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Authors

Holbrook, Janet T
Sugar, Elizabeth A
Burke, Alyce E
et al.

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Dissociations of the Fluocinolone Acetonide Implant: The Multicenter Uveitis Steroid Treatment (MUST) Trial and Follow-up Study

Janet T. Holbrook, PhD[1], **Elizabeth A. Sugar, PhD**[1,2], **Alyce E. Burke, MS**[1], **Albert T. Vitale, MD**[3], **Jennifer E. Thorne, MD, PhD**[1,4], **Janet Davis, MD**[5], **Douglas A. Jabs, MD, MBA**[1,6], and **for the Multicenter Uveitis Steroid Treatment (MUST) Trial Research Group**[7]

[1]Department of Epidemiology, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD

[2]Department of Biostatistics, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD

[3]Moran Eye Center and Department of Ophthalmology, University of Utah School of Medicine, Salt Lake City, UT

[4]Wilmer Eye Institute and the Department of Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, MD

[5]Bascom Palmer Eye Institute and Department of Ophthalmology, University of Miami School of Medicine, Miami, FL

[6]Departments of Ophthalmology and Medicine, Icahn School of Medicine at Mount Sinai, New York, NY

Abstract

Purpose—To describe fluocinolone acetonide implant dissociations in the Multicenter Uveitis Steroid Treatment (MUST) Trial.

Design—Randomized clinical trial with extended follow-up.

Methods—Review of data collected on the first implant in the eye(s) of participants. Dissociation was defined as the drug pellet no longer being affixed to the strut and categorized as spontaneous or surgically-related.

Corresponding author: Douglas A. Jabs, MD, MBA, Department of Ophthalmology, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, Box 1183, New York, NY 10029. **Phone:** 212-241-6752 **Fax:** 212-241-5764 douglas.jabs@mssm.edu.

[7]Members of the MUST Research Group are listed at www.ajo.com.

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Results—250 eyes (146 patients) had at least one implant placed. Median time follow-up time after implant placement was 6 years (range 0.5 to 9.2). Thirty-four dissociations were reported in 30 participants. There were 22 spontaneous events in 22 participants; 6-year cumulative risk of a spontaneous dissociation was 4.8% (95% confidence interval (CI): 2.4%–9.1%). The earliest event occurred 4.8 years after placement. Nine of 22 eyes with data had a decline in visual acuity ≥5 letters temporally related to the dissociation. 39 implant removal surgeries were performed, 33 with replacement. Twelve dissociations were noted during implant removal surgeries in 10 participants (26%, 95% CI 15%–48%); 5 of these eyes had a decline in visual acuity ≥5 letters after surgery. The time from implant placement to removal surgery was longer for the surgeries at which dissociated implants were identified than for those without one (5.7 vs 3.7 years, $p < 0.001$). Overall, visual acuity declined 15 or more letters from pre-implant values in 22% of affected eyes; declines were frequently associated with complications of uveitis or it's treatment.

Conclusion—There is an increasing risk of dissociation of Retisert implants during follow-up, the risk is greater with removal/exchange surgeries, but both the risk of spontaneous and surgically related events increase with longevity of the implants. In 22% of affected eyes visual acuity declined by 15 letters. In the context of eyes with moderate to severe uveitis for years, this rate is not unexpected.

Introduction

The fluocinolone acetonide intraocular implant (Retisert®, Bausch and Lomb, Bridgewater, New Jersey) is a Food and Drug Administration (FDA)-approved treatment for non-infectious intermediate, posterior, and panuveitis.[1,2] The fluocinolone acetonide implant is designed to allow sustained release of corticosteroid for approximately 2.5 years. The implant is made of a non-biodegradable polymer, and consists of suture strut that anchors the implant to the eye wall and a drug pellet containing fluocinolone acetonide, which is glued to the strut. The pellet can become unglued from the strut, which is referred to as a "dissociation"; if the pellet also separates from the strut it is characterized as a "dislocated" pellet.

Dissociation of the drug pellet, with or without dislocation, is a recognized complication of treatment with the fluocinolone acetonide implant and typically has been reported to occur without serious sequelae or visual loss. A retrospective study of 224 patients with 407 implants from 2 centers with a median follow-up of 3.4 years (range 0.9 to 12 years) reported 17 spontaneous dislocations of the drug pellet; the major risk factor for spontaneous dislocations was time since placement of the implant.[3] Three other retrospective case series have reported a total of 9 cases of spontaneous implant dislocations discovered on clinical examination after patients noticed visual symptoms; these events occurred between two and seven years after implant placement.[4–6] Dissociations, with or without dislocations, have also been reported in conjunction with surgeries to remove and replace implants. Nicholson and colleagues[7] reported that the pellet was noted to be dissociated from the strut in 40% of 27 surgical procedures occurring between 2001 and 2010; Itty and colleagues[3] reported a lower frequency, 14% of 77, noted at the time of implant exchange.

