Implantable Miniature Telescope for the Treatment of Visual Acuity Loss Resulting from End-Stage Age-Related Macular Degeneration: 1-Year Results

*Henry L. Hudson, MD,[1] Stephen S. Lane, MD,[2] Jeffrey S. Heier, MD,[3] R. Doyle Stulting, MD, PhD,[4] Lawrence Singerman, MD,[5] Paul R. Lichter, MD,[6] Paul Sternberg, MD,[7] David F. Chang, MD,[8] IMT-002 Study Group**

Purpose: To evaluate the safety and efficacy of an implantable visual prosthetic device (IMT; VisionCare Ophthalmic Technologies, Saratoga, CA) in patients with bilateral, end-stage age-related macular degeneration (AMD).

Design: Prospective, open-label, multicenter clinical trial with fellow eye controls.

Participants: A total of 217 patients (mean age, 76 years) with AMD and moderate to profound bilateral central visual acuity loss (20/80–20/800) resulting from bilateral untreatable geographic atrophy, disciform scars, or both were enrolled.

Methods: A visual prosthetic device (implantable telescope), designed to enlarge retinal images of the central visual field, was implanted monocularly in the capsular bag after lens extraction. Fellow eyes were not implanted to provide peripheral vision and served as controls. Study patients participated in 6 visual rehabilitation visits after surgery.

Main Outcome Measures: Best-corrected distance visual acuity (BCDVA) and best-corrected near visual acuity (BCNVA), quality-of-life scores from the National Eye Institute 25-item Visual Function Questionnaire (NEI VFQ-25) and the Activities of Daily Life scale, endothelial cell density (ECD), and incidence of complications and adverse events.

Results: At 1 year, 67% of implanted eyes achieved a 3-line or more improvement in BCDVA versus 13% of fellow eye controls ($P<0.0001$). Fifty-three percent of implanted eyes achieved a 3-line or more improvement in both BCDVA and BCNVA versus 10% of fellow eyes ($P<0.0001$). Mean BCDVA and BCNVA improved 3.5 lines and 3.2 lines, respectively, in implanted eyes versus 0.8 lines and 1.8 lines, respectively, in fellow eyes ($P<0.0001$). Change in visual acuity was not related to lesion type. Mean NEI VFQ-25 scores improved by more than 7 points from baseline ($P<0.01$) on 7 of 8 relevant subscales. Eleven eyes did not receive the device because of an aborted procedure. Endothelial cell density was reduced by 20% at 3 months and 25% at 1 year. The decrease in ECD was correlated with postsurgical edema ($P<0.0001$), and there was no evidence that endothelial cell loss is accelerated by ongoing endothelial trauma after implantation.

Conclusions: This implantable visual prosthesis can improve visual acuity and quality of life in patients with moderate to profound visual impairment caused by bilateral, end-stage AMD. *Ophthalmology 2006; 113:1987–2001 © 2006 by the American Academy of Ophthalmology.*

As the principal cause of legal blindness in the United States, age-related macular degeneration (AMD) has considerable impact on public health.[1,2] Advanced AMD, either neovascular or atrophic, affects nearly 1.8 million people in

Originally received: October 18, 2005.
Accepted: July 6, 2006. Manuscript no. 2005-1000.

[1] Retina Centers, Tucson, Arizona.

[2] Associated Eye Care, Stillwater, Minnesota.

[3] Ophthalmic Consultants of Boston, Boston, Massachusetts.

[4] Emory University Eye Center, Atlanta, Georgia.

[5] Retina Associates of Cleveland, Beachwood, Ohio.

[6] Kellogg Eye Center, University of Michigan, Ann Arbor, Michigan.

[7] Vanderbilt Eye Institute, Nashville, Tennessee.

[8] Altos Eye Physicians, Los Altos, California.

Neither the authors nor any of the participants in the IMT002 Study Group has a direct financial or proprietary interest with the subject matter. Drs Heier, Hudson, Lane, and Stulting serve on the medical advisory board for the study sponsor as consultants. All authors served as investigators in the clinical research trial of the Implantable Miniature Telescope (Dr Isaac Lipshitz), sponsored by VisionCare Ophthalmic Technologies, Inc., Saratoga, California.

Correspondence to Henry L. Hudson, MD, 6585 North Oracle Road, Suite A, Tucson, AZ 85704.

*See "Appendix" for Study Group participants.

ISSN 0161-6420/06/$–see front matter
doi:10.1016/j.ophtha.2006.07.010

the United States[3,4] and is bilateral in approximately one third or more of these individuals.[5,6] The characteristic central scotoma of late-stage AMD decreases visual acuity and limits the ability to engage in most daily activities, especially those that require detailed central vision such as self-care, social interaction, and reading. This may cause depression, increased levels of dependency, and an overall decrease in the quality of life.[7–9] Remarkably, healthcare providers significantly underestimate the deleterious effects of this condition on quality of life and the economic burden it imposes.[9,10]

Although a number of treatments are available or are being developed for neovascular AMD,[11–13] no medical or surgical treatment is available for improving visual acuity and quality of life in patients with end-stage AMD (i.e., bilateral AMD resulting from geographic atrophy, disciform scars associated with choroidal neovascularization, or both). Attempts to use a teledioptric system to project images onto a preferred retinal location were not successful.[14] More recently, retinal-based prosthetic implants have been proposed, but clinical application has been limited to blindness caused by retinitis pigmentosa.[15] Furthermore, a Veterans Administration review of visual rehabilitation appliances concluded that there is not quality evidence to document the benefits of such appliances. The authors note that most studies to date have used reading tasks in a controlled indoor setting as their end point, which does not address the clinically relevant impact of an intervention on the social and emotional facets of a patient's daily life.[16]

The AMD visual prosthetic device used in this study (IMT; VisionCare Ophthalmic Technologies, Saratoga, CA) was developed to reduce visual impairment caused by end-stage AMD. The prosthesis is a fixed-focus telescopic system comprised of ultraprecision quartz glass wide-angle micro-optics. In conjunction with the cornea, the device produces a telephoto effect that enlarges the objects in a patient's central visual field. This design is intended to allow the individual to distinguish and discern more visual information in the central field for improved function. Because a 20° to 24° forward field of view is projected onto approximately 55° of the retina, the peripheral field in the treated eye is reduced.

Lipshitz et al[17] designed this visual prosthesis and described the first model and associated surgical technique. To achieve the desired retinal image, the device is implanted monocularly in the anterior segment for central vision. Therefore, the fellow eye is able to provide peripheral vision for orientation and mobility. Implantation of the device allows patients to participate in both static and dynamic activities at near, intermediate, and distance vision ranges.

Results of a phase I trial demonstrated acceptable safety and initial efficacy in a limited number of patients.[18] Recently, a pivotal multicenter trial was conducted to determine whether the device can improve visual acuity and quality of life in patients with moderate to profound visual impairment resulting from bilateral end-stage AMD; this report describes the 1-year safety and efficacy results of this study.

Patients and Methods

Study Device

The visual prosthesis is a fixed-focus telescopic optical device integrated in a carrier with 2 rigid continuous haptics (Fig 1A). It is a compound micro-optical system comprised of anteriorly and posteriorly positioned wide-angle micro-optics housed in a quartz cylinder. Clear anterior and posterior windows are located on each end of the cylinder, which is also encircled by a blue polymethyl methacrylate light restrictor. The external surfaces of the device consist of biocompatible polymethyl methacrylate and quartz glass that contact the aqueous and intraocular structures. There are 2 models of the visual prosthesis, which differ in image enlargement only (2.2X and 3X; the latter is nominally 2.7X). The device cylinder is 4.4 mm long and 3.6 mm in diameter and weighs 115 mg in air and 60 mg in aqueous. Positioned within the capsular bag, the device typically protrudes through the pupil by approximately 0.1 to 0.5 mm, which allows for a clearance of approximately 2.5 mm between the device and corneal endothelium (Fig 1B, C).

Refraction by the cornea, wide-angle micro-optics, and refractive air spaces provide the overall refractive power to produce an enlarged retinal image of the central visual field, that is, approximately 55° of the central and peripheral retina, rather than a 15° to 20° macular region. The central visual field is enlarged nominally 2.2 to 3 times (depending on the device model used) that of an image normally projected by the cornea and crystalline lens, and the nominal forward field of view is 24° or 20°, respectively. The optical output is designed to allow the patient to recognize images that previously were difficult or impossible to discern because of the reduced resolving power at the preferred retinal locus used for fixation. The depth of focus is maintained from 1.5 m up to 10 m (optimal depth, 3 m), which is ideal for intermediate distance visual activities. After surgery, standard prescription spectacles are dispensed for distance and near vision correction to enhance the focus of the enlarged retinal image for distance and near activities.

Study Design

This prospective, open-label, multicenter clinical trial was conducted under an investigational device exemption from the United States Food and Drug Administration. Patients were enrolled at 28 vitreoretinal, multispecialty, and anterior segment ophthalmic practices in the United States. All study sites obtained institutional review board approval before study initiation, and all enrolled patients provided written informed consent. Implanted patients were followed up for 12 months for efficacy and safety, and visits were scheduled through 24 months for longer-term safety surveillance.

The primary efficacy end point was a gain of 2 or more lines of distance or near best corrected visual acuity (BCVA) at 12 months after surgery. The more common evaluation criterion of 3-line improvement is also presented in this report. The secondary outcome measure was self-assessment of functional vision and quality of life as determined by National Eye Institute 25-item Visual Function Questionnaire (NEI VFQ-25) and Activities of Daily Living (ADL) scale. Change in BCVA, endothelial cell density (ECD), and incidence of adverse events and complications were identified as safety outcome measures. Patients were asked to participate in 6 visual rehabilitation visits to learn how to use their new visual status in activities of daily living, including learning to alternate viewing between eyes for peripheral and central visual tasks.

