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ORIGINAL RESEARCH

# Long-term (60-month) results for the implantable miniature telescope: efficacy and safety outcomes stratified by age in patients with end-stage age-related macular degeneration

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**Background:** The purpose of this study was to evaluate the long-term results of an implantable miniature telescope (IMT) in patients with bilateral, end-stage, age-related macular degeneration (AMD).

**Methods:** A prospective, open-label, multicenter clinical trial with fellow eye controls enrolled 217 patients (mean age 76 years) with AMD and moderate-to-profound bilateral central visual acuity loss (20/80–20/800) resulting from untreatable geographic atrophy, disciform scars, or both. A subgroup analysis was performed with stratification for age (patient age 65 to <75 years [group 1; n=70] and patient age ≥75 years [group 2; n=127]), with a comparative evaluation of change in best-corrected distance visual acuity (BCDVA), quality of life, ocular complications from surgery, adverse events, and endothelial cell density (ECD). Follow-up in an extension study was 60 months.

**Results:** Data were available for 22, 38, and 31 patients in group 1 and 42, 46, and 32 patients in group 2 at 36, 48, and 60 months, respectively. Mean BCDVA improvement from baseline to 60 months was 2.41±2.69 lines in all patients (n=76), with 2.64±2.55 lines in group 1 and 2.09±2.88 lines in group 2. Quality of life scores were significantly higher in group 1. The most common significant surgery-related ocular complications in group 1 were iritis >30 days after surgery (7/70; 10%) and persistent corneal edema (3/70; 4.3%); and in group 2 were a decrease in BCDVA in the implanted eye or IMT removal (10/127 each; 7.9%), corneal edema >30 days after surgery (9/127; 7.1%), and persistent corneal edema (6/127; 4.7%). Significant adverse events included four corneal transplants, comprising two (2.9%) in group 1 and two (1.6%) in group 2. At 60 months, one patient in group 1 (3.2%) and three patients in group 2 (9.4%) had lost ≥2 lines of vision. The IMT was removed in one (1.4%) and ten (7.9%) patients in group 1 and group 2, respectively. Mean ECD loss was 20% at 3 months. Chronic loss was 3% per year. ECD loss was less in group 1 than in group 2 (35% versus 40%, respectively) at 60 months.

**Conclusion:** Long-term results show substantial retention of improvement in BDCVA. Chronic ECD loss was consistent with that reported for conventional intraocular lenses. The IMT performed as well in group 1 (the younger group) as it did in group 2 through month 60. Younger patients retained more vision than their older counterparts and had fewer adverse events. Although not a specified outcome for this study, patients younger than 65 years also fared better than those in group 2 and retained more vision with fewer adverse events through month 60.

**Keywords:** end-stage age-related macular degeneration, implantable miniature telescope, low vision

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## Introduction

Advanced age-related macular degeneration (AMD; geographic atrophy or neovascular AMD) affects as many as 1.8 million people in the USA[1,2] and is bilateral

in at least 33% of these people.[3,4] Bilateral late AMD has an estimated incidence of 60,000–80,000 in the USA each year, with most cases occurring in elderly people.[1,3,5] Late-stage AMD is defined as large drusen, pigment changes in the retina, or both, with accompanying vision loss due to choroidal neovascularization, geographic atrophy, or both. End-stage AMD is defined as moderate (20/80 or worse) to profound (20/600 or worse) vision impairment due to bilateral central scotomas resulting from geographic atrophy, disciform scar, or both. As a result of significant visual impairment, patients experience a substantial reduction in quality of life, increased dependency on caregivers, and depression.[6–9] A reported 63% reduction in quality of life for those with advanced AMD is similar to that reported by patients with advanced prostatic cancer or severe stroke.[10] Loss of central vision is so debilitating for those with end-stage AMD that most are willing to give up as much as half their remaining life in exchange for healthy, normal vision.[8] The cost to society cannot be overlooked either. Depending upon a patient's visual acuity, annual costs for caregiving can exceed $47,000.[11]

