# Cataract Development After Trabeculectomy With Mitomycin C: A 1-Year Study

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**Purpose:** To measure cataract changes quantitatively in the crystalline lens after trabeculectomy with mitomycin C and to identify associated clinical factors.

**Methods:** Forty-one consecutive trabeculectomy patients (41 eyes) were enrolled in this prospective study. The enrollment criteria were: phakic eye, no history of intraocular surgeries or inflammation, and no corneal opacification. The transparency of the lens was measured and analyzed by an anterior segment analysis system preoperatively and 1, 3, and 12 months postoperatively. Cataract development was correlated with clinical factors using a multivariate regression analysis.

**Results:** During the first postoperative month, changes occurred primarily in the anterior segment of the lens, but later, deeper lenticular areas also started to show an increase in light scattering intensity. Multivariate regression analyses demonstrated that some clinical factors were associated with cataract development.

**Conclusions:** Slight cataractous changes develop after trabeculectomy with mitomycin C as early as 1 month postoperatively, and they gradually increase in extent and in intensity during the next 11 months. **Jpn J Ophthalmol 2000;44:52–57** © 2000 Japanese Ophthalmological Society

**Key Words:** Cataract, filtering surgery, glaucoma, mitomycin C, Scheimpflug photography.

## Introduction

Filtering surgery, the most effective and sight-saving method of reducing intraocular pressure (IOP) in the treatment of glaucoma, carries a risk of cataract development.[1–7] The intraoperative use of mitomycin C during trabeculectomy makes it possible to achieve highly successful IOP control, but this antiproliferative agent has a toxic effect on healthy cells in vivo.[8,9] The intraoperative use of mitomycin C may facilitate cataract development or cataract progression in the eye after trabeculectomy.[10–14] Postoperative complications, such as shallow anterior chamber and hypotony, may further aggravate cataractous changes.[1–3,5,13,15] Even some ocular or systemic clinical factors unrelated to filtering surgery, such as diabetes mellitus, systemic hypertension, use of pilocarpine, and refractive error, could be responsible for cataract development and/or progression.[16–24]

Most of the studies describing cataract development after trabeculectomy are retrospective.[1,3–5,7] Only a few investigators use a quantitative method like lenticular measurement with the Lens Opacity Meter for detecting postoperative lenticular opacity value.[2,6] No reports have been made regarding quantitative detection of increased lenticular opacification after trabeculectomy with mitomycin C by applying densitometric analysis of Scheimpflug photographs. The Scheimpflug method is superior to other methodologies of observing the lenticular changes because it enables us to observe the tangential section objectively. Our previous study[25] has demonstrated quantitative lenticular change detected by an anterior segment analysis system, which operates on the Scheimpflug principle,[26–27] during a 3-month postoperative follow-up. Because progressive lenticular change was detected even within the 3-month follow-up

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period, longer follow-up study seemed advisable. The purpose of this study is to report the 1-year postoperative change in the crystalline lens using the same quantitative analysis system and to identify ocular or systemic clinical factors possibly associated with postoperative cataract development and progression.

## Materials and Methods

From June 1995 to January 1997, we prospectively enrolled consecutive trabeculectomy cases into the study who met the following criteria: phakic eye, no history of intraocular surgery, no corneal opacification that could disturb clear observation of the lens, and the first eye operated on when both eyes were involved. There were 41 eyes belonging to 41 subjects, 26 (63%) were men and 15 (37%) were women. Ages ranged from 21 to 77 years with a mean ± SD of 59 ± 15 years; 5 patients were in their 20s, 2 were in their 30s, 3 were in their 40s, 7 were in their 50s, 15 were in their 60s, and 9 were in their 70s. Five cases suffered from non-insulin–dependent diabetes mellitus; two cases had a 15-year history of the disease; one case had a 9-year history; and two cases had a 4-year history. Twenty-eight (68%) eyes had primary open-angle glaucoma, 6 (15%) eyes had normal-tension glaucoma, 2 (5%) eyes had developmental glaucoma, 4 (10%) eyes had capsular glaucoma, and 1 (2%) had primary angle-closure glaucoma. Twenty-six cases had at least a 6-month history of pilocarpine use.