Patient Screening and Enrollment

Enrolled patients were at least 55 years of age, had bilateral, stable, central visual acuity loss caused by untreatable end-stage AMD (geo-

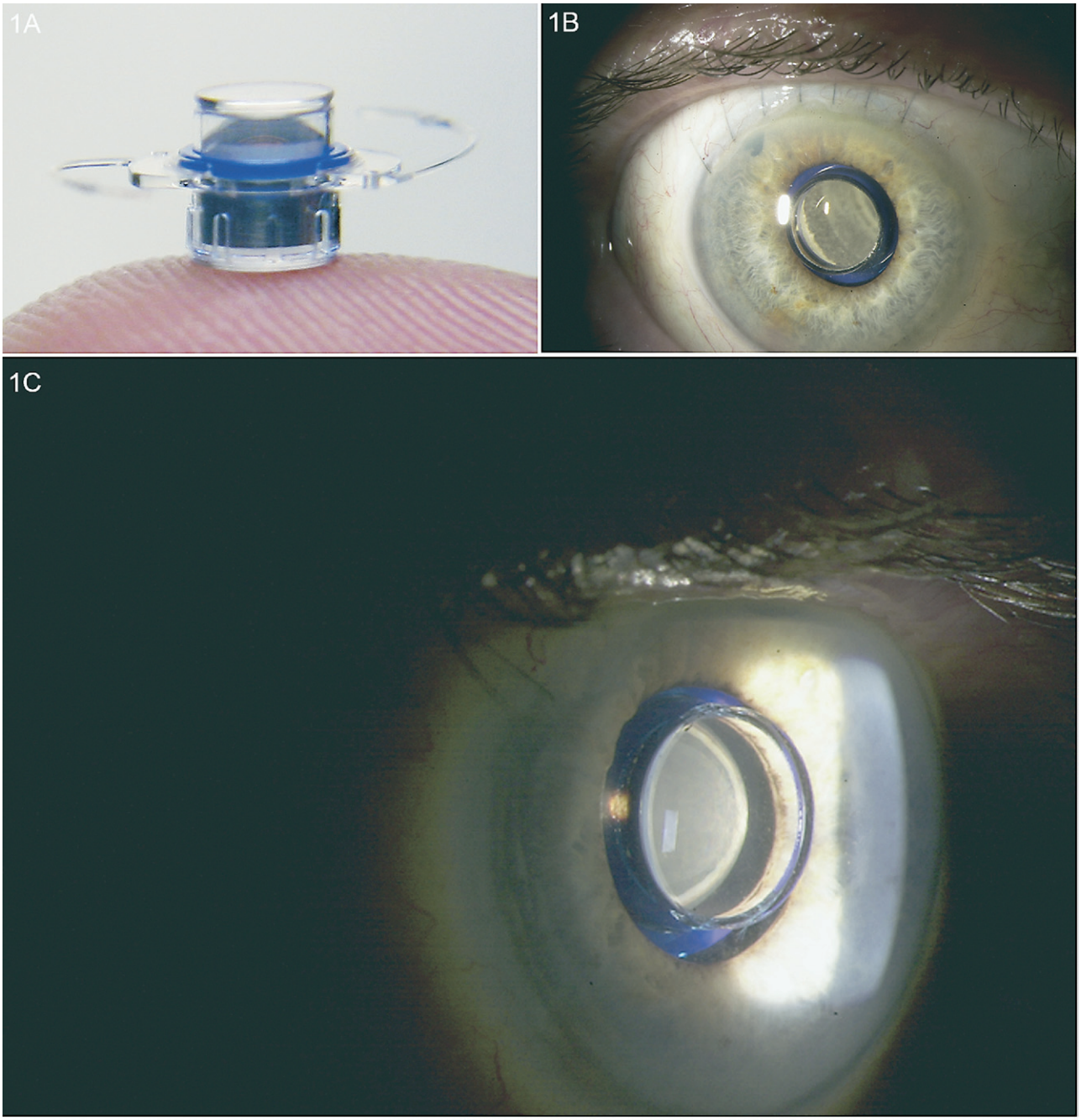

Figure 1. **A**, Side view of the implantable miniature telescope (top is anterior aspect of the device). The anterior quartz high-plus wide-angle micro-optic is positioned behind the front window and a refractive air space. The posterior wide-angle micro-optic is not visible, because it is hidden inside the bushing that prevents light scatter in the posterior portion of the device cylinder. **B**, Implanted study eye 6 weeks after surgery. The blue light restrictor can be seen behind the iris. Photograph credit: James P. Gilman. **C**, The anterior micro-optical element can be seen illuminated behind the front window of the device. The front window protrudes marginally through the iris plane. Photograph credit: James P. Gilman.

graphic atrophy, disciform scar, or both), as determined by fluorescein angiography, and were phakic with evidence of cataract in the study eye. Bilateral best-corrected distance visual acuity (BCDVA) was between 20/80 and 20/800 on the Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity chart, and there were no ophthalmic pathologic features that could compromise functional peripheral vision in the fellow eye. A monocular external telescope (field of view limited to approximately one half of implantable device) was provided to the patients to allow evaluation of the loss of binocularity at home for at least 3 days. To be eligible for enrollment, patients had to achieve at least a 5-letter improvement on the ETDRS chart with an external telescope in the eye scheduled for implantation. Patients were informed that they would experience an overall reduction in field of view because of field restriction in the implanted eye, and that the overall field could be expected to be that of the nonstudy eye (approximately 140°).

If 1 or both eyes had better than 20/200 BCDVA, the visual prosthesis was placed in the eye with poorer visual acuity. If both eyes had BCDVA worse than 20/200, the selection of the eye to implant was made by the investigator and patient. Choice of device magnification was based on the patient's preoperative experience with 2.2X and 3X external telescopes. The planned operative eye was required to have an anterior chamber depth of 2.5 mm or more as determined by A scan. Patients also were requested to be available for the duration of the study and to be willing to attend all visits for evaluation, testing, and rehabilitation. Details of patient exclusion criteria were described previously[18] and included active choroidal neovascularization (CNV), treatment of CNV in the preceding 6 months, history of intraocular or corneal surgery in the study eye, ECD less than 1600 cells/mm^2, and narrow angle (less than Schaffer grade 2).

Surgical Procedure and Postoperative Regimen

A surgical technique for implantation of the AMD visual prosthesis has been summarized previously for an earlier version of the device.[18] The unique and substantial dimensions of the device require a distinct and challenging implantation technique. First, anesthesia was induced by retrobulbar or peribulbar anesthesia, and mydriatic agents were used for pupil dilation. Lens extraction was performed through a 6.5-mm capsulorrhexis. A 10- to 11-mm limbal or scleral tunnel incision was created to provide sufficient vertical clearance for implantation without trauma to the corneal endothelium and to provide adequate space to implant the rigid haptic loops. A peripheral iridectomy was performed, the surgical wound was closed with 6 to 8 sutures, and a sub-Tenon's steroid injection was delivered. A 3-month postoperative regimen of steroids and anti-inflammatory medications was prescribed, and cycloplegic drops were prescribed for the first 3 to 4 postoperative weeks. For an example of the surgical technique, see Video 1 (available at http://aaojournal.org).

Examination Methods

Patients underwent a preoperative evaluation, including a comprehensive ophthalmic examination, fundus photography, measurement of intraocular pressure and visual acuity, cataract evaluation, and specular microscopy. Patients were examined after surgery on days 1 and 7 and at months 1, 3, 6, 9, and 12. Patients participated in visual rehabilitation sessions at weeks 1, 2, 4, 6, 10, and 12. Quality of life was evaluated before and after surgery by administration of the NEI VFQ-25 and ADL scale. All NEI VFQ-25 subscales were analyzed for change from baseline, including vision-related subscales (i.e., General Vision, Near Activities, Distance Activities, Color Vision) and vision-targeted psychosocial subscales (i.e., Dependency, Mental Health, Role Difficulties, and Social Functioning) that were considered relevant in a recent advanced AMD trial and to the current intervention.[19] The Activities of Daily Vision Scale[20] was modified to be more applicable to end-stage AMD by excluding driving-related questions and modifying questions involving vision for fine details designed for a cataract population with central vision. The resulting ADL questionnaire contains questions regarding level of difficulty performing visual tasks such as watching television, using money bills, performing household activities, and reading.

As described previously,[18] distance BCVA was measured by ETDRS and best-corrected near visual acuity (BCNVA) was measured at 20 cm (8 inches) and 40 cm (16 inches) with the New ETDRS chart 1, using M-unit equivalents for each line of acuity measured. The value used for BCNVA change was the better of the 2 measurement distances.

Specular Microscopy

Specular microscopy was performed preoperatively and at 3, 6, 9, and 12 months after surgery in implanted and fellow eyes. Three acceptable specular microscopy images were taken with a noncontact specular microscope using the automatic function (Konan Robo, Konan Medical, Hyogo, Japan). If the endothelium was not located successfully using the automatic function, then the manual function was used. All endothelial images were assessed by a specular microscopy reading center (Emory University), and the mean ECD from the 3 images was used for analysis.

Statistical Methods

The level for statistical significance in this study was $P<0.05$. The sample size was based on the ability to detect a specified change in the primary efficacy end point, that is, an improvement of 2 lines or more in either BCDVA or BCNVA in 50% of implanted eyes at 12 months after surgery, and primary safety end point, that is, mean decrease in ECD of 17% or less at 1 year after surgery based on published literature involving large-incision cataract surgery.[21,22] A paired *t* test was used to determine whether the mean logarithm of the minimum angle of resolution visual acuity change or NEI VFQ-25 score change from baseline was equal to 0, the null hypothesis of no change. For the near BCVA graph, a small amount of random noise (jitter) was added to each data point to separate overlapping points. The McNemar test was used to determine differences between the implanted eyes and the fellow eyes in mean line improvement in BCVA from preoperative levels. The analysis of variance test was used for testing differences among AMD lesion groups in BCDVA. A 2-sample *t* test was used to compare visual acuity line changes from preoperative with change in NEI VFQ-25 scores. The Student *t* test was used for testing the mean percentage ECD change. Paired *t* tests and signed rank tests were used to determine whether there were any differences between operated and fellow eyes in ECD change.

Results

Demographics and Patient Retention

A total of 32 anterior segment surgeons performed the surgical procedures. Baseline characteristics and demographic information are shown in Table 1. Of the 217 enrolled eyes, 11 had aborted procedures, resulting in 206 implanted eyes. Five procedures were aborted before device insertion and 6 procedures were aborted after device implantation, but before completion of the surgery. Reasons for abortion of the procedure were posterior capsule rupture (n = 7), choroidal effusion (n = 1), choroidal hemorrhage (n = 2), or zonular dehiscence (n = 1). These eyes were implanted with an intraocular lens. In addition, 2 eyes required device removal 1 month after implantation because of condensation inside the telescope cylinder. These failures were caused by mechanical damage to the device either during device handling or at the time of the procedure. The explanted devices were replaced with a standard intraocular lens. These 13 eyes were followed up until a stable outcome was achieved. Complications and last available BCDVA from this cohort are presented separately in "Safety Outcomes" below. With an implantable device trial design, the 1-year outcomes assess the affects of the device in situ (i.e., overall results include eyes with the implant in place at 12 months).

