively, could continuation of cell loss lead to corneal decompensation in a patient's lifetime? The available literature suggests that cell loss tapers after an ocular surgical procedure after an initial accelerated loss, and that 500 cells/mm^2 is the critical required cell density for proper corneal function [17–19]. At or below this level, edema and corneal decompensation may occur. The model developed by Armitage and colleagues indicated critical cell density for corneal graft survival to be 500 cells/mm^2 [17]. In a graft with 2000 cells/mm^2 before surgery, critical density would be reached in 20 years. Olsen and Eriksen noted corneal thickness to increase in a small number of eyes when ECD dropped below 500 cells/mm^2 [18], and Bates and colleagues reported patients presenting with bullous keratopathy after cataract surgery had ECD of 515 cells/mm^2 [19].

Considering the expected life span of patients affected by end-stage AMD, and the expected cell loss per year after implantation, one can expect good corneal health will continue through a patient's lifetime after implantation with this AMD visual prosthesis, given that an adequate cell density exists preoperatively. For younger persons 60–65 years of age, an additional 22 years of life can be expected for a total life span of 82–87 years [20]. If a person in this age group has a minimum cell density of 2500 cells/mm^2 preoperatively, a 3% decline per year postoperatively (estimated mean loss/year after an initial 1 year 25% ECD decrease) would result in approximately 1000 cells/mm^2 at the age of 82–87. This is above the critical value for the predicted life span of this patient. At the other end of the age scale, a person over age 90 with a minimum cell count of 1600 cells/mm^2 could expect to live another 5 years and, with a 3% cell loss per year, would have an ECD of approximately 1062 cells/mm^2.

Conclusion

While new treatments such as photodynamic therapy and anti-VEGF compounds have shown promise in the treatment of neovascular AMD, end-stage disease remains the major cause of severe and irreversible vision loss in the United States and the developed world. No medical treatment is currently available, and patients with advanced disease have only the use of frustrating external low vision aids for static tasks requiring central vision. Now, with the development of this AMD visual prosthesis, patients with bilateral, end-stage AMD may have a unique opportunity for improved visual acuity and quality of life. Patients implanted with the prosthetic device in the Phase II/III study experienced clinically and statistically significant gains in visual acuity, with 89% and 86% gaining two or three more lines, respectively, of best-corrected near or distance visual acuity at 6 months. The device was generally safe and well tolerated, but careful surgical technique and experience are required to minimize the expected ECD decrease found in this study.

Appropriate patient selection, setting realistic expectations, and proper screening of corneal risk factors are important for successful outcomes with the procedure. Preoperative cell counts obtained through specular microscopy can eliminate patients with low baseline ECD. If a patient has a healthy cornea before implantation, we would not expect many implanted eyes to fall below 500 cells/mm^2 and approach levels of imminent corneal decompensation. The decline in cell loss after 3 months in the Phase II/III study suggests that initial cell loss was related to surgical trauma during the procedure, and that the ongoing presence of the visual prosthesis in the anterior segment did not compromise corneal endothelial integrity in the long term.

A multidisciplinary approach that allows each specialist to play a defined role in treatment of these patients is essential. The visual rehabilitation program is a key factor to a successful outcome, as it allows the patients to leverage their improved visual acuity into performance of everyday activities. The retina specialist and/or anterior segment surgeon must screen for patient willingness to commit to the program.

In this patient population with moderate-to-profound bilateral visual impairment, older age, and no accepted treatment options, the rewards of improved vision and quality of life with this monocular device appear to outweigh the associated risks of the surgical procedure.

These risks can be low and rewards high with careful surgical technique, the multidisciplinary approach, and adherence to a patient selection protocol. Until medical treatments are available to prevent end-stage disease, implantation of this AMD visual prosthesis can provide improved central vision and allow some of the independent function that these patients greatly desire.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:
• of special interest
•• of outstanding interest
Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 109).

1 Friedman DS, O'Colmain BJ, Munoz B, *et al*. Eye Diseases Prevalence Research Group. Prevalence of age-related macular degeneration in the United States. Arch Ophthalmol 2004; 122:564–572.

2 Age-Related Eye Disease Study Research Group. Potential health impact of age-related eye disease study results. AREDS report no. 11. Arch Ophthalmol 2003; 121:1621–1624.

3 Williams RA, Brody BL, Thomas RG, *et al*. The psychosocial impact of macular degeneration. Arch Ophthalmol 1998; 116:514–520.

4 Casten RJ, Rovner BW, Tasman W. Age-related macular degeneration and depression: a review of recent research. Curr Opin Ophthalmol 2004; 15: 181–183.

5 Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin – TAP Report 2. Arch Ophthalmol 2001; 119:198–207.

6 The Anecortave Acetate Clinical Study Group. Anecortave acetate as monotherapy for treatment of subfoveal neovascularization in age-related macular degeneration. Ophthalmology 2003; 110:2372–2385.

7 Gragoudas ES, Adamis AP, Cunningham ET, *et al*. Pegaptanib for neovascular age-related macular degeneration. N Engl J Med 2004; 351:2805–2816.

8 • Fine SL. Age-related macular degeneration 1969–2004: A personal perspective. Am J Ophthalmol 2005; 139:405–420.
This paper is an excellent recent review of the pathogenesis of AMD and the published studies on available treatments.

9 Peli E. The optical functional advantages of an intraocular low-vision telescope. Optom Vis Sci 2002; 79:225–233.

10 Lane SS, Kuppermann BD, Fine IH, *et al*. A prospective multicenter clinical trial to evaluate the safety and effectiveness of the Implantable Miniature Telescope. Am J Ophthalmol 2004; 137:993–1001.

11 Zetterstrom C, Laurell CG. Comparison of endothelial cell loss and phacoemulsification energy during endocapsular phacoemulsification surgery. J Cataract Refract Surg 1995; 21:55–58.

12 Kosrirukvongs KR, Slade SG, Berkeley RG. Corneal endothelial changes after divide and conquer versus chip and flip phacoemulsification. J Cataract Refract Surg 1997; 23:1006–1012.

13 O'Brien PD, Fitzpatrick P, Kilmartin DJ, Beatty S. Risk factors for endothelial cell loss after phacoemulsification surgery by a junior resident. J Cataract Refract Surg 2004; 30:839–843.

14 Domingues FG, Moraes HV Jr. Yamane R. Corneal endothelial cell density comparative study after phacoemulsification by 'divide and conquer' and 'quick chop' techniques. Arq Bras Oftalmol 2005; 68:109–115 [Epub 30 March 2005].

15 Bourne WM, Nelson LR, Hodge DO. Continued endothelial cell loss 10 years after implantation. Ophthalmology 1994; 101:1014–1023.

16 Panton RW, Viana MG, Panton PJ, Panton JH. Long-term follow-up of Leiske closed-loop anterior chamber intraocular lenses. J Cataract Refract Surg 2000; 26:590–596.

17 Armitage WJ, Dick AD, Bourne WM. Predicting endothelial cell loss and long-term corneal graft survival. Invest Ophthalmol Vis Sci 2003; 44:3326–3331.

18 Olsen T, Eriksen JS. Corneal thickness and endothelial damage after intraocular lens implantation. Acta Ophthalmol (Copenh) 1980; 58:773–786.

19 Bates AK, Cheng H, Hiorns RW. Pseudophakic bullous keratopathy: relationship with endothelial cell density and use of a predictive cell loss model. A preliminary report. Curr Eye Res 1986; 5:363–366.

20 Arias E. United States life tables, 2002. National vital statistics reports; vol. 53 no. 6. Hyattsville, Maryland: National Center for Health Statistics; 2004.