Most clinical studies and published reports on AMD concentrate on slowing or arresting vision impairment related to late AMD associated with choroidal neovascularization. Several therapies, including laser photocoagulation, photodynamic therapy, and intravitreal anti-vascular endothelial growth factor injections, are commercially available for the treatment of choroidal neovascularization. There are no commercially available treatments for geographic atrophy. Therapeutic options for patients with bilateral moderate to profound vision impairment caused by central scotomas associated with end-stage AMD are very limited. Even low vision rehabilitation does not provide uniformly improved quality of life in this patient population.[12]

An implantable miniature telescope (IMT; VisionCare Ophthalmic Technologies, Saratoga, CA, USA) prosthetic device was designed specifically for patients with end-stage AMD. The IMT is a fixed-focus telescopic system comprised of an ultraprecision quartz glass wide-angle micro-optics. In conjunction with the cornea, the device produces a telephoto effect that enlarges the visual 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°–24° forward field of view is projected onto approximately 55° of the retina, the peripheral field in the treated eye is reduced. The device is implanted in one eye only, leaving the fellow eye to compensate for peripheral vision. Outcomes and surgical implantation techniques from Phase II/Phase III studies have been previously published.[13–15] Results from the IMT-002 clinical study (ClinicalTrials.gov identifier NCT00976235) led to US approval for the improvement of patients with stable severe-to-profound vision impairment (best corrected distance visual acuity 20/160 to 20/800) caused by bilateral central scotomas associated with end-stage AMD. The initial US approval limited the indication to patients older than 75 years of age because of concerns about potential safety risks in a younger cohort. Approvals by Canadian and European regulatory health authorities included younger age groups.

Herein we report the results of an extension study (ClinicalTrials.gov identifier NCT00976235) evaluating the long-term (60-month) efficacy and safety outcomes in all patients who had completed both the IMT-002 study and a long-term monitoring extension study (IMT-002-LTM). In addition, in order to explore whether younger patients have similar or better visual outcomes after implantation with the IMT than their older counterparts, we performed a retrospective subgroup analysis for two patient subgroups, ie, those aged 65 to <75 years (group 1) and those older than 75 years of age (group 2). The findings of this extension study subgroup analysis resulted in the US label expansion to include patients aged 65–75 years.

## Materials and methods

In IMT-002-LTM, an extension study of IMT-002, patients were followed to 60 months. IMT-002 had an endpoint of 24 months, after which time patients exited the study. At the request of the US Food and Drug Administration, an extension study was initiated, with the original patients solicited for enrollment and follow-up to 60 months. Visual acuity, quality of life, ocular complications from surgery, adverse events (AEs), acute and long-term change in endothelial cell density (ECD), vision loss in both implanted eyes and nonimplanted fellow eyes, telescope removal, and telescope malfunction were analyzed for the entire patient group and then further stratified by age in both the original and extension studies.

Details on the surgical implantation methods and original IMT-002 study methods, including relevant preoperative screening evaluations, were previously published[13–15] and are summarized here. The surgery is similar to standard phacoemulsification, but the incision size is 12 mm to account for the size of the implant. Once the telescope's haptics are in the capsular bag and fixed in position, the wound is sutured closed and a peripheral iridectomy is performed.

Postoperative follow-up is similar to postoperative follow-up after standard phacoemulsification surgery as well, with the addition of postoperative education that includes both low vision specialists and optometrists. The postoperative education takes 3–6 months.