Patient retention was high. More than 93% (192/206) of patients were available for analysis at 12 months; 10 eyes were discontinued (7 because of patient death unrelated to the device

Table 1. Demographic and Baseline Information for Enrolled Patients

Variable	Mean (Standard Deviation) or n (%)
Enrolled patients	217
Underwent surgery but not implanted	11
Successfully implanted patients*	206
Age (yrs)	
Mean (SD)	75.6 (7.3)
Range	55–93
<65	20 (9.2%)
65–74	70 (32.3%)
75–84	105 (48.4%)
85 and older	22 (10.1%)
Gender: female; male	103 (47.5%); 114 (52.5%)
Race	
White	208 (95.9%)
Black	3 (1.4%)
Hispanic	5 (2.3%)
Asian	1 (0.5%)
BCDVA mean (SD)	
Implant eye	1.20 logMAR (0.22) (VA = 20/316)
Fellow eye	1.07 logMAR (0.24) (VA = 20/233)
BCNVA mean (SD), better of 8" or 16" distance	
Implant eye	1.10 logMAR (0.23) (VA = 20/250)
Fellow eye	1.00 logMAR (0.26) (VA = 20/200)
Visual impairment classification (ICD-9-CM) of study eye	
Moderate (<20/60–≥20/160)	20 (9.7%)
Severe (<20/160–≥20/400)	125 (57.6%)
Profound† (<20/400–≥20/1000)	71 (32.7%)
NEI VFQ-25 (mean, SD)	43.9/100 (13.3)
ADL (mean, SD)	41.4/100 (15.7)
Macular lesion (study eye)	
Disciform scar resulting from CNV	106 (48.8%)
Geographic atrophy	93 (42.9%)
Mixed	18 (8.3%)
Implant model: 2.2X; 3.0X	122 (56.2%); 95 (43.8%)

ADL = Activities of Daily Life; BCDVA = best-corrected distance visual acuity; BCNVA = best-corrected near visual acuity; CNV = choroidal neovascularization; ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification; logMAR = logarithm of the minimum angle of resolution; NEI VFQ-25 = National Eye Institute 25-item Visual Function Questionnaire; SD = standard deviation.
*217 patients were enrolled; 5 procedures were aborted before device insertion, and in 6 patients implantation was attempted, but not completed.
†20/800 Snellen-equivalent visual acuity (VA) was minimum for study enrollment.

and 3 because of explant), and only 4 patients were missing or were lost to follow-up. Last available BCDVA are presented for this cohort. In several cases, specular microscopy results were missing; subsequently, ECD data are available for 192, 198, 190, and 186 eyes at 3, 6, 9, and 12 months, respectively.

Visual Acuity Outcomes

Figure 2 illustrates the change in mean lines in BCDVA and BCNVA for implanted and fellow (control) eyes at 12 months, and Figure 3 shows the proportion of implanted and fellow eyes that gained at least 2 or 3 lines in both BCDVA and BCNVA. The effect of baseline imbalance in visual acuity was assessed by subtracting the change in lines from baseline reported for the fellow eye from that of the implanted eyes. Results revealed that implanted eyes achieved a significant mean improvement by paired *t* tests of at least 2.5 lines ($P<0.0001$) from baseline at 3 months and beyond for the implanted eye over the fellow eye. Cumulative distribution of change in lines of BCDVA and BCNVA at 12 months, implanted versus fellow eyes, is shown in Figure 4. Overall, 90% of implanted patients at 1 year achieved at least a 2-line improvement in BCDVA or BCNVA, as compared to 50% required for the primary efficacy end point. A stricter 3-line improvement criterion was also achieved, either matched or exceeded by 87% of implanted eyes at 1 year. The loss of BCDVA at 12 months was significantly greater in fellow eyes than in the implanted eyes ($P = 0.005$), with loss of 2 or more lines observed in 8.9% of fellow eyes as compared with 2.1% if implanted eyes. There was no relationship between lesion type (geographic atrophy, disciform scar, or both) and mean logarithm of the minimum angle of resolution line change at 1 year (Table 2).

Preoperative BCDVA and BCNVA did not differ significantly between the eyes that were to be implanted with the 2.2X or 3X device. A significant positive correlation was observed between improvement in BCDVA and in BCNVA for both the 2.2X and 3X devices ($R = 0.5881$; $P<0.0001$); however, eyes implanted with the 3X device had greater improvement in BCDVA than those implanted with the 2.2X device ($P = 0.0006$). A similar, nonsignificant ($P = 0.1240$) trend was observed in BCNVA. Figures 5 and 6 compare preoperative and 12-month postoperative BCDVA and BCNVA, respectively. These figures show that the vast majority of patients, with either device model implanted, demonstrated improved BCVA.

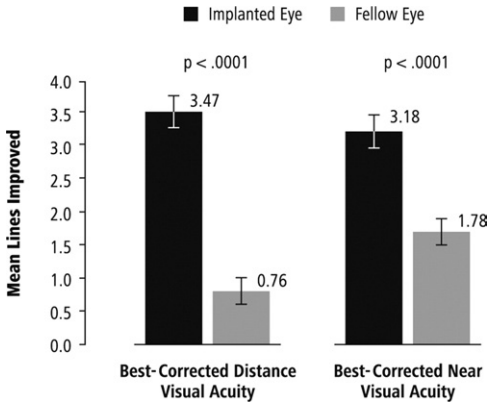

Figure 2. Bar graph comparing mean line change in logarithm of the minimum angle of resolution best-corrected distance and near visual acuity at 12 months between implanted and fellow eyes. Implanted eyes achieved a doubling of the visual angle (3-line improvement) at both distances, a statistically significant improvement over fellow eye controls.

Quality of Life and Functional Outcomes

As shown in Table 3, statistically and clinically significant (considered 5 points or more)[23] mean improvement from baseline was observed in 7 of the 8 relevant NEI VFQ-25 subscales. Of the 3 nonrelevant subscales, the Peripheral Vision subscale decreased significantly from preoperative levels, whereas the Ocular Pain and Driving subscales were relatively unchanged. Overall, the mean NEI VFQ-25 composite score improved significantly by 6.1±14.4 points from baseline ($P<0.0001$). A separate analysis by device model did not reveal any significant differences with regard to the NEI VFQ-25. Improvement in the NEI VFQ-25 composite score for the relevant subscales was correlated with improvement in BCVA: patients with a gain of at least 2 lines of BCDVA and BCNVA had a significantly greater NEI VFQ-25 point increase than patients who did not experience a gain of 2 or more lines ($P = 0.0175$; Fig 7).

Age was not significantly correlated with the change in BCDVA or BCNVA from the preoperative examination to 12 months after surgery. However, increasing age of implanted patients was slightly negatively correlated with overall NEI VFQ-25 composite score ($R = -0.1550$, $P = 0.0314$), suggesting less overall change in quality of life with increasing age.

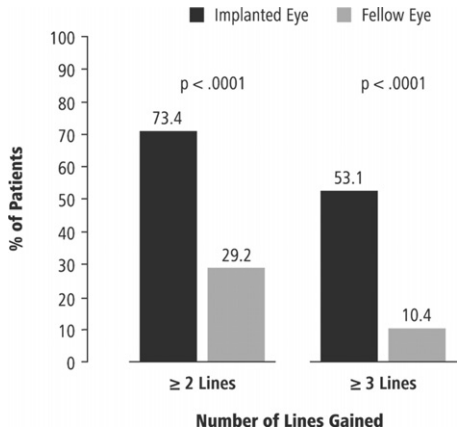

Figure 3. Bar graph comparing the percent of implanted and fellow eyes improving 2 or more and 3 or more lines in both best-corrected distance and near visual acuity at 12 months. Of implanted eyes, 53.1% achieved a doubling of the visual angle (3-line improvement) versus 10.4% of fellow eye controls. Improvement in fellow eye visual acuity may be the result of visual rehabilitation.

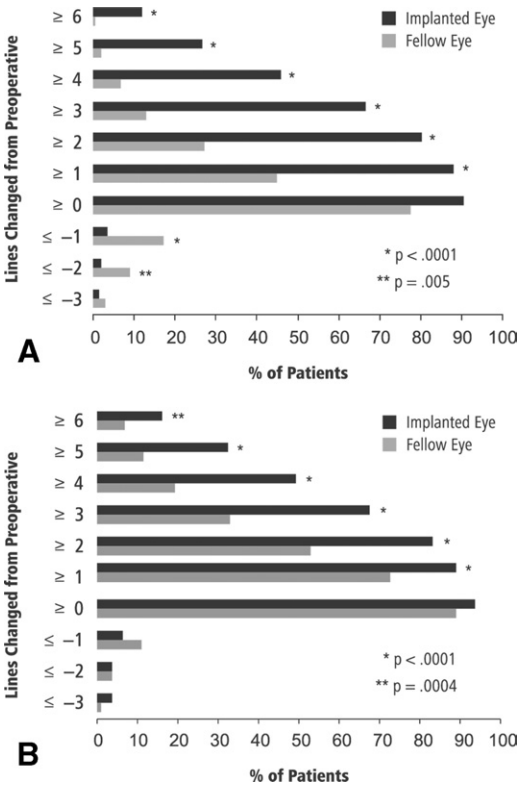

Figure 4. **A**, Bar graph showing cumulative distribution of best-corrected distance visual acuity (BCDVA) line change at 12 months in implanted and fellow (control) eyes. One hundred twenty-eight (66.7%) of 192 operated eyes gained 3 or more lines (doubling of visual angle) of BCDVA versus 24 (12.5%) of 192 of the fellow eye controls ($P<0.0001$). **B**, Bar graph showing cumulative distribution of best-corrected near visual acuity (BCNVA) line change at 12 months. One hundred thirty (67.7%) of 192 implanted eyes gained 3 or more lines (doubling of visual angle) of BCNVA versus 64 (33.3%) of 192 of the fellow eye controls ($P<0.0001$).