The risk of dissociation and dislocation of fluocinolone acetonide implants has not been evaluated prospectively. We reviewed data from the cohort of patients who were enrolled and followed in the Multicenter Uveitis Steroid Treatment (MUST) Trial and Follow-up Study to evaluate the risks of implant dissociation and dislocation and effects on visual acuity. The trial enrolled 255 participants with noninfectious intermediate, posterior or panuveitis for which systemic corticosteroids were indicated;[8] participants were randomly assigned to receive either fluocinolone acetonide implants or systemic treatment for uveitis. The results of the MUST Trial after 2 years and 4.5 years of follow-up have been reported;[9–11] vision preservation was similar in both groups; the implant was more effective for suppressing uveitis activity but was associated with more ocular side-effects, such as cataract and elevated intraocular pressure, and a higher incidence of glaucoma than systemic treatment.[9–11] Herein, we report the occurrence of dissociations and dislocations for the first fluocinolone acetonide implant placed in each eye with uveitis in the MUST Trial and Follow-up Study.

Methods

Participants

Details regarding the design, surgical techniques, baseline characteristics, and 2-year and 4.5-year results of the original MUST Trial are reported elsewhere.[8–11] Briefly, eligible patients 13 years of age or older were enrolled in the MUST Trial at 23 centers in the United States, the United Kingdom, and Australia between December 2005 and December 2008. Patients meeting the eligibility criteria in both eyes were assigned to receive the same treatment in both eyes. Participants under follow-up at the end of the trial period (December 2010) were invited to continue follow-up in the MUST Follow-up Study that commenced in January 2011 and currently is ongoing. All participants signed informed consent statements for the trial approved by the clinical center institutional review boards (IRBs). Participants that continued in MUST Follow-up Study signed a second IRB-approved consent statement for that study. The clinical trial is registered at ClinicalTrials.gov (NCT00132691). Both MUST studies are in compliance with HIPAA regulations.

Data collection

Participants were seen every 3 months during the MUST Trial period (December 2005 to December 2010) and every 6 months in the MUST Follow-up Study (January 2011 to data base closure for this analysis in March 2015). Visits include slit lamp and indirect ophthalmic examinations, color fundus photography, and best-corrected visual acuity assessments according to Early Treatment Diabetic Study procedures.[9–12] Placement and removal of implants were performed by MUST Trial-certified ophthalmic surgeons, and data regarding these surgeries were collected.

This analysis includes all eyes that received a fluocinolone acetonide implant during the course of the MUST Trial or Follow-up Study between December 2005 and March 2015, regardless of the original treatment assignment or uveitis status at baseline. Results are limited to the first implant(s) a participant received in an eye(s) with uveitis during the trial or follow-up study.

Main outcomes measures

The main outcome was dissociation of the implant; dissociated implants were further classified as being dislocated (separated from the strut) or not. There were two circumstances under which the dissociations were identified: 1) spontaneous events identified or confirmed by clinical examination; and 2) events that were identified during implant removal surgery. For events identified during surgery it was not possible to definitively distinguish between pre-existing events and those caused by surgery. Hence, we grouped both types of surgery-related events together in this report. A decline or improvement in visual acuity was defined as a change of 5 or more letters; stable vision was defined as a visual acuity measurements within 5 letters of the comparator measurement.

Statistics

Time to spontaneous dissociation was measured from the date that the implant was placed until the date of the discovery or confirmation of a spontaneous dissociation at a clinic visit. Implanted eyes without a spontaneous dissociation were censored at the date of removal or the date of last follow-up, whichever came first. Kaplan-Meier estimates of the survivor function were used to graphically display the cumulative proportion with a spontaneous dissociation.[13] For surgical dissociations, generalized estimating equations were used to fit regression models while accounting for between-eye correlation. Logistic regression was used to estimate the 95% confidence interval (CI) of the point estimate for probability of dissociation, and linear regression was used to compare the time from implantation to surgery for those who had a dissociation as compared to those that did not. Robust standard error estimates were computed.[14] Statistical analyses were performed using SAS (SAS/STAT User's Guide Version 9.2, SAS Institute, Cary, NC) and R (The R Project for Statistical Computing, version 2.13.1, http://www.r-project.org/).