The primary efficacy endpoint of the IMT-002 study was visual acuity, as determined using the Early Treatment Diabetic Retinopathy Study protocol charts. The intraocular telescope implantation procedure was considered successful in patients with bilateral end-stage AMD if there was an improvement of ≥2 lines in either near or distance acuity in 50% of the implanted eyes at 12 months post-implantation. Quality of life was a secondary outcome measurement. The validated National Eye Institute Visual Function Questionnaire 25-item survey was used. A 5-point change in composite score or any individual survey subscale represents a clinically significant change.[16]

## Inclusion/exclusion criteria

All patients who were successfully enrolled in IMT-002 were eligible for continued observation in IMT-002-LTM. Of the original 217 patients enrolled in IMT-002, 20 were aged 55–65 years and were excluded from data analysis on age stratification due to the small number of patients in the cohort. While excluded from extensive discussion in this manuscript, the efficacy and safety performance of this small cohort of patients was consistent with results in group 1. Of the remaining 197 potential patients eligible for enrollment in groups 1 or 2 in the extension study, there were a combined 64, 84, and 63 eyes with data available at 36, 48, and 60 months, respectively.

Results were thus stratified into two groups: group 1, comprising patients aged 65 to <75 years, and group 2, comprising patients ≥75 years of age. Where age is identified or discussed, it is the age of the patient at the time of device implantation in study IMT-002.

All authors received approval of an institutional review board at each clinical study site. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Declaration of Helsinki of 1975, as revised in 2000 and 2008. Informed consent was obtained from all patients before inclusion in the study.

# Results

A total of 217 patients were enrolled in the IMT-002 study. There were 63 patients with 60 months of follow-up in IMT-002-LTM (31 patients in group 1 and 32 patients in group 2). Overall, similar to the reported 1-year and 2-year results,[14,15] the 60-month results reflect a continued benefit in this patient population, and a somewhat better outcome in group 1 than in group 2.

## Efficacy

Overall, patients experienced a mean improvement in BCDVA of 3.2 lines at 24 months, the end of study IMT-002, and 2.4 lines at 60 months, the end of study IMT-002-LTM. At the final study visit (60 months), 62% maintained a clinically significant 2-line improvement in BCDVA. Mean change in BCDVA in patients stratified by age is presented in Table 1.

Retention of visual acuity gains was higher in group 1 than in group 2. In group 1, mean BCDVA improvement was 3.3 lines at 24 months and 2.6 lines at 60 months. In group 2, mean BCDVA improvement was 3.1 lines at 24 months and 2.1 lines at 60 months. A substantially larger percentage of patients in group 1 retained ≥3 lines of vision at month 60 than in group 2 (58% versus 38%, respectively).

At 60 months, one patient in group 1 and three patients in group 2 had lost >2 lines of BCDVA (3.2% and 9.4%, respectively, see Table 2). Vision loss in the fellow (nonimplanted)

**Table 1** Best-corrected distance visual acuity in implanted with the implantable miniature telescope, stratified by age group

| | 12 months | 24 months | 36 months | 48 months | 60 months |
|---|---|---|---|---|---|
| **Age 65 to <75 years (group 1)** | | | | | |
| n | 65 | 60 | 22 | 38 | 31 |
| Gain ≥3 lines | 43 (66.2%) | 37 (61.7%) | 11 (50.0%) | 22 (57.9%) | 18 (58.1%) |
| Gain ≥2 lines | 52 (80.0%) | 45 (75.0%) | 15 (68.2%) | 26 (68.4%) | 21 (67.7%) |
| Mean ± SD line change | 3.6±2.1 lines | 3.3±2.0 lines | 2.4±2.8 lines | 2.7±2.6 lines | 2.7±2.7 lines |
| **Age ≥75 years (group 2)** | | | | | |
| n | 109 | 95 | 42 | 46 | 32 |
| Gain ≥3 lines | 72 (66.1%) | 55 (57.9%) | 24 (57.1%) | 19 (41.3%) | 12 (37.5%) |
| Gain ≥2 lines | 87 (79.8%) | 71 (74.7%) | 31 (73.8%) | 29 (63.0%) | 19 (59.4%) |
| Mean ± SD line change | 3.4±2.2 lines | 3.1±2.2 lines | 3.0±1.8 lines | 2.2±2.6 lines | 2.1±2.9 lines |