The ADL questionnaire showed a mean 14.1-point improvement to 55.8 (±19.6) from the mean baseline score of 41.4 points ($P<0.0001$; Fig 8). The ADL subscales improved significantly for distance, intermediate, and near activities for both static and dynamic dimensions. The mean ADL score improvement correlated with improvement in the NEI VFQ-25 composite score ($R = 0.7339$; $P<0.0001$).

Safety Outcomes

A small subset of implanted eyes, 10 eyes (5.2%), experienced a loss of more than 2 lines in BCDVA or BCNVA at 12 months without a 2-line improvement in the other test distance. The most commonly reported (≥5%) adverse events or complications are listed in Table 4. In 2 implanted eyes (1.0 %), corneal decompensation was diagnosed between 9 and 12 months after surgery. One eye had intraoperative iris prolapse and a shallow anterior chamber after surgery. In this eye, ECD eventually decreased to 463 cells/mm^2 at the 9-month visit. The other eye had intraoperative iris prolapse and the implant was decentered inferiorly because of 1 haptic being located in the sulcus. In this eye, ECD eventually decreased to 385 cells/mm^2 after 9 months. Both eventually un-

Table 2. Differences among Age-Related Macular Degeneration Lesion Groups for Best-Corrected Distance Visual Acuity

Lesion Group	Mean Preoperative Best-Corrected Distance Visual Acuity (Standard Deviation)	Mean Best-Corrected Distance Visual Acuity at 12 Months (Standard Deviation)	Change in Best-Corrected Distance Visual Acuity*
Geographic atrophy (n = 80)	1.18 (0.22)	0.86 (0.26)	−0.32
Disciform scar (n = 95)	1.20 (0.21)	0.84 (0.20)	−0.35
Mixed (n = 14)	1.32 (0.19)	0.84 (0.21)	−0.46
Analysis of variance		$P = 0.102$	

[†]A −0.1 logarithm of the minimum angle of resolution change indicates 1-line improvement in visual acuity.

derwent successful device removal and corneal transplantation (more than 12 months after initial surgery). There were no retinal adverse events or complications of more than 1% in incidence.

Figure 9 shows last available safety BCDVA outcomes for the subpopulation of eyes with an aborted implantation procedure, device explant, or unattainable 12-month BCVA because the patient died, missed a visit, or was lost to follow-up. Complications in eyes with aborted procedures or device failure are noted in Table 5.

Figure 10 shows the mean ECD over time for implanted eyes. Mean ECD loss from baseline to 3 months was 20%, and at 12 months after surgery, mean ECD loss was 25%. The difference in percent ECD change over time between consecutive specular microscopy postoperative visits for study eyes versus all fellow eyes was statistically significant during the 3- to 6-month interval only (−2.7%; $P = 0.015$). No statistically significant differences in ECD at postoperative visits were observed between implanted and pseudophakic fellow eyes (Fig 11).

When 3-month ECD was stratified by amount of corneal edema on postoperative day 1, the difference between the eyes with greater edema (≥+2) and the eyes with +1 or no edema was

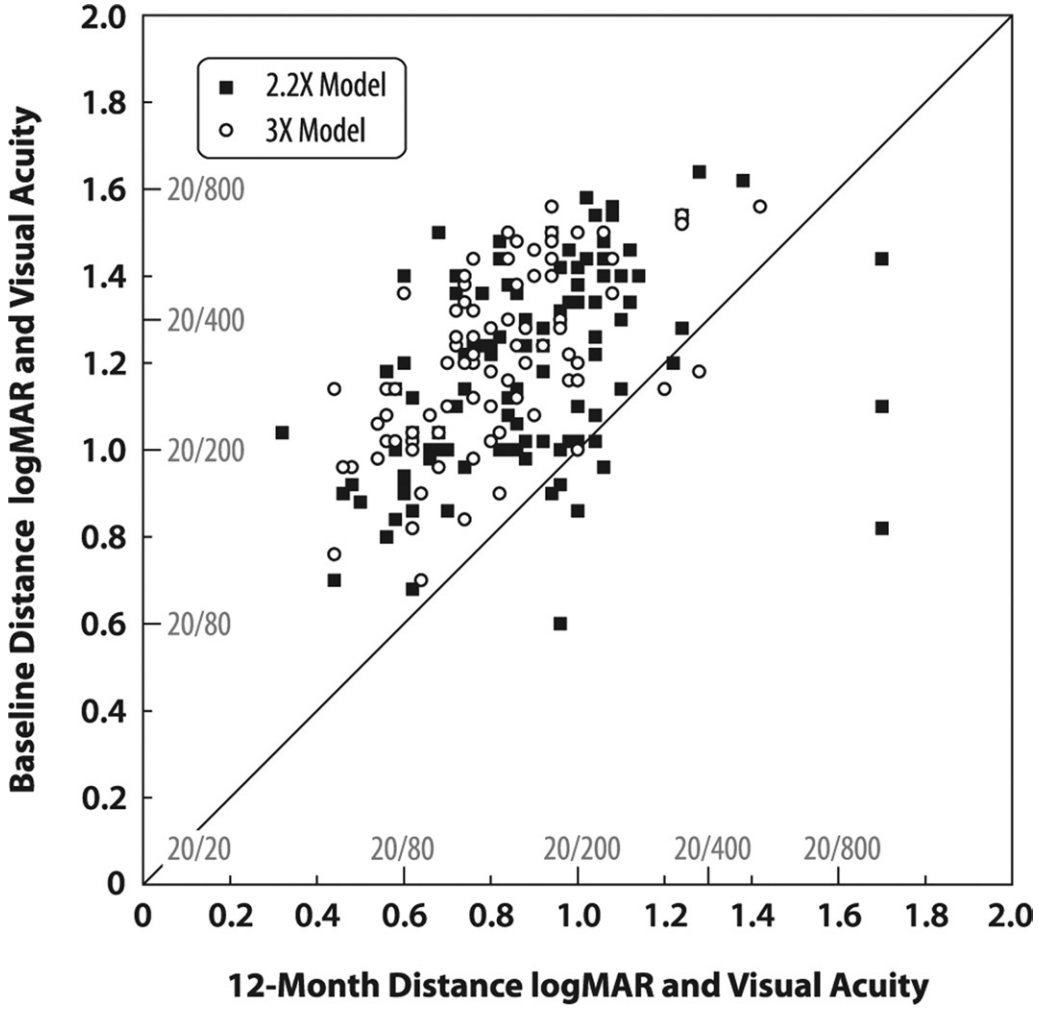

Figure 5. Scatterplot showing the change in logarithm of the minimum angle of resolution (logMAR) distance best-corrected visual acuity 12 months after the implantable telescope procedure (n = 192: 110 model 2.2X, 82 model 3X). Snellen equivalents are shown in grey.

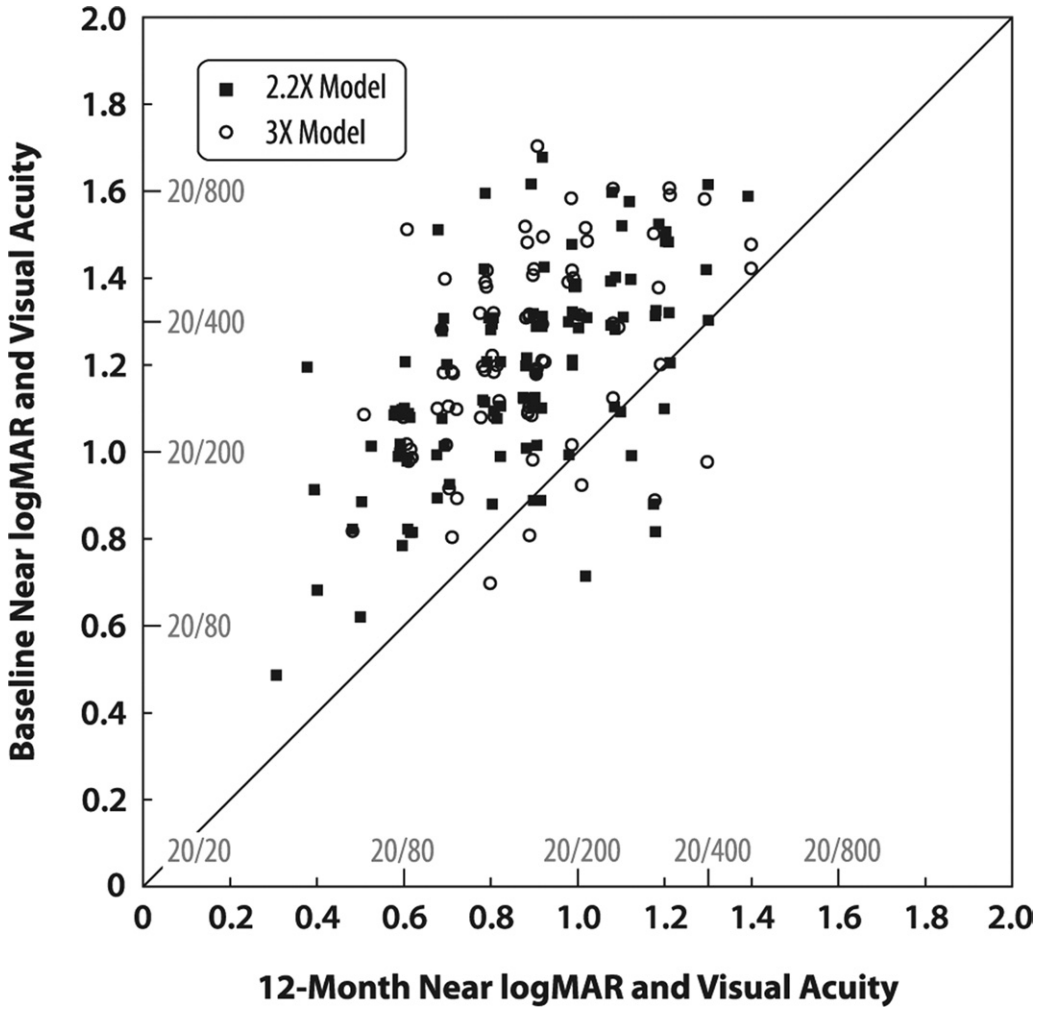

Figure 6. Scatterplot showing the change in logarithm of the minimum angle of resolution (logMAR) near best-corrected visual acuity 12 months after the implantable telescope procedure (n = 186: 106 model 2.2X, 80 model 3X). Snellen equivalents are shown in grey.

statistically significant ($P<0.0001$; Table 6). This remained significant through the 12-month visit.