Results

Between December 2005 and March 2015, 320 implants were placed; 250 were first implants, 67 were second implants, and 3 were third implants (Figure 1). The 250 first implants were placed in the eye(s) of 146 of the 255 participants enrolled in the trial and form the basis of this report. Most of these participants, 71% (104 of 146), had implants placed in both eyes. The characteristics of the participants at the visit prior to implant placement surgery were similar to the overall MUST Trial cohort at baseline (Table 1).[8] Sixty-two percent these participants had posterior or panuveitis, and 27% of participants had uveitis associated with a systemic disease. Most participants (59%) self-identified as white, and most were women (74%). The median time since diagnosis of uveitis was 4.5 years (range 0 to 40.5 years) at the time of implantation. Median baseline visual acuity in the eye(s) with uveitis at baseline was 65 letters, which corresponds to a logMAR of 0.4 and a Snellen equivalent of 20/50. The median follow-up time after placement of the first study implant was 6.0 years (range 0.5 to 9.2 years). Of the 250 first implants, a total of 34 implants were identified as having dissociated, 29 with dislocation; these events occurred in 30 participants, four participants had dissociated implants in both eyes.

Spontaneous dissociations

Spontaneous dissociations were identified in 22 eyes of 22 participants between 4.8 and 8.6 years after placement (Table 2). In all cases the drug pellet was dislocated from the strut as well. Only one event was observed before 5 years (at 4.8 years) and the cumulative risk climbed to 4.8% (95% CI: 2.4%–9.1%) by 6 years (Figure 2). Most events (68%) were identified after the participant reported visual symptoms such as black spots, blurred or decreased vision; 7 events (32%) were asymptomatic and identified during a clinical examination.

Thirteen of the dislocated implants and 7 of the corresponding struts were surgically removed; 11 were removed without significant complications. Two eyes had retinal detachments associated with surgery and one of these eyes required a second surgery to remove the dislocated drug pellet. A second implant was placed in 6 of the 12 eyes: 4 during and 2 prior to the surgery to remove the first implant.

Twelve eyes had follow-up data on visual acuity after the dissociation. Visual acuity declined by more than one line (5 letters) in 6 of the 12 eyes as measured within 5 months of dissociation (Table 2; Supplemental Figure 1). Three of the 6 eyes with declines ranging from 33 to 91 letters, did not recover to pre-dissociation visual acuity, although 2 of the 3 showed substantial improvement. i.e., 20 to 63 letters. Three eyes with declines ranging from of 9 to 13 letters temporally related to dissociation, subsequently improved to a visual acuity exceeding the pre-event acuity. The remaining 6 eyes with follow-up had stable visual acuity after the discovery of the dissociation. Causes cited for the persistent declines were exudative retinal detachment, post-operative air-fluid vitrectomy and sub-retinal fibrosis, and epiretinal membrane with corneal opacity and a macular hole; other causes of decline cited were macular hole; chorioretinal atrophy; and hypotony with vitreous haze. Overall 6 of 11 eyes with sufficient data to evaluate had visual acuity ranging from −5 to +19 letters of the value measured prior to implant surgery 5.8 to 9 years after the implant was placed. In the 4 eyes with a declines ranging from 6 to 47 letters 6 to 9 years after surgery, only 1 was directly linked to the removal surgery. In the other 3 cases complications sited as affecting visual acuity were: macular edema (2), retinal atrophy (2), retinal detachment (1), and hypotony with vitreous haze (1). See supplement for details on individual cases.

Nine dislocated implants were not removed as of October 2015. We did not systematically record the rationale for not removing implants, although some forms noted that there were no vision loss or troublesome symptoms associated with the event so the decision was to continue observation. The observation time after the dislocated implant was identified in these 9 eyes ranged from 0 to 24 months, with a median time of 12 months (Table 2, Supplemental Figure 2). Three of these nine eyes had a decline in visual acuity of more than one line at the first measurement available after the dissociation was identified. One eye with a history of corneal clarity problems, macular edema recovered to pre-dissociation visual acuity within 4 months. The remaining two eyes in with persistent visual acuity loss had other complications: one that declined to −10 letters had cystoid macular edema and an epiretinal membrane; and the other hypotony and corneal edema associated with migration of a sustained-release dexamethasone pellet (Ozurdex®, Allergan, Inc., Irvine, CA) into the

anterior chamber. One eye with poor visual acuity prior to implantation (−10 letters) continued to have poor visual acuity throughout follow-up. The remaining 5 eyes had stable visual acuity after the discovery of the dissociation and continued to be stable or improved for the remainder of follow-up. In comparison to the visual acuity prior to implant placement, 4 of these 9 eyes had visual acuity decreases of more than 5 letters 6.2 to 9.1 years after implant surgery. In addition to the two cases noted above, two other eyes had 9 and 13 letter declines from their pre-surgery visual acuity that were attributed to glaucoma and corneal clarity with macular dysfunction, respectively. See supplemental Figure 2 for details.