**Abbreviation:** SD, standard deviation.

**Table 2** Vision loss stratified by age group

| | 12 months | 24 months | 36 months | 48 months | 60 months |
|---|---|---|---|---|---|
| **Age 65 to <75 years (group 1)** | | | | | |
| n | 65 | 60 | 22 | 38 | 31 |
| Loss ≥2 lines | 1 (1.5%) | 0 (0.0%) | 2 (9.1%) | 2 (5.3%) | 3 (9.4%) |
| **Age ≥75 years (group 2)** | | | | | |
| n | 109 | 95 | 42 | 46 | 32 |
| Loss ≥2 lines | 2 (1.8%) | 2 (2.1%) | 0 (0.0%) | 2 (4.3%) | 3 (9.4%) |
| **Fellow (non-implanted) eyes** | | | | | |
| **Age 65 to <75 years (group 1)** | | | | | |
| n | 65 | 60 | 22 | 38 | 31 |
| Loss ≥2 lines | 4 (6.2%) | 3 (5.0%) | 2 (9.1%) | 4 (10.5%) | 5 (16.1%) |
| **Age ≥75 years (group 2)** | | | | | |
| n | 109 | 95 | 42 | 46 | 32 |
| Loss ≥2 lines | 10 (9.2%) | 12 (12.5%) | 6 (14.3%) | 6 (13.0%) | 9 (28.1%) |

eye was substantially higher at all time points in both groups, suggesting that potential disease progression and/or other binocular comorbidities may be causative factors.

## Subjective outcomes

Self-reported quality of life at 12 months was assessed by the National Eye Institute's Visual Function Questionnaire 25-item scores. The survey was not repeated at subsequent follow-up time points, as it is believed the most substantial differences would be noted initially and not over longer periods of time. Overall, there were clinically significant improvements in the composite score and vision-specific subscales (general vision, near activities, and distance activities) as well as psychosocial vision-targeted subscales (social functioning, mental health, role difficulties, and dependency). In subscales where no improvement or a decline in performance was expected (color vision, driving, ocular pain, and peripheral vision), performance was stable or declined. A 5-point change in individual subscales or the composite scale is clinically significant.[16]

In the age stratification (Table 3), both groups showed clinically significant quality of life improvement from baseline in the majority of subscales. Quality of life gains were highest in group 1 for the number of subscales with significant improvement, the changes in subscale scores, and changes in composite score.

## Ocular complications

Ocular complications were defined as events directly related to the surgical procedure for intraocular telescope implantation, whether successful or not, occurring in the operative and immediate postoperative period, defined as the first 3 months. Events occurring after the immediate postoperative period were classified as AEs. Significant ocular complications reported for the IMT-002 and IMT-002-LTM studies are provided in Table 4.

There were 217 patients included in the safety analysis and 206 telescope-implanted eyes in study IMT-002. Reasons for patient exclusions (11/217) in the efficacy analysis have been previously discussed for all age groups.[14,15] In IMT-002-LTM, group 2 had the highest cumulative incidence of complications in 13 (87%) of 15 categories. Only iris damage and iris prolapse occurred more frequently in group 1.

There were 17 events that qualified as significant AEs, but there were no reported events of endophthalmitis, retinal

**Table 3** Results for quality of life questionnaire

| NEI VFQ-25 subscale* | Age 65 to <75 years (group 1) | Age ≥75 years (group 2) |
|---|---|---|
| | Change from preoperative mean score (95% CI) n=65 | Change from preoperative mean score (95% CI) n=109 |
| General vision | 20 (14, 26) | 9 (5, 13) |
| Near activities | 14 (9, 20) | 8 (5, 12) |
| Distance activities | 12 (6, 17) | 5 (0, 9) |
| Color vision | 6 (0, 12) | 1 (–4, 6) |
| Social functioning | 17 (6, 21) | 6 (1, 10) |
| Mental health | 15 (10, 21) | 5 (1, 9) |
| Role difficulties | 16 (10, 22) | 3 (–1, 8) |
| Dependency | 13 (6, 19) | 7 (2, 12) |
| Ocular pain | 3 (–1, 8) | –1 (–4, 3) |
| Driving | 0 (–1, 2) | –1 (–3, 0) |
| Peripheral vision | –8 (–16, 0) | –4 (–10, 2) |
| Overall composite | 10 (6, 13) | 3 (1, 6) |

**Note:** *Not all patients completed the questionnaire.
**Abbreviations:** NEI, National Eye Institute; CI, confidence interval; VFQ-25, Visual Function Questionnaire 25-item.