Discussion

Despite ongoing basic and clinical research, effective treatments to improve visual acuity and quality of life for patients with advanced forms of AMD have not been identified, and the condition remains the leading cause of functional vision loss in the United States.[2–4] After implantation of the telescope visual prosthesis, visual acuity increased to clinically meaningful levels in this end-stage AMD study population. Ninety percent of implanted eyes achieved a 2-line minimum improvement in BCDVA or BCNVA, and 53% of eyes gained more than 3 lines (a doubling of the visual angle) in both BCDVA and BCNVA at 12 months. Reduction in ECD was 25% at 1 year, exceeding the 17% end point defined in the study protocol.

Similar to several recent ophthalmic trials[19,24–27] that included patients' subjective outcome assessments, this study examined whether objective visual acuity improvement resulted in concomitant vision-related quality-of-life improvements. A correlation between objective improvement in visual acuity and NEI VFQ-25 quality-of-life scores after the telescope prosthetic device procedure was observed.

The NEI VFQ-25 was developed based on interviews with focus groups of patients with ocular pathologic conditions, including AMD, and its questions are important to our study population.[28,29] It is not surprising that the mean preoperative NEI VFQ-25 composite score for this end-stage AMD study population indicated a very low level of visual functioning, lower than that reported for other ocular pathologic features and less advanced forms of AMD.[30] This instrument also has been shown to be a reliable and valid health-related quality-of-life assessment tool[4,31] that is responsive to changes over time after an intervention.[32]

A 5-point improvement on the NEI VFQ-25 subscales is considered clinically meaningful.[23,32] In this trial, the mean overall composite score, as well as the scores for almost all relevant subscales, achieved this level. Not only was there an improvement in vision-specific subscales, which would

Table 3. Change from Preoperative in National Eye Institute 25-item Visual Function Questionnaire Scores*

Visual Function Questionnaire Subscale	Preoperative Mean Score (Standard Deviation), (n = 206)	12-Month Mean Score (Standard Deviation), (n = 192)	Mean Change from Preoperative (Standard Deviation)	P Value†
General Health	63.2 (24.3)	58.7 (23.2)	−5.1 (21.7)	0.03
General Vision	35.4 (15.4)	50.3 (19.7)	14.0 (21.9)	<0.0001
Near Activities	25.5 (14.2)	37.3 (18.8)	11.2 (19.3)	<0.0001
Distance Activities	34.3 (18.4)	42.4 (23.2)	7.9 (24.7)	<0.0001
Color Vision	63.9 (27.8)	67.2 (26.4)	3.4 (24.6)	NS
Social Functioning	49.3 (24.5)	58.3 (22.2)	8.6 (26.6)	<0.0001
Mental Health	39.8 (24.2)	49.3 (26.4)	9.3 (22.5)	<0.0001
Role Difficulties	37.4 (23.7)	44.8 (26.6)	7.3 (26.1)	0.0002
Dependency	37.2 (27.2)	48.3 (27.4)	10.0 (27.5)	<0.0001
Ocular Pain‡	88.0 (16.1)	88.5 (16.9)	0.8 (19.2)	NS
Driving‡	2.1 (8.9)	1.9 (8.7)	−0.3 (7.3)	NS
Peripheral Vision‡	67.6 (27.2)	62.9 (22.4)	−5.9 (31.0)	0.0009
Overall Composite§	43.9 (13.3)	50.3 (14.7)	6.1 (14.4)	<0.0001

*National Eye Institute 25-item Visual Function Questionnaire (NEI VFQ-25) scores on a scale of 0 (low) to 100 (maximum).
†Value for testing that VFQ change = 0.
‡NEI VFQ-25 components not relevant to outcome associated with the visual prosthetic device.
§General Health not included in Overall Composite per NEI VFQ-25 scoring guidelines.

be expected with a doubling of visual acuity, there was also a significant improvement on the psychosocial vision-targeted dependency, mental health, role difficulties, and social functioning subscales. Results suggest that patients are less dependent on others, less worried or frustrated with their visual acuity, less limited in their activities related to visual acuity, more able to visit others, and better able to recognize facial expressions.

Nonrelevant NEI VFQ-25 subscale scores either remained unchanged or declined. General Health and Peripheral Vision subscales had significant, but not unexpected, declines. The overall health of this aged study population, with a mean age of 76 years, is expected to decline over time as shown by a decrease in the Medical Outcomes Study 36-Item Short-Form Health Survey scores in a large, 18-month prospective study of Medicare beneficiaries.[33] Before surgery, study patients were told that device implantation would involve a tradeoff of decreased peripheral field of view in 1 eye for potentially improved central vision. In light of this tradeoff, which could have potential safety implications, it is encouraging to know that there were only 4 bone fractures (2%) reported in the study

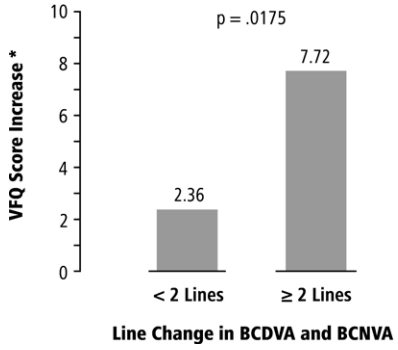

Figure 7. Bar graph showing the National Eye Institute 25-item Visual Function Questionnaire (VFQ) score change from baseline at 12 months for patients with implanted eyes gaining 2 lines or more in both distance best-corrected visual acuity (BCDVA) and near best-corrected visual acuity (BCNVA) versus patients whose implanted eyes did not gain 2 lines in both BCDVA and BCNVA. A 5-point difference on VFQ subscales is considered clinically meaningful and is associated with a 2-line difference in visual acuity (Globe DR, Wu J, Azen SP, et al. The impact of visual impairment on self-reported visual functioning in Latinos. The Los Angeles Latino Eye Study. Ophthalmology 2004;111:1141–9). Study patients who achieved a 2-line or more improvement in both BCDVA and BCNVA gained 7.72 points on the VFQ composite score versus 2.36 points for patients who did not gain 2 lines ($P = 0.0175$). Fellow eye controls did not show this association between visual acuity improvement and VFQ score change ($P = 0.5291$). *Nonrelevant subscales were excluded (i.e., ocular pain, driving, and peripheral vision).

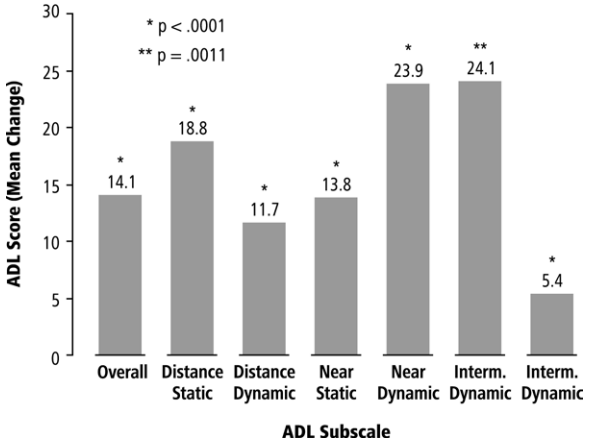

Figure 8. Bar graph showing Activities of Daily Life (ADL) scale overall and subscale score change from baseline to 12 months. Subscales represent activities of daily living grouped by 2 variables: type of activity (static or dynamic) and focusing distance (distance, intermediate, or near). The overall ADL score and each subscale showed statistically significant improvement. The ADL scale is a modified version of the Activities of Daily Living scale (Mangione CM, Phillips RS, Seddon JM, et al. Development of the "Activities of Daily Vision Scale." A measure of visual functional status. Med Care 1992;30:1111–26) designed for patients with cataract and central vision. The Activities of Daily Living scale question content was modified to apply to a population with central visual loss.

Table 4. Ocular Adverse Events and Complications in All Implanted Eyes

Event	1-Year after Surgery (n = 192)	Cumulative (n = 206)
Ocular adverse events (>5%)*		
Inflammatory deposits on device	23 (12%)	44 (21%)
Pigment deposits on device	11 (6%)	20 (10%)
Guttae	14 (7%)	16 (8%)
Posterior synechiae	8 (4%)	13 (6%)
Ocular complications (>5%)		
Increased IOP within 7 days requiring treatment	0 (0%)	57 (28%)
Corneal edema within 30 days	0 (0%)	14 (7%)
Iris prolapse	0 (0%)	12 (6%)
Corneal abrasion	0 (0%)	11 (5%)

IOP = intraocular pressure.
*Less commonly reported adverse events include iritis beyond 30 days after implant (3.9%), foreign body sensation (3.4%), increased IOP beyond 7 days after implant requiring treatment (2.9%), device removal (2.9%), anterior chamber inflammation beyond 30 days after implant (2.4%), corneal edema beyond 30 days after implant (1.0%), and device dislocation (1.0%). There were no reports of endophthalmitis or hypopyon. There were no reports of retinal detachment or retinal adverse events or complications >1% in incidence.

as nonocular adverse events. None of the fractures were reported as caused by the device. The 5-year cumulative incidence in the 70- to 79-year-old age group has been reported to be 13.7%.[34] The Ocular Pain subscale scores improved marginally, but this measure has little relationship with visual acuity.[32] Few patients answered the Driving subscale questions, because patients were informed not to attempt driving after the procedure. Patients with substantial but moderate visual impairment, averaging 20/100 visual acuity, have reported that driving is impossible (Massof RW, Deremeik JT, Park WL. Self-reported importance and difficulty of driving for a low vision clinic population. Invest Ophthalmol Vis Sci 46:E-Abstract 1903, 2005).

Scores from the ADL questionnaire showed that patients enjoyed an improvement in activities of daily life for both static and dynamic tasks at distance, intermediate, and near ranges. One explanation for these improvements is that the device provides patients with the functional ability to use natural eye movements for detailed near and distance activities. Also, the absence of any manual controls facilitates the performance of dynamic activities.