Dissociations associated with surgery

There were a total of 39 implant removal/exchange surgeries performed (excluding surgeries performed to remove implants that spontaneously dissociated) at 12 centers to remove the first implant (n=6) or to replace the initial implant (n=33). Twelve (26%, 95% CI: 15%–48%) implant dissociations were noted during surgery in 10 participants (Table 3); 7 of these implants were dislocated from the anchoring struts. No complications were noted during surgery for 10 eyes; in the remaining two eyes the drug pellet dislocated during surgery and was not removed. The time from implant placement to removal surgery was longer for the surgeries at which a dissociation was identified compared to those without a dissociation, 5.5 vs 3.7 years ($p < 0.001$).

Visual acuity measurements were available from these eyes 2 to 46 months after surgery. Five eyes had a decline of more than one line noted after surgery (Table 3, Supplemental Figure 3). Causes cited for the decline were macular atrophy or macular edema (3), and glaucoma and retinal scarring (1); for one eye no reason was cited. Visual acuity subsequently returned to within one line of pre-surgery levels in 4 of 5 eyes and within 7 letters in the remaining eye. Over all follow-up since implantation, 4 of the 12 eyes with surgically-related dissociations had visual acuity loss of more than 5 letters from the pre-implant measurement; losses ranged from 10 to 37 letters. Reasons for visual loss were cited as a macular hole (1), uveitis (1) and not specified in 2 cases. See supplemental Figure 3 for details.

Overall 56% of the affected eyes (18 of 32 with follow-up) visual acuity was better or the same at the last recorded measurement as compared to the acuity measured prior to placement of implants, 5.8 to 9.2 years after the first implant was placed. The remaining 14 eyes with dissociation of the first implant had a decline in vision of least 1 line and 7 of which had a decline of 15 letters or more: 6 with spontaneous dissociations and 1 with a surgically related dissociation. There were multiple factors cited as contributing to vision decline, the most common was macular edema or atrophy. In only 1 case was visual acuity loss directly linked to dissociation, i.e., an air-fluid vitrectomy was a complication of removal of a dislocated implant.

Discussion

In patients with fluocinolone acetonide implants followed prospectively from implantation according to a study protocol we found the rate of spontaneous dissociation and dislocation

to be low, 4.8% at 6 years, and to increase with time since implant placement. Spontaneous dissociations all involved dislocation of the drug pellet, at least by the time they were observed. Time since implantation was also linked to dissociations that occurred during surgery. In all of the observed cases, it is likely that drug pellets were empty and not therapeutically effective since the estimated drug delivery time for the Retisert is 2.5 years. These findings are consistent with the low rates of spontaneous dislocation that increased over time reported in a large retrospective study done at two centers.[3]

Short-term visual acuity losses were common among participants with spontaneous dissociations (9 of 21) and with dissociations discovered during surgery (5 of 12). However, the visual acuity recovery was lower in the spontaneous dissociations (3 of 9) versus the surgical cases (4 of 5). Over the longer term the visual outcomes for most participants with dissociated implants were similar regardless of the how the dissociation was identified or whether the implant was removed, 50% to 58% had visual acuity that was stable or better than the pre-implant acuity 6 to 9 years after implantation, which is a good outcome. About 22% of eyes (7 of 32 with data) with dissociated implants experienced visual acuity loss of 15 letters or more 6 to 9 years after the original surgery, 6 of these were in eyes with spontaneous dissociations. In most of these cases it is impossible to disentangle the direct effect of the dissociated implant or its' removal from the effects of uveitis or other treatments on visual acuity; macular edema or atrophy were frequently cited as a contributing cause. Hence, our results are not directive as to whether implants should be removed, before or after dissociation. Complications related to spontaneous events are likely dependent on what happens to the drug pellet after dislocation. A free floating drug pellet is more likely to cause visual symptoms and poses greater risk of causing complications than one that becomes lodged in the inferior uvea. Removal of the pellet entails other risk associated with surgery, however, we noted only one of which was definitively linked to the operative procedure, i.e., complications of air-fluid vitrectomy.

In the retrospective study by Itty and colleagues[7] reporting 17 dislocated implants, visual acuity declined in 5 of 17 eyes (29%); 4 with the dislocated implant removed, and 1 under observation. The apparent larger immediate impact on visual acuity seen in our study (13 of 33 eyes, 39%) is likely due to the fact that we measured the impact based on visual acuity assessments obtained 1 to 18 months before the dislocated implants were detected rather than at the time of detection. Regardless, it is encouraging that extended follow-up showed that visual acuity recovered or exceed pre-dislocation levels in 58% of affected eyes, including 6 of the 13 eyes with immediate declines. Others have reported retinal tears, hemorrhage or corneal edema associated with dislocated implants.[3–7]