**Table 4** Significant ocular complications in the operated eye through 60 months

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

detachment, or retinal tear (Table 5). Group 2 reported more AEs in eleven of the 14 reported category events (79%).

There was a decrease in BCDVA of >2 lines in 15/217 patients (7%) at the last available visit compared with baseline in the operated eye. There were 31 nonoperated fellow eyes reported with BCDVA loss of ≥2 lines (16%). The number of patients and percentage of patients with BCDVA loss was highest in group 2 for both operated eyes and nonoperated fellow eyes (Table 6).

Baseline mean ECD was 2,496 cells/mm$^2$ in the 206 IMT-implanted eyes, and 3 months after telescope implantation, the mean ECD was 1,995 cell/mm$^2$; the acute mean percent ECD loss was 20%. Reasons for the ECD loss have been discussed previously,[13–15] and are likely a result of the 12 mm corneal incision and manipulation of the telescope during implantation. At all follow-up visits (months 3, 12, 24, 36, 48, and 60) in the extension study, the percentage of patients with ECD <1,000 cells/mm$^2$ was highest in group 2,

**Table 5** Significant adverse events in operated eyes through 60 months

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

**Abbreviation:** BCDVA, best corrected distance visual acuity.

**Table 6** Visual acuity loss in the nonimplanted eyes through month 60

| | Age 65 to <75 years (n=70) | | Age ≥75 years (n=127) | |
|---|---|---|---|---|
| | n | % | n | % |
| Decrease >2 lines in BCDVA in nonimplanted fellow eye | 7 | 10.0 | 24 | 18.9 |

**Abbreviation:** BCDVA, best corrected distance visual acuity.

as was the percent of patients with ECD <750 cells/mm$^2$, except for months 36 and 60. Table 7 describes the corneal ECD counts through month 60 (only those eyes enrolled in both IMT-002 and IMT-002-LTM). Of the 206 implanted eyes in IMT-002, 21 (10%) were reported with ECD <750 cells/mm$^2$ at two consecutive visits or at the last visit (by month 24).

## Explantation

The telescope was removed from 12 (5.8%) of 206 IMT-implanted eyes in the first 24 months. In all cases, a conventional intraocular lens replaced the explanted telescope.[14,15] The telescope was removed in ten patients in group 2, one patient in group 1, and one patient in the youngest patient cohort (aged 55–65 years). Possible surgical trauma to two devices during implantation resulted in formation of condensation inside the telescope, necessitating telescope explant. Two telescopes were removed during corneal transplant procedures, and eight devices were removed due to patient dissatisfaction.

# Discussion

In study IMT-002-LTM, 60 months after telescope implantation in patients with bilateral end-stage AMD, the mean BCDVA gain was 2.41 lines, with 36/76 (47.4%) achieving a 3-line gain and 47/76 (61.8%) achieving a 2-line gain. Although not a designated arm of this study, patients younger than 65 years were followed and received the same care/evaluations as those in groups 1 or 2. This group had better mean BCDVA, with a higher percent achieving both 2-line and 3-line gains by 60 months: 77.8% (n=14) had gained ≥2 lines of vision by month 24. A total of 13 patients in this youngest age group reached 60 months; of those, 46.2% (n=6) had gained ≥3 lines of vision, with a mean gain of 2.58±2.58 lines. They also had fewer overall complications. Of the 20 initial patients in the youngest age group, there was a total of five AEs, three of which were posterior capsule rupture.