The importance of postoperative visual rehabilitation cannot be overemphasized. Patients with central vision loss must maximize their available vision to achieve functional goals requiring detailed vision. Working with a visual rehabilitation specialist is important in ensuring translation of visual improvement achieved into their daily activities. This surgical medical model of visual rehabilitation will require a high level of cooperation between retina, anterior segment, and visual rehabilitation specialists to achieve the best outcomes for the patient.

Both device models in this study significantly improved both BCDVA and BCNVA. The 3X model improved both distance and near acuities more than the 2.2X model, but the difference in near vision performance was not significant. Because the 3X version has a slightly smaller field of view than the 2.2X version (20° versus 24°), a smaller field of view may offset an increase in central visual acuity with the model that produces greater magnification. Although visual acuity gains were substantial with both models, macular lesion in the study cohort precluded the potential theoretical improvement that might have been achieved after device implantation in normal, healthy eyes without macular pathologic features. With the mean visual acuity improvement in implanted eyes demonstrated in this study, patients with visual acuities differing by more than 2 to 3 lines between eyes may not be recommended for implantation in the lesser-seeing eye. Simulations of the expected field of view and scotoma reduction effect on visual acuity could aid future patients in selecting the most appropriate implant model. Simulators, which also would aid in expectation management, are being developed. In short, visual and quality-of-life benefits of this visual prosthesis were significant and clinically important.

Although implantation of this device was associated with a significant reduction in ECD, exceeding the 17% end point at 3 months after surgery, it is important to note that beyond 3 months after surgery, the rate of change in ECD decreased and was similar to changes observed in pseudophakic fellow eyes. There was significant correlation between postoperative ECD and the level of corneal edema present on the first postoperative day, suggesting that endothelial damage occurred during surgery, rather than during the postoperative period.

Endothelial cell loss associated with modern cataract surgery has been reported to be between 2% and 14% after 3 months[22,35] and between 10% to 20% at 1 year after surgery.[22,36] Bourne et al[36] reported, after adjusting for age and preoperative ECD, a 16% mean loss in ECD at 1 year after phacoemulsification. The authors also reported that age was associated with higher ECD loss. Normal annual ECD reduction in nonoperated eyes with healthy corneas has been reported to be 0.6%.[37] Pseudophakic fellow eyes in our patient population had a 14% lower ECD at presentation than study eyes before implantation of the study device. At all postoperative visits, ECD was similar in study eyes and pseudophakic fellow eyes. Although no data are available, these findings suggest that the aged population with AMD may experience a greater decrease and larger annual loss in ECD after routine cataract surgery than the general population. Despite the ECD reduction found in the study, corneal clarity remained high, with only 2 cases of corneal decompensation at 1 year.

The 11 aborted surgical cases and operative complications attest to the unique geometrical considerations of this device and the resulting complexity of the surgical procedure. Large incisions, careful wound construction, and dexterous handling are essential for successful implantation to accommodate the 4.4-mm height of the device on entry into the anterior chamber. Eventually, 2 eyes required a corneal transplantation, underscoring that considerable endothelial damage from implantation is possible. For each patient, the risk of corneal decompensation should be weighed carefully against the potential for improved visual acuity and quality of life with this monocular device. Screening for preoperative risk factors, such as Fuchs dystrophy, a shallow anterior chamber, and low preoperative

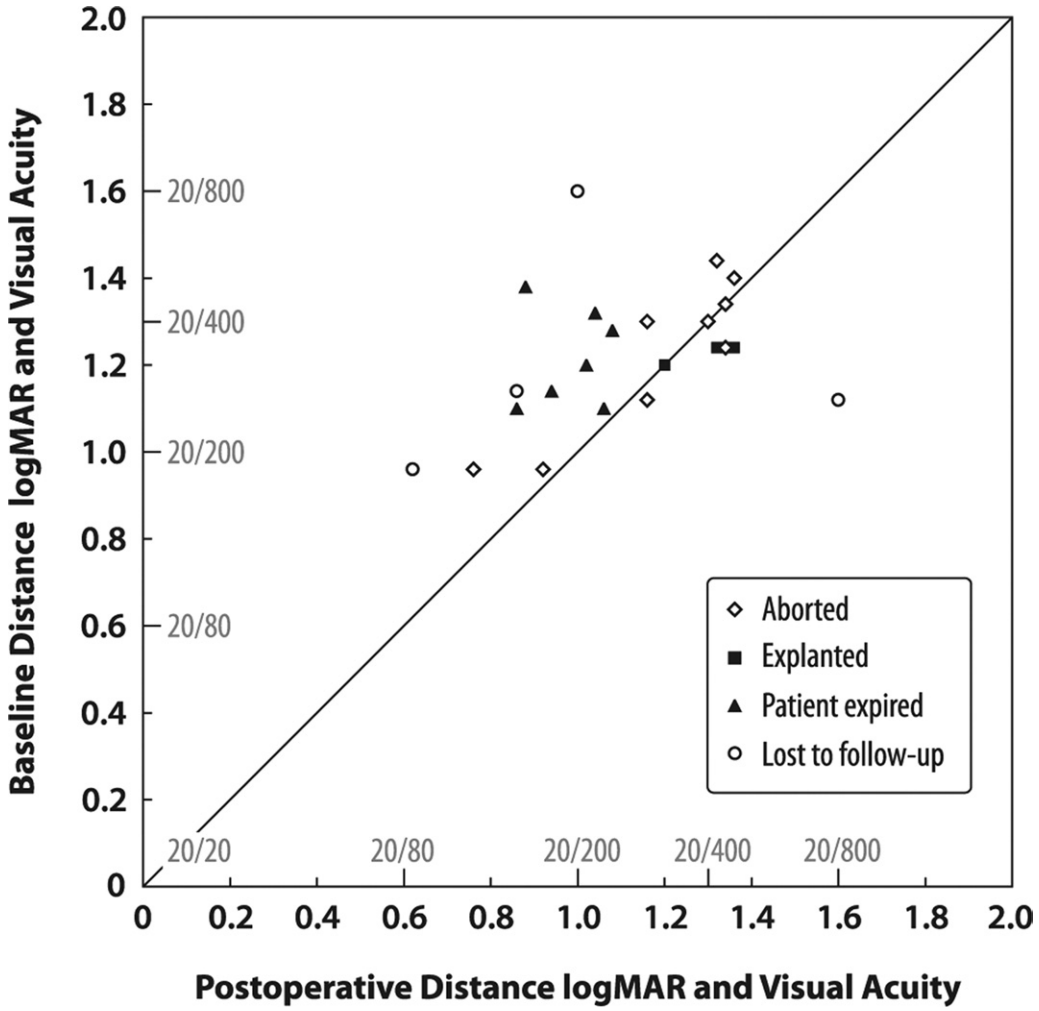

Figure 9. Scatterplot showing the change in logarithm of the minimum angle of resolution (logMAR) distance best-corrected visual acuity at last available follow-up for study eyes with an aborted implantation procedure (n = 11), device explant (n = 3), patient death (n = 10), or missed visit/lost-to-follow-up (n = 4) association. The 14 eyes with an aborted procedure or device explant were followed up for at least 1 month or until stable outcome was achieved. Last available distance best-corrected visual acuity (BCVA), recorded for 12 eyes, was 1.21 logMAR (mean follow-up time of 5.2 months) compared with 1.23 logMAR at baseline ($P = 0.5688$). None of these eyes lost 3 or more lines of BCVA during follow-up. Snellen equivalents are shown in grey.

ECD, as well as good surgical technique, may decrease the risk of corneal decompensation. Despite the large incision required to maximize vertical clearance to the cornea, our surgeons did not report astigmatism to be an issue. There were no reports of uncorrectable astigmatism.

The retinal status entry criteria were validated. There were no cases of retinal detachment and only 1 case of CNV recurrence, which was treated successfully by argon laser photocoagulation through the micro-optics of the device. If there is minor bleeding adjacent to the cicatricial lesion, the vitreoretinal specialist determines if this is the result of wound contraction and whether active CNV can be ruled out. The recent approval of anti–vascular endothelial growth factor compounds[11–13] will make recurrence of choroidal neovascularization relatively easier to treat in eyes implanted with this visual prosthesis.

The extent of visual acuity improvement in this prospective study is remarkable for this patient population with limited treatment options. However, the current study does have limitations. Adherence to a randomized control trial for this clinical situation was problematic for ethical and practical reasons. A control group of eyes that received an IOL was considered, but review of the literature suggested potential improvement only in early stages of AMD (soft drusen), especially with regard to contrast sensitivity and minor degrees of optical degradation.[38] Patients with scotoma resulting from advanced AMD, similar to our study population, have not been shown to benefit from cataract surgery.[39–41] Therefore, it was not considered ethical to include such an elective procedure for a control group. A rehabilitation control also was considered; however, no standardized or accepted rehabilitation protocol has been identified,[42] and a current study defines usual care as patients on a waiting list for low vision services (Stelmack J, Mancil R, Mancil G, et al. Veterans Affairs Low Vision Intervention Trial. Invest Ophthalmol Vis Sci 46:E-Abstract 1920, 2005). Moreover, short-term outcomes (<3 months) of visual rehabilitation appliances have shown limited effectiveness[43] and no clinically relevant change on psy-

Table 5. Complications in Eyes with Aborted Procedure (n = 11) or Device Failure (n = 2)

	No.
Complications on day of surgery	
Posterior capsular rupture	7
Vitreous loss requiring vitrectomy	6
Choroidal detachment	2
Vitreous loss	2
Choroidal hemorrhage	2
Cortical remnants	1
Iris damage	1
Zonular dehiscence	1
Complications within 7 days of surgery	
Increased IOP	2
Iritis	1
Vitreous hemorrhage	1
Wound leak	1
Complications within 1 month of surgery	
Distorted pupil	2
Floaters	1
Iris transillumination defects	1
Subretinal hemorrhage	1
Zonular dehiscence	1
Complications beyond 1 month of surgery	
Iris atrophy	1 (at 12 mos)
Iris transillumination defects	1 (at 12 mos)

IOP = intraocular pressure.

chosocial aspects of a patient's life,[16] whereas longer-term multidisciplinary studies (6–12 months) have not shown effectiveness or improvement in ability to perform everyday activities.[44,45] Therefore, the lack of any generally accepted rehabilitation control, paucity of data, and inherent patient compliance issues resulted in the conclusion that no rehabilitation-only control group could be identified.