The frequency of dissociations discovered at or occurring during surgical removal of the implant was 26% in our study, compared to 11% and 41% of surgeries by others.[3,7] In all of these reports, dissociations were associated with the implant residing within the eye for a longer time period. Our results are consistent with those reported by Itty and colleagues,[3] i.e., implants that were dissociated at surgery had resided in eyes for a mean time of 5.5 years whereas those that did not were in place for a mean of about 3.7 years. Nicholson and colleagues[7] reported a similar effect but with shorter time periods, mean times since placement of 3.9 versus 2.7 years for dissociated and intact implants, respectively. One

reason for the discordant estimates for the rate of surgicallyrelated dissociations and the shorter time periods could be that the Nicholson[7] series may have included more of the first generation implants. Manufacturing processes were re-engineered after the manufacturer noted higher than acceptable rates of dissociation in quality assurance testing. However, Nicholson[7] did not detect difference in the dissociation rates between the two “generations” of implants. Some of those earlier implants were included in the study by Itty;[3] but our study only included only the re-engineered version of the implant. There could also have been differences in operative technique that influenced dissociations. We observed 7 of 12 cases in which the drug pellet was found to be dislocated or dislocated during surgery, whereas Itty[3] reported no such occurrences and Nicholson[7] reported only 2 of 11 cases. Furthermore, details about the event may have been missing in the retrospective studies. We also report a greater, albeit transient, impact on visual acuity than either of these two series.[3,7] However, both of those studies used pre-operative visual acuity assessment as a baseline whereas we used the last assessment 1 to 18 months prior to surgery and 5.8 to 9.6 years prior to placement of the implant to evaluate short and long-term associations with visual acuity, respectively.

The results of all of the studies published to date suggest that implant dissociations that are discovered or caused by surgical removal of implants are not likely to cause permanent damage to vision and are usually uncomplicated. We agree with others that surgeons should be prepared for the possibility of dissociation and dislocation on fluocinolone acetonide removal, which should include informing patients about that risk and the potential need for additional surgical maneuvers to extract a dissociated implant, e.g., vitrectomy. Surgical strategies that have been recommended to reduce risk of dissociation include use of infusion ports, making larger scleral wounds to facilitation removal, grasping drug pellet with forceps, and gaping the wound to ensure clearance.[7,15] It may also be advisable to routinely remove implants when new fluocinolone acetonide implants are placed. Furthermore, if it is anticipated that a patient will require replacement, it may be advisable to perform those surgeries at the earliest indication rather than observing the patient for a prolonged period. The cumulative experience also indicates that the risk of spontaneous dislocation of implants increases with time and have a higher risk of complications and vision loss. Monitoring of patients with fluocinolone acetonide implants should include an attempt to visualize the integrity of the implant at each clinical assessment. Decisions about removal of a dissociated and dislocated implant identified on clinical examination will depend on the particular circumstances of the patient including the presence of visual symptoms, uveitis activity and presence of other complications.

Strengths of our analysis is that we have regular follow-up on all participants with implants and uniform procedures for measuring visual acuity, so our results are less likely to be affected by ascertainment bias. However, the results are limited to implants manufactured between 2003 and 2011. The implant manufacturing process was re-engineered in 2001 and again in 2011, both times to strengthen the attachment between the drug pellet and the anchoring strut.[1] Hence, our results do not apply to implants manufactured before 2001, and there has not been enough experience to date with the implant re-designed in 2011 to determine whether the modifications prevent or reduce dissociations. Furthermore, we don’t know what would have happened to the visual acuity in these eyes if no implant was ever