The initial US approval for IMT implantation was in patients older than 75 years. However, this long-term study has shown that over the first 60 months post-implantation, patients aged 65–75 years have a favorable efficacy and safety profile after implantation of the IMT for the treatment of end-stage AMD compared with the older cohort. Telescope implantation does not expose patients aged 65 to <75 years (or even patients <65 years of age) to a higher undue safety risk as compared with patients ≥75 years of age. Patients in group 1 (the younger group) had fewer surgical complications, which supports other studies suggesting that increasing age itself is a risk factor for surgical complications, including posterior capsule rupture and corneal edema.[17,18] In this study, these were two of the three most common complications (the third being iris prolapse) across all groups. Corneal edema affected 7.9% of those in group 2, 4.3% of those in group 1, and 5% of those in the youngest group (under 65 years of age). Iris prolapse affected an equal number of patients in groups 1 and 2, and was not reported in the youngest age group.

**Table 7** Corneal endothelial cell density in implanted eyes through month 60 in IMT-002-LTM

| | Baseline | 3 months | 12 months | 24 months | 36 months | 48 months | 60 months |
|---|---|---|---|---|---|---|---|
| **Age 65 to <75 years (group 1)** | | | | | | | |
| n | 68 | 65 | 65 | 59 | 22 | 35 | 28 |
| Mean ECD | 2,444 | 1,984 | 1,866 | 1,775 | 1,569 | 1,618 | 1,552 |
| 95% CI | 2,362, 2,525 | 1,849, 2,118 | 1,731, 2,002 | 1,637, 1,914 | 1,323, 1,815 | 1,429, 1,808 | 1,325, 1,779 |
| Mean change in ECD | | –18% | –23% | –27% | –33% | –32% | –35% |
| 95% CI | | –23, –13 | –28, –18 | –32, –21 | –43, –24 | –39, –25 | –44, –27 |
| **Age ≥75 years (group 2)** | | | | | | | |
| n | 119 | 111 | 102 | 94 | 39 | 42 | 29 |
| Mean ECD | 2,499 | 1,957 | 1,823 | 1,762 | 1,677 | 1,579 | 1,576 |
| 95% CI | 2,433, 2,564 | 1,843, 2,072 | 1,703, 1,943 | 1,631, 1,893 | 1,475, 1,880 | 1,385, 1,772 | 1,333, 1,819 |
| Mean change in ECD | | –22% | –28% | –30% | –34% | –38% | –40% |
| 95% CI | | –26, –18 | –32, –24 | –35, –25 | –41, –27 | –45, –31 | –48, –32 |

**Note:** Not all patients were available for all follow-up visits.
**Abbreviations:** CI, confidence interval; ECD, endothelial cell density.

Numerous complications occurred only in group 2, including aborted surgery, choroidal detachment or hemorrhage, phthisis, vitreous hemorrhage/loss, and vitreous in the anterior chamber, once again adding to the literature that age itself is a factor for potential surgical complications. There were, in fact, no complications that occurred more frequently in younger patients than in group 2.

In all other measured outcomes, the group 1 patients had a greater BCDVA gain and retention, lower rates of AEs, and a lower percentage of corneal ECD loss compared with their older counterparts in group 2. However, 50% of those in group 1 who developed persistent corneal edema (n=4) needed a corneal transplant, compared with only 22% of those in group 2 who developed persistent corneal edema (n=9). There were also more eyes in group 1 that developed persistent iritis (n=7) compared with group 2 (n=5), but otherwise more significant AEs occurred in the older cohort. It is interesting to note, however, that none of the patients in the youngest group developed persistent iritis, and only one patient developed persistent corneal edema resulting in a corneal transplant.