Without the ability to mask patients undergoing this procedure and the absence of a separate control group, one could hypothesize that the improvements observed in the study population in part may be the result of visual rehabilitation or placebo effect rather than the study device. Although this investigation did not include a randomized control, we believe

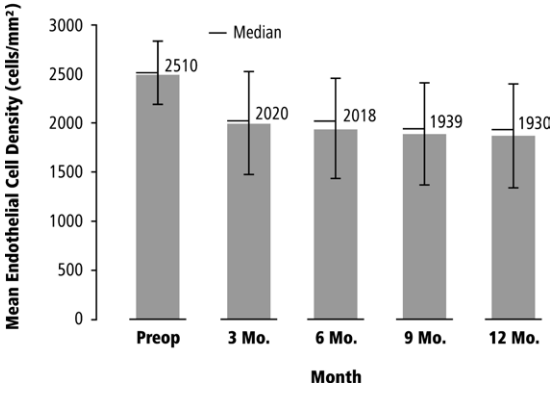

Figure 10. Bar graph showing the mean and median endothelial cell density through 12 months. endothelial cell density decreased 20% at 3 months and 25% at 12 months. At 12 months, mean endothelial cell density was 1870 cells/mm^2, compared with 2492 cells/mm^2 at baseline. Preop = preoperative.

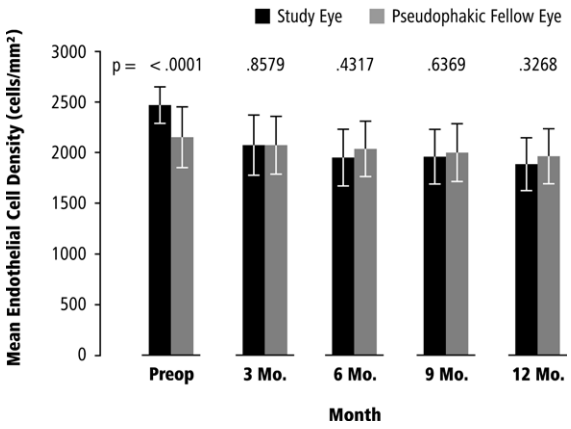

Figure 11. Bar graph showing the mean endothelial cell density (ECD) in a consistent cohort of implanted and pseudophakic fellow eye controls (n = 30). Mean ECD was not statistically significantly different from immediately after surgery through 1 year after surgery. Preop = preoperative.

that the overall improvements in visual acuity and quality-of-life outcomes of this study are attributable to the device, with integration of the new visual status into daily activities by postoperative rehabilitation. First, fellow eyes served as a control in the study, and even though both study and fellow eyes underwent 6 sessions of visual rehabilitation, implanted eyes showed a significant improvement in visual acuity as compared with fellow eye controls. Second, at 1 year of follow-up, patients with implanted eyes that gained at least 2 lines in BCDVA and BCNVA had an improved NEI VFQ-25 score of 7.7 points versus an improvement of only 2.4 points for those who did not gain at least 2 lines in BCDVA and BCNVA in their implanted eye ($P = 0.0175$). Fellow eye controls did not show this association ($P = 0.529$). Also of note, statistically significant and clinically meaningful outcomes were evident 1 year after surgery and 9 months after completion of rehabilitation sessions. In contrast, patients with bilateral advanced AMD participating in an observation arm of surgical clinical trials showed no substantial change in NEI VFQ-25 scores.[27,46]

When counseling eligible patients about this treatment approach, ophthalmologists should manage patient expectations carefully by explaining the potential benefits with the associated tradeoffs. First, the potential improvement and complications presented in this report should be explained along with the biocular postoperative visual status: use of the implanted eye for central vision and the unimplanted eye for peripheral vision. The latter is aided by the external telescope simulation. Also, ophthalmologists should enlist the other members of the

Table 6. Percent Change in Endothelial Cell Density from Baseline at Month 3 Stratified by Corneal Edema Level on Postoperative Day 1

Corneal Edema on Postoperative Day 1	Mean % Change in Endothelial Cell Density from Baseline (95% Confidence Interval)
Normal to +1	−12.8 (−16.4, −9.60)
≥+2	−35.1 (−40.7, −29.6)
	$P<0.0001$

multidisciplinary team to help educate patients on field-of-view implications, monocular central visual field enlargement, and the importance of postoperative rehabilitation to integrate their new visual status into activities of daily living. Education and explanation of all these factors will better align patient expectations before surgery. Moreover, the multidisciplinary team can aid the ophthalmologist in patient selection by collaborating on implant model selection and patient compliance issues. The fact that patients with intolerable disruption of binocularity can self-exclude themselves during simulations is an inherent advantage of the preoperative assessment. After surgery, practitioners should inform patients that diplopia is expected to occur on their path to integrating their visual status into daily activities. This is a signal that the visual system strongly perceives the enlarged image in the implanted eye.

In summary, the population of patients in this investigation experienced clinically meaningful and statistically significant improvements in both visual acuity and quality of life. The outcomes of this clinical trial show that the telescope visual prosthesis reduces the impact of the central scotoma on visual function in patients with end-stage AMD. Notably, there was an improvement in vision-targeted psychosocial status, and study participants reported less difficulty performing activities of daily living. After being approved for use, this telescope visual prosthesis will be the first surgical treatment for patients with visual impairment resulting from end-stage AMD. The implantation procedure is complex, and surgeons must exercise caution to preserve corneal endothelial integrity by following a unique implantation protocol. As with all new therapies, careful patient selection and management of expectations will be of importance. Furthermore, maximal success with this device requires comprehensive management of these patients by retina, anterior segment, and visual rehabilitation specialists. Future studies will consider optimal patient management in the multidisciplinary medical model.

References

1. Leibowitz HM, Krueger DE, Maunder LR, et al. The Framingham Eye Study monograph: an ophthalmological and epidemiological study of cataract, glaucoma, diabetic retinopathy, macular degeneration, and visual acuity in a general population of 2631 adults, 1973–1975. Surv Ophthalmol 1980; 24(suppl):335–610.
2. Gohdes DM, Balamurugan A, Larsen BA, Maylahn C. Age-related eye diseases: an emerging challenge for public health professionals. Prev Chronic Dis [serial online] 2005;2:A17. Available at: http://www.cdc.gov/pcd/issues/2005/jul/04_0121.htm. Accessed August 13, 2005.
3. Eye Diseases Prevalence Research Group. Prevalence of age-related macular degeneration in the United States. Arch Ophthalmol 2004;122:564–72.
4. Age-Related Eye Disease Study Research Group. Potential public health impact of age-related eye disease study results: AREDS report no. 11. Arch Ophthalmol 2003;121:1621–4.
5. Wang JJ, Mitchell P, Smith W, Cumming RG. Bilateral involvement by age related maculopathy lesions in a population. Br J Ophthalmol 1998;82:743–7.
6. Sunness JS. The natural history of geographic atrophy, the advanced atrophic form of age-related macular degeneration. Mol Vis [serial online] 1999;5:25. Available at: http://www.molvis.org/molvis/v5/a25/v5a25-sunness.pdf. Accessed August 14, 2006.
7. Williams RA, Brody BL, Thomas RG, et al. The psychosocial impact of macular degeneration. Arch Ophthalmol 1998;116: 514–20.
8. Casten RJ, Rovner BW, Tasman W. Age-related macular degeneration and depression: a review of recent research. Curr Opin Ophthalmol 2004;15:181–3.
9. Brown MM, Brown GC, Stein JD, et al. Age-related macular degeneration: economic burden and value-based medicine analysis. Can J Ophthalmol 2005;40:277–87.
10. Brown GC, Brown MM, Sharma S. Difference between ophthalmologists' and patients' perceptions of quality of life associated with age-related macular degeneration. Can J Ophthalmol 2000;35:127–33.
11. 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: two-year results of 2 randomized clinical trials–TAP report 2. Arch Ophthalmol 2001; 119:198–207.
12. Anecortave Acetate Clinical Study Group. Anecortave acetate as monotherapy for treatment of subfoveal neovascularization in age-related macular degeneration. Twelve-month clinical outcomes. Ophthalmology 2003;110:2372–83, discussion 2384–5.
13. Gragoudas ES, Adamis AP, Cunningham ET Jr, et al. Pegaptanib for neovascular age-related macular degeneration. N Engl J Med 2004;351:2805–16.
14. Koziol JE, Peyman GA, Cionni R, et al. Evaluation and implantation of a teledioptric lens system for cataract and age-related macular degeneration. Ophthalmic Surg 1994;25: 675–84.
15. Chow AY, Chow VY, Packo KH, et al. The artificial silicon retina microchip for the treatment of vision loss from retinitis pigmentosa. Arch Ophthalmol 2004;122:460–9.
16. Adams E, Flynn K, Alligood E, Johnson T. VA Technology Assessment Program report. Optical devices for adults with low vision: a systematic review of published studies of effectiveness. Boston: Department of Veterans Affairs; 2003. Available at: http://www.va.gov/VATAP/pubs/lowvision.PDF. Accessed August 14, 2006.
17. Lipshitz I, Loewenstein A, Reingewirtz M, Lazar M. An intraocular telescopic lens for macular degeneration. Ophthalmic Surg Lasers 1997;28:513–7.
18. Lane SS, Kuppermann BD, Fine IH, et al. A prospective multicenter trial to evaluate the safety and effectiveness of the implantable miniature telescope. Am J Ophthalmol 2004;137: 993–1001.
19. Cahill MT, Stinnett SS, Banks AD, et al. Quality of life after macular translocation with 360° degrees peripheral retinectomy for age-related macular degeneration. Ophthalmology 2005;112:144–51.
20. Mangione CM, Phillips RS, Seddon JM, et al. Development of the "Activities of Daily Vision Scale." A measure of visual functional status. Med Care 1992;30:1111–26.
21. Evaluation Team (OCTET). Oxford Cataract Treatment and Long-term corneal endothelial cell loss after cataract surgery: results of a randomized controlled trial. Arch Ophthalmol 1986;104:1170–5.
22. Beltrame G, Salvetat ML, Driussi G, Chizzolini M. Effect of incision size and site on corneal endothelial changes in cataract surgery. J Cataract Refract Surg 2002;28:118–25.
23. Globe DR, Wu J, Azen SP, et al. The impact of visual impair-