placed. Uveitis is a chronic disease and visual acuity loss is not unexpected. Continued follow-up of the MUST Trial cohort will allow us to address that question in the future as well as enabling further precision of the quantification of the risk of dissociation and dislocation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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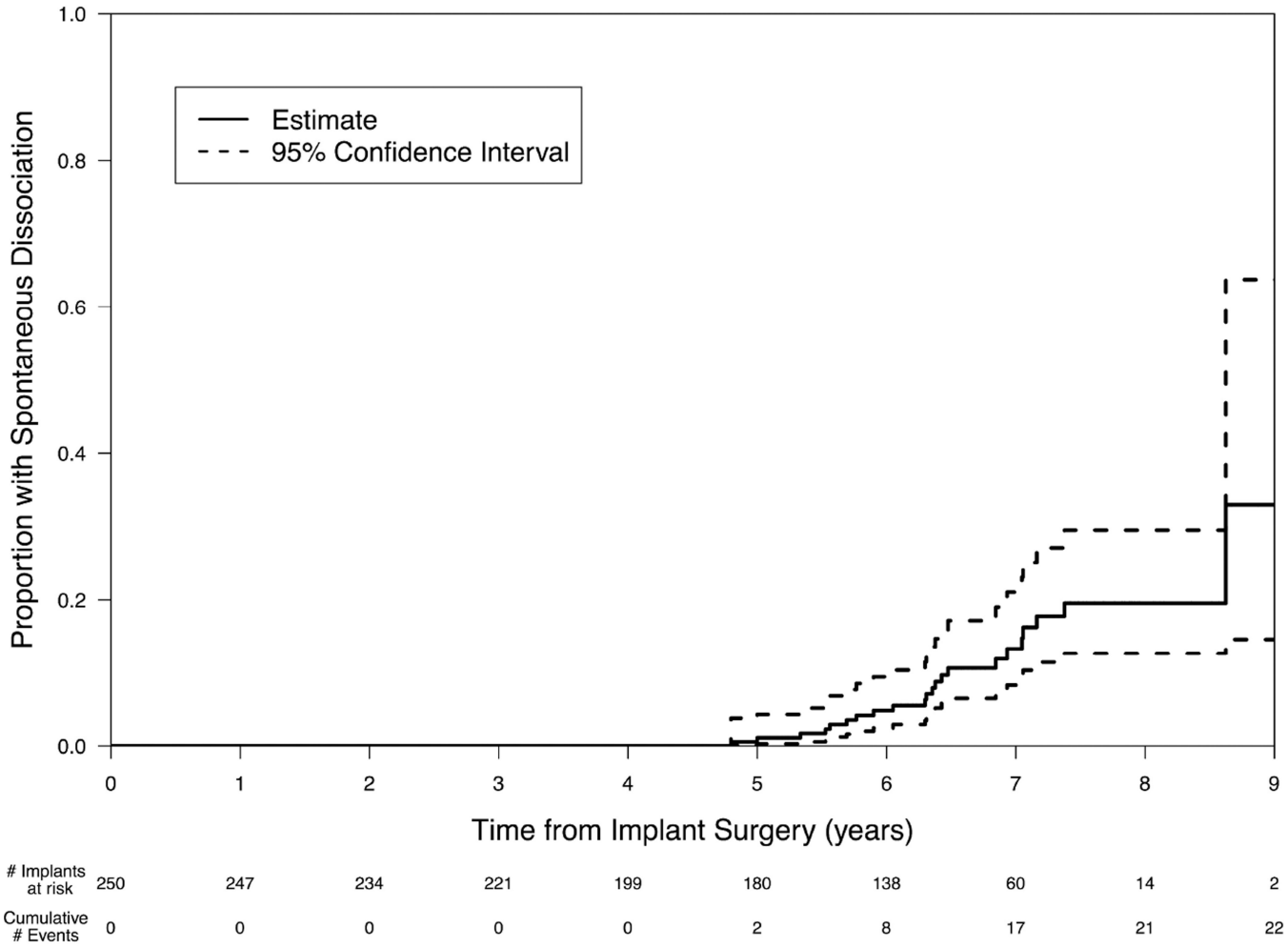

Figure 1.

Fluocinolone acetonide implant placements and dissociations in the MUST Trial and Follow-up Study (December 2005 to March 2015)