In our study, 3-month ECD loss in group 1 (18%) and group 2 (22%) is similar to the higher rates reported in other high-risk patient populations.[19–22] These rates are likely a result of the surgical trauma itself since the rates declined over the remaining follow-up visits, although they never reverted to "normal" cell density decreases of about 0.6% per year in healthy eyes.[23] The ECD losses reported in this analysis (20% at 3 months) are consistent with large incision cataract surgery (19% at 2 months).[24]

While bilateral end-stage AMD is a different disease entity from cataract, and the IMT, which has a unique and clinically important benefit/risk equation, is different in function and size from an intraocular lens, there is a mild additional risk of ECD loss over time for patients aged 65 to $<$75 years as a result of longer life span than for patients aged $\geq$75 years. In our study, group 1 had a lower percentage of ECD loss than group 2 by month 60, but had approximately the same mean number of endothelial cells by month 60, ie, 1,552 in group 1 and 1,576 in group 2. In the youngest group, the mean number of endothelial cells was much higher (1,770 by month 60), but still represented a 31% loss from baseline.

However, our rates of cell loss are not anomalistic to published studies: one study found corneal endothelial cell loss to be 18%–19% in an aged group (75+ years) one month after cataract surgery.[25] Surgical implantation of a device has resulted in higher rates of cell loss, even without chronic degenerative disease being present.[24,26–31] The 3% (upper 95% confidence interval 4.4%) mean annual ECD percent loss in all patients was consistent with reports in the literature of an annual chronic mean cell loss of 2.8% in patients undergoing large incision conventional cataract surgery and intraocular lens implantation.[24]

In group 2 (the older cohort), there was a higher ECD loss in patients with shallow chambers. However, their shorter life span likely offsets the general risk of acute and long-term loss. In theory, a patient with substantial ECD loss at the time of surgery yielding only 1,000 cells/mm$^2$ post-surgery would have 694 cells/mm$^2$ at 12 years (the average life expectancy of a female aged 75 years) postoperatively and 596 cells/mm$^2$ at 17 years postoperatively, assuming an average ECD loss of 3% per year.

This study is not without its limitations. The investigators were unable to perform all measurements on all patients during the follow-up visits. As noted, the original point of exit for IMT-002 was 24 months; at the request of the US Food and Drug Administration, the extension study was undertaken and not all patients chose to continue. There are numerous reasons that could account for the low number of patients enrolled in the extension study compared with the original study, among them distance to participating site, lost to follow-up, disinterest in continued monitoring on a particular schedule, or difficulty arranging transport. This may have skewed the results in favor of the group with the higher number of participants because various outliers would not be as obvious. However, in our extension study, the group with the smaller numbers (group 1) had consistently better results across all parameters monitored. This suggests the device functions at least as well for the younger cohort as it does for the older cohort.

End-stage AMD is more likely to occur in an older patient, and our study demographics reflect real-world settings, accounting for the low number of patients in the youngest group (aged 55–65 years). Another potential limitation is the study's strict exclusion criteria based on ECD (among other variables). It is possible that the clinical results from the 5-year analysis of study patients may not be reflective of real-world clinical settings, as often occurs. Finally, as with any open-label study, our research brings with it all the potential biases of investigators in an unmasked study.

There are several strengths to this extension study. This is the first analysis of the long-term results of an implantable optical device for this particular end-stage disease. Younger patients fared better in terms of BCDVA and AEs, but that was somewhat expected as younger patients are also unlikely

to have as many comorbidities as their older counterparts. This study analyzed the data stratified by age to determine what, if any, differences occurred in outcomes between a younger cohort and an older cohort and found all outcomes were more favorable in the younger group.

## Conclusion

The long-term (60-month) results in patients implanted with the IMT show substantial BCDVA improvement and retention, both of which were better in a younger group of patients (aged 65–75 years) than in an older group (older than 75 years). Chronic ECD loss across all patients was consistent with that reported in the literature. Younger patients also had fewer reported AEs than their older counterparts. The IMT performed as well in the 20 patients aged 55–65 years as in those aged 65–75 years.

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## Author contributions

The named authors meet the International Committee of Medical Journal Editors criteria for authorship of this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval of the version to be published.

## Disclosure

Data from this paper have been presented in part at the Annual Meeting of the Association for Research in Vision and Ophthalmology, 2015. Neither the authors nor any of the participants in the IMT-002 study group has a direct financial or proprietary interest with the subject matter. The authors report no conflicts of interest in this work.

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