ment on self-reported visual functioning in Latinos. The Los Angeles Latino Eye Study. Ophthalmology 2004;111:1141–9.
24. Slakter JS, Stur M. Quality of life in patients with age-related macular degeneration: impact of the condition and benefits of treatment. Surv Ophthalmol 2005;50:263–73.
25. Krummenauer F, Braun M, Dick HB. Clinical outcome and subjective quality of life after photodynamic therapy in patients with age-related macular degeneration. Eur J Ophthalmol 2005;15:74–80.
26. Tranos PG, Topouzis F, Stangos NT, et al. Effect of laser photocoagulation treatment for diabetic macular oedema on patient's vision-related quality of life. Curr Eye Res 2004;29:41–9.
27. Submacular Surgery Trials (SST) Research Group. Surgery for hemorrhagic choroidal neovascular lesions of age-related macular degeneration: quality-of-life findings. SST report no. 14. Ophthalmology 2004;111:2007–14.
28. Mangione CM, Berry S, Spritzer K, et al. Identifying the content area for the 51-item National Eye Institute Visual Function Questionnaire: results from focus groups with visually impaired persons. Arch Ophthalmol 1998;116:227–33.
29. Mangione CM, Lee PP, Gutierrez PR, et al. Development of the 25-item National Eye Institute Visual Function Questionnaire. Arch Ophthalmol 2001;119:1050–8.
30. Mangione CM, Gutierrez PR, Lowe G, et al. Influence of age-related maculopathy on visual functioning and health-related quality of life. Am J Ophthalmol 1999;128:45–53.
31. Mangione CM, Lee PP, Pitts J, et al. Psychometric properties of the National Eye Institute Visual Function Questionnaire. Arch Ophthalmol 1998;116:1496–504.
32. Submacular Surgery Trials Research Group. Responsiveness of the National Eye Institute Visual Function Questionnaire to changes in visual acuity: findings in patients with subfoveal choroidal neovascularization—SST report no. 1. Arch Ophthalmol 2003;121:531–9.
33. Martin DC, Berger ML, Anstatt DT, et al. A randomized controlled open trial of population-based disease and case management in a Medicare Plus Choice health maintenance organization. Prev Chronic Dis [serial online] 2004;1:A05. Available at: http://www.pubmedcentral.gov/articlerender.fcgi?artid=1277945. Accessed August 13, 2005.
34. Klein BE, Moss SE, Klein R, et al. Associations of visual function with physical outcomes and limitations 5 years later in an older population. The Beaver Dam Eye Study. Ophthalmology 2003;110:644–50.
35. Oshika T, Eguchi S, Oki K, et al. Clinical comparison of Healon5 and Healon in phacoemulsification and intraocular lens implantation: randomized multicenter study. J Cataract Refract Surg 2004;30:357–62.
36. Bourne RR, Minassian DC, Dart JK, et al. Effect of cataract surgery on the corneal endothelium. Modern phacoemulsification compared with extracapsular cataract surgery. Ophthalmology 2004;111:679–85.
37. Bourne WM, Nelson LR, Hodge DO. Central corneal endothelial cell changes over a ten-year period. Invest Ophthalmol Vis Sci 1997;38:779–82.
38. Shuttleworth GN, Luhishi EA, Harrad RA. Do patients with age related maculopathy and cataract benefit from cataract surgery? Br J Ophthalmol 1998;82:611–6.
39. Armbrecht AM, Findlay C, Kaushal S, et al. Is cataract surgery justified in patients with age related macular degeneration? A visual function and quality of life assessment. Br J Ophthalmol 2000;84:1343–8.
40. Armbrecht AM, Findlay C, Aspinall PA, et al. Cataract surgery in patients with age-related macular degeneration: one-year outcomes. J Cataract Refract Surg 2003;29:686–93.
41. Schein OD, Steinberg EP, Cassard SD, et al. Predictors of outcome in patients who underwent cataract surgery. Ophthalmology 1995;102:817–23.
42. Vision rehabilitation: care and benefit plan models. Literature review. Rockville, MD: Agency for Healthcare Research and Quality; 2002. Available at: http://www.ahrq.gov/clinic/vision/vision3.htm#models. Accessed August 13, 2005.
43. Scott IU, Smiddy WE, Schiffman J, et al. Quality of life of low-vision patients and the impact of low-vision services. Am J Ophthalmol 1999;128:54–62.
44. Reeves BC, Harper RA, Russell WB. Enhanced low vision rehabilitation for people with age related macular degeneration: a randomized controlled trial. Br J Ophthalmol 2004;88:1443–9.
45. Hinds A, Sinclair A, Park J, et al. Impact of an interdisciplinary low vision service on the quality of life of low vision patients. Br J Ophthalmol 2003;87:1391–6.
46. Submacular Surgery Trials (SST) Research Group. Surgery for subfoveal choroidal neovascularization in age-related macular degeneration: quality-of-life findings. SST report no. 12. Ophthalmology 2004;11:1981–92.

Appendix: IMT002 Study Group

Participating Clinical Centers

Altos Eye Physicians, Los Altos, California: David Chang, MD,* David Yang, OD, Karen Harker, Susan Olsen; *Associated Eye Care, Stillwater, Minnesota:* Stephen Lane, MD,* Alan Downie, MD, Terri Flom, Jane Verness; *Associated Retinal Consultants, Royal Oak, Michigan:* Michael Trese, MD,* Robert Lesser, MD, Susan Hahn, OD, Mary Zajechowski; *Cullen Eye Institute, Baylor College of Medicine, Houston, Texas:* M. Bowes Hamill, MD,* Douglas Koch, MD, Anna Perez, OD, Swati Modi, OD, Pam Spurling; *Dean A. McGee Eye Institute, Oklahoma City, Oklahoma:* Robert Leonard, MD,* Cynthia Bradford, MD, Connie Dwiggins, Lisa Ogilbee; *Discover Vision Centers, Independence, Missouri:* Doug Dehning, MD,* Kristi Chevalier, OD, Robert Weixeldorfer, OD, Pam Taylor, Judy Rosenthal; *Doheny Retina Institute, University of Southern California, Los Angeles, California:* Srinivas Sadda, MD,* John Irvine, MD, Frances Walonker, Lori Levin, Jesse Garcia; *Duke University Eye Center, Durham, North Carolina:* Sharon Fekrat, MD,* Terry Kim, MD, Deborah LaPolice, Mikki O'Neal; *Emory University Eye Center, Atlanta, Georgia:* Daniel Martin, MD,* R. Doyle Stulting, MD, PhD, Susan Primo, OD, Kenneth Rosengren, OD, Gina Holecek, Jayne Brown; *Fine, Hoffman & Packer, Eugene, Oregon:* Howard Fine, MD,* Richard Hoffman, MD, Mark Packer, MD, Lee Aspiroz, OD, Tina Callina, Laurie Brown, Peggy Coffman; *Kellogg Eye Center, University of Michigan, Ann Arbor, Michigan:* Paul Lichter, MD,* Donna Wicker, OD, Cheryl Terpening Frueh, Carole Standardi; *Kraff Eye Institute, Chicago, Illinois:* Manus Kraff, MD,* Colman Kraff, MD, Mark Rzadkowski; *Massachusetts Eye and Ear Infirmary, Boston, Massachusetts:* Joan Miller, MD,* Kathyrn Colby, MD, PhD, Ursula Lord, OD, Erin Peters, Nicholas Emmanuel; *Medical Center Ophthalmology Associates, San Antonio, Texas:* Steven Fisher, MD,* Michael Singer, MD, Michael Orozco, OD, Robin Hartman; *Ophthalmic Consultants of Boston, Boston, Massachusetts:* Jeffrey Heier, MD,* Michael Raizman, MD, Mark Kirstein, OD, Joy Bankert, Sean Mahoney, Alison Nowak; *Paducah Retinal*

Center, Paducah, Kentucky: Carl Baker, MD,* Mark Gillespie, MD, Gregg Batts, OD, Tracey Caldwell; *Retina Associates of Cleveland, Beachwood, Ohio:* Lawrence J. Singerman, MD,* Martin Markowitz, MD, Susan Garber, Kim DuBois; *Retina Centers, Tucson, Arizona:* Henry Hudson, MD,* George Novalis, MD, Kristin Carter, MD, Robert Kershner, MD, Tom Perski, Trish Wilkins, Rita Lennon; *Retina Group of Washington, Chevy Chase, Maryland:* Daniel Berinstein, MD,* Thomas Clinch, MD, Neil Martin, MD, Suleiman Alibhai, OD, Joulia Haziminas; *Sarasota Retinal Institute, Sarasota, Florida:* Keye Wong, MD,* Marc Levy, MD, Julian Newman, OD, Christine Holland; *South East Clinical Research, Charlotte, North Carolina:* Donald Stewart, MD,* Michael Rotberg, MD, Michael Spicola, OD, Alison Stallings, Amy Rogers; *Eye Institute, Medical College of Wisconsin, Milwaukee, Wisconsin:* Dennis Han, MD,* Steven Koenig, MD, Scott Robison, OD, Troy Drescher, Christine Lang; *University of California Irvine, Orange, California:* Baruch Kuppermann, MD, PhD,* Lawrence Chao, MD, Jeff Grijalva, Rosie Magallon; *Vanderbilt Eye Institute, Nashville, Tennessee:* Paul Sternberg, MD,* Jeffrey Horn, MD, Jeffrey Sonsino, OD, Sandy Owings; *Vitreoretinal Foundation, Memphis, Tennessee:* Seth Yoser, MD,* John Linn, MD, Alyce Miles, OD, Felicia Jones; *Vitreous-Retina-Macula Consultants of New York, New York, New York:* Jason Slakter, MD,* Sidney Mandelbaum, MD, Sharon Shaw, OD; *Wills Eye Hospital, Philadelphia, Pennsylvania:* Brian Connolly, MD,* Jack Dugan, MD, Susan Edmonds, OD, Scott Edmonds, OD, Christina Centinaro, Michele Formoso; *Wilmer Ophthalmological Institute, Johns Hopkins University, Baltimore, Maryland:* Oliver Schein, MD,* Gislin Dagnelie, PhD, Ava Bittner, OD, James Deremeik.

*Principal investigators.

Specular Microscopy Reading Center

Emory University Eye Center, Atlanta, Georgia: Bernard McCarey, PhD, Henry Edelhauser, PhD.