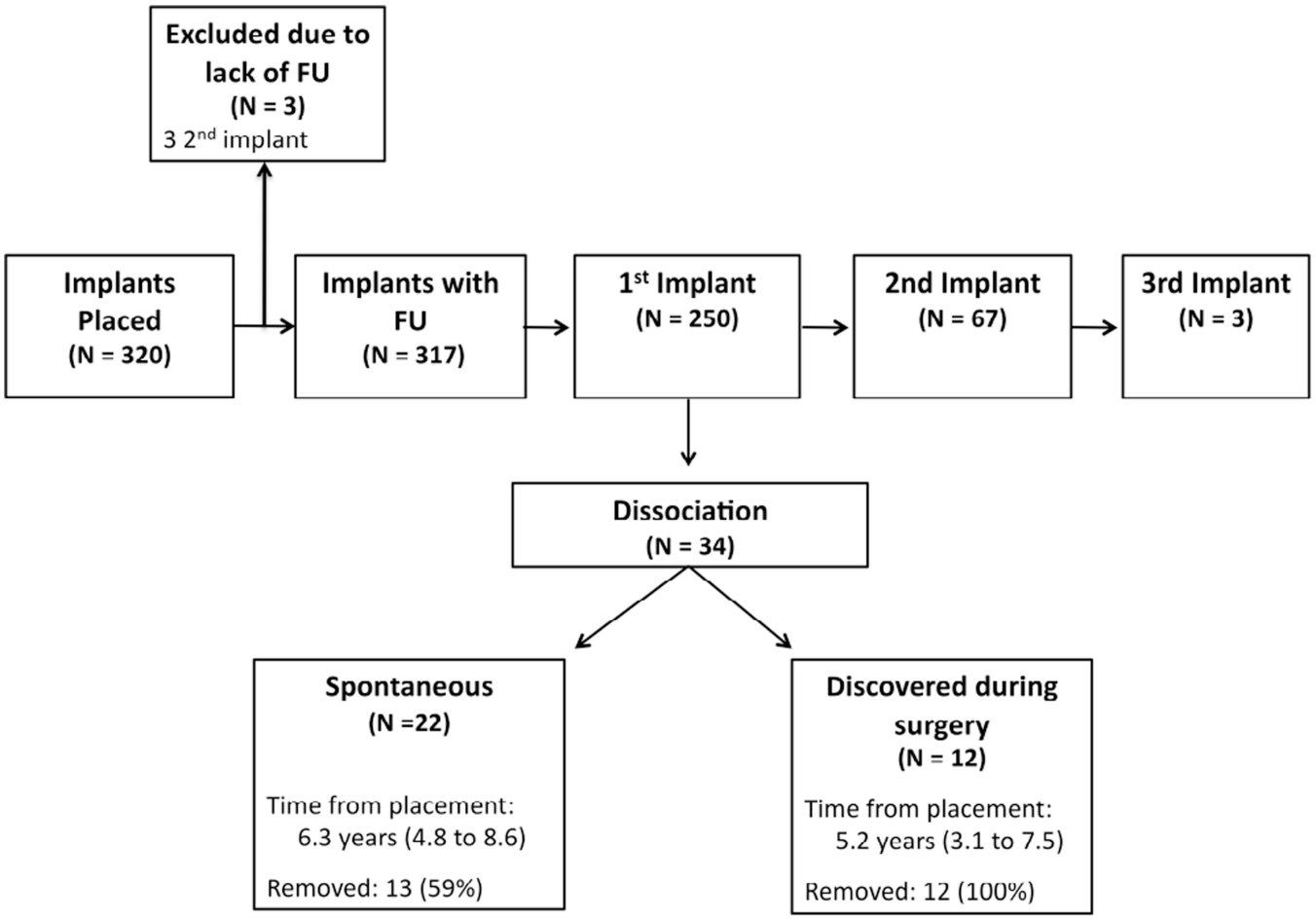

Figure 2.

Kaplan Meier curve of time to spontaneous dissociations of fluocinolone acetonide implants in the Multicenter Uveitis Steroid Treatment (MUST) Trial and Follow-up Study.

Table 1

Demographic, disease, and eye characteristics at the study visit prior to implantation of fluocinolone acetonide implants in the Multicenter Uveitis Steroid Treatment Trial and Follow-up Study.

Characteristics	Result
Number patients	146
Median age at first implantation, years, (range)	48 (13, 87)
Male, number (%)	38 (26%)
Race, number (%)	
Caucasian	86 (59%)
African American	20 (14%)
Hispanic	37 (25%)
Other	3 (2%)
Associated systemic disease, number (%)	39 (27%)
Posterior/panuveitis, number (%)	90 (62%)
Bilateral uveitis, number (%)	131 (90%)
Bilateral implants, number (%)	104 (71%)
Eye-level characteristics	
Number eyes	250
Median years since onset of uveitis (range)*	4.5 (0.1, 40.5)
Median visual acuity, letters (range)*	65 (−10, 96)
Median visual acuity, Snellen equivalent*	20/50
Macular edema, number (%)*	83 (36%)
Observation years from first implant (range)	6.0 (0.5, 9.2)

*Number observations for years of onset of uveitis = 245, visual acuity = 248, and macular edema = 230.

Table 2

Participants with spontaneous dissociation of fluocinolone acetonide Implants in the Multicenter Uveitis Steroid Treatment (MUST) Trial and Follow-up Study

Participant number - eye	Detection method	Years in place	Visual acuity in logarithmic acuity chart letters* (months from reference point)				Visual acuity status	
			Prior to implant	Prior to dissociation	At/after dissociation	Last measured	Prior to dissociation vs at/after dissociation	Prior to implant vs last follow-up
Implant Removed								
S6-right eye	Symptoms	4.8	54 (−0.9)	45 (−4)	36 (0)	66 (32)	Declined†	Improved‡
S16-left eye	Symptoms	5.0	75 (−2.6)	81 (−3)	70 (0)	82 (9)	Declined	Improved
S7-right eye	Symptoms	5.3	61 (−2.5)	82 (−18)	70 (2)	80 (23)	Declined	Improved
S12-left eye	Exam	5.7	37 (−1.3)	49 (−3)	−10 (3)	−10 (3)	Declined	Declined
S26-right eye	Exam	6.1	66 (−1.7)	35 (−1)	65 (1.1)	66 (1.1)	Stable	Stable
S4-left eye	Symptoms	6.3	70 (−0.4)	36 (−4)	3 (2)	23 (14)	Declined	Declined
S15-left eye	Symptoms	6.3	71 (−0.2)	60 (−4)	55 (0)	67 (3)	Stable	Stable
S11-left eye	Symptoms	6.4	NA	59 (−2)	60 (0)	36 (5)	Stable	NA
S10-left eye	Symptoms	6.5	93 (−0.9)	85 (−2)	86 (3)	87 (8)	Stable	Declined
S8-right eye	Symptoms	7.1	77 (−1.3)	81 (−3)	−10 (1)	53 (8)	Declined	Declined
S29-right eye	Symptoms	7.2	43 (−11)	44 (−3)	44 (3)	44 (3)	Stable	Stable
S9-right eye	Symptoms	7.4	69 (−0.5)	51 (−7)	NA¶	NA	NA	NA
S28-right eye	Exam	8.6	76 (−0.5)	12 (−4)	36 (5)	36 (5)	Stable	Declined
Implant remains in eye								
S1-right eye	Symptoms	5.5	61 (−2.1)	77 (−3)	85 (1)	87 (8)	Stable	Improved
S2-left eye	Symptoms	5.6	61(−1.3)	47 (−6)	43 (0)	48 (19)	Stable	Declined
S27-left eye	Exam	5.8	−10 (−1.6)	−10 (−6)	−10 (0)	−10 (0)	Stable	NA
S3-right eye	Exam	5.9	46 (−0.9)	85 (−8)	58 (0)	−10 (18)	Declined	Declined
S5-right eye	Exam	6.4	52 (−1.7)	42 (−1)	25 (5)	23 (24)	Declined	Declined
S13-left eye	Symptoms	6.4	37 (−1.0)	58 (−1)	60 (0.7)	60 (5)	Stable	Improved
S17-left eye	Symptoms	6.8	78 (−0.7)	69 (−2)	55 (0)	69 (4)	Declined	Declined

Participant number - eye	Detection method	Years in place	Visual acuity in logarithmic acuity chart letters* (months from reference point)				Visual acuity status	
			Prior to implant	Prior to dissociation	At/after dissociation	Last measured	Prior to dissociation vs at/after dissociation	Prior to implant vs last follow-up
S14-right eye	Exam	6.9	77 (−0.1)	75 (−1)	70 (0)	82 (8)	Stable	Stable
S30-right eye	Symptoms	7.0	38 (−0.7)	66 (−2)	66 (4)	80 (12)	Stable	Improved

*85 letters = 20/20, 70 letters = 20/40, 50 letters = 20/100, and 35 letters = 20/200.

†Decline = decrease in visual acuity of more than one line (5 letters) from pre-dissociation visit or from pre-implant visits.

‡Improved = increase in visual acuity of more than one line;

¶NA= not available.

Table 3

Participants with dissociations of fluocinolone acetonide implants noted during implant removal or exchange surgery in the Multicenter Uveitis Steroid Treatment (MUST) Trial and Follow-up Study

Participant number - eye	Years in place	Implant replaced (yes/no)	Visual acuity in logarithmic acuity chart letters* (months from reference point)				Visual acuity status	
			Prior to implant	Prior to dissociation	At/after dissociation	Last measured	Prior to dissociation vs at/after dissociation	Prior to implant vs last follow-up
S18-right eye	3.1	Yes	56 (−1.8)	63 (−3)	62 (2)	44 (45)	Stable†	Declined
S20-right eye	4.4	Yes	74 (−0.5)	79 (−4)	73 (2)	74 (19)	Declined†	Stable
S20-left eye	5.2	Yes	34 (−0.5)	67 (−4)	61 (2)	62 (14)	Declined	Improved‡
S21-right eye	5.0	Yes	38 (−0.7)	33 (−2)	50 (5)	53 (11)	Stable	Improved
S1-left eye	5.2	Yes	72 (−1.4)	73 (−6)	57 (1)	66 (5)	Declined	Declined
S23-right eye	5.3	Yes	92 (−0.2)	86 (−1)	90 (5)	55 (34)	Stable	Declined
S23-left eye	6.4	Yes	93 (−0.7)	81 (−6)	86 (2)	88 (20)	Stable	Stable
S22-left eye	5.6	Yes	87 (−0.9)	91 (−6)	90 (1)	81 (22)	Stable	Declined
S24-left eye	6.1	Yes	91 (−1.8)	91 (−1)	92 (6)	93 (24)	Stable	Stable
S25-left eye	6.1	Yes	25 (−0.4)	75 (−2)	73 (7)	62 (46)	Stable	Improved
S19-left eye	6.7	No	54(−0.4)	58 (−3)	33 (5)	59 (10)	Declined	Stable
S8-left eye	7.5	Yes	75 (−0.4)	75 (−6)	50 (0)	71 (2)	Declined	Stable

*85 letters = 20/20, 70 letters = 20/40, 50 letters = 20/100, and 35 letters = 20/200.

†Decline = decrease in visual acuity of more than one line (5 letters) from pre-dissociation visit or from pre-implant visits.

‡Improved = increase in visual acuity of more than one line.