The follow-up of the patients is explained elsewhere.[25] Every subject had corrected visual acuity testing, applanation tonometry, anterior eye segment examinations with a slit-lamp biomicroscope, and fundus examination. After maximal (diameter >5 mm) dilatation of the pupil with 0.5% phenylephrine hydrochloride–0.5% tropicamide (Mydrin P™; Santen, Osaka), the clarity of the lens was analyzed by an anterior eye segment analysis system (EAS-1000; Nidek, Gamagori), which makes use of the Scheimpflug principle and permits objective, reproducible analysis of anterior segment pathology.[26,27] Images were taken 1 day before the surgery and 1, 3, and 12 months postoperatively. The camera unit was used to obtain a two-dimensional linear image of the cross-section of the anterior segment along the 0°, 45°, 90°, and 135° meridians; the power of the light source was set at 200 W.

All changes in the crystalline lenses were objectively diagnosed through documented images using an analysis mode. As described elsewhere,[25] we arbitrarily divided the Scheimpflug lens images into the most anterior 10 pixels, anterior cortex, and nuclear zones. It was sometimes difficult to take slit-image photos deep enough to obtain good pictures of the posterior cortex and posterior subcapsular region of the lens because of the thicker lenses in elderly patients (even with maximal dilatation). Axial densitometry of the integrated area was performed on each lens zone. The light scattering intensity in the slit photos from each meridian was measured along the lines parallel to the optical axis between −75 and +75 pixels in discrete steps taken at every 15 pixels. Then the average of *cct* (the intensity of light scattering per one pixel of each layer) obtained along the four meridians was calculated. The intensity of light scattering was evaluated in 256 steps (minimum intensity, 0; maximum, 255) and *cct* was used as the unit.

A stepwise regression analysis with a 0.15 significance level was performed using the PC-SAS software[28] to correlate the percent increase of cataract change at 12 months after trabeculectomy in the most anterior 10 pixels, anterior cortex, and nuclear zones. The independent clinical factors included: age, gender, refraction, preoperative lens density level, postoperative IOP (mean IOP during the follow-up period), difference between preoperative and postoperative IOPs, period of preoperative use of pilocarpine, history of diabetes mellitus, systemic hypertension, bleb revision and development of postoperative shallow anterior chamber (depth less than half of the postoperative), or hypotony (5 mm Hg or less).

The surgical procedure has been described previously.[29] Briefly, all surgeries were performed according to a modification of Cairn's technique: a limbal-based conjunctival flap and a 4 × 4 mm half-layer scleral flap were made. Next, mitomycin C was applied for 5 minutes, and the wound was irrigated with 250 mL of balanced salt solution. Then a 0.5 × 3 mm limbal block was dissected and a peripheral iridectomy was performed. The scleral flap was snugly closed with interrupted 10-0 nylon sutures; the anterior chamber was reformed by injecting balanced salt solution. The conjunctival wound was closed with a continuous 10-0 nylon shoelace suture. After surgery, 1.2 mg of dexamethasone sodium phosphate, topical atropine (1%), and antibiotics were given. All patients received a similar topical medical regimen in the postoperative period, including 0.1% topical betamethasone, 1% topical atropine sulfate, and

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0.3% ofloxacine. All patients were followed up at the Department of Ophthalmology, Gifu University School of Medicine.

## Results

The preoperative IOP ranged from 14 to 35 mm Hg with a mean ± SD of 22.6 ± 6.6 mm Hg. The IOP ranged from 2 to 18 mm Hg (mean = 8.6 ± 3.3 mm Hg) at 1 month, and it was between 6 and 18 mm Hg (mean = 11.1 ± 2.9 mm Hg) during the following 11 months. The preoperative visual acuity ranged from 0.04 to 1.5 (logarithmic mean = 0.59); it was from hand motion to 1.5 (logarithmic mean = 0.45) at the first postoperative month and it was between 0.01 and 1.5 (logarithmic mean = 0.43) 12 months postoperatively. Eleven patients (27%) showed a decrease in best corrected visual acuity of two lines or more 1 month postoperatively, and 14 patients (35%) showed a decrease 12 months postoperatively. One case required cataract surgery because of the development of mature cataract during the first postoperative month: visual acuity decreased from 0.3 to hand motion. Four months later, the patient underwent phaco surgery with intraocular lens implantation, and visual acuity improved to 0.7. During the early postoperative period, 5 eyes had shallow anterior chamber, 16 eyes showed an IOP of 5 mm Hg or less. Six eyes had a bleb revision.

Analysis of the changes that the slit images recorded disclosed that the largest increase in light scattering intensity developed in the anterior part of the lens. Figure 1 demonstrates a case of cataract development during the 12-month follow-up as detected in slit-image photos taken by the EAS-1000 system. The average of light scattering intensity in 40 eyes increased from 61.5 ± 14.2 *cct* preoperatively to 65.4 ± 21.7 *cct* (7.3 ± 9.7% increase) at 1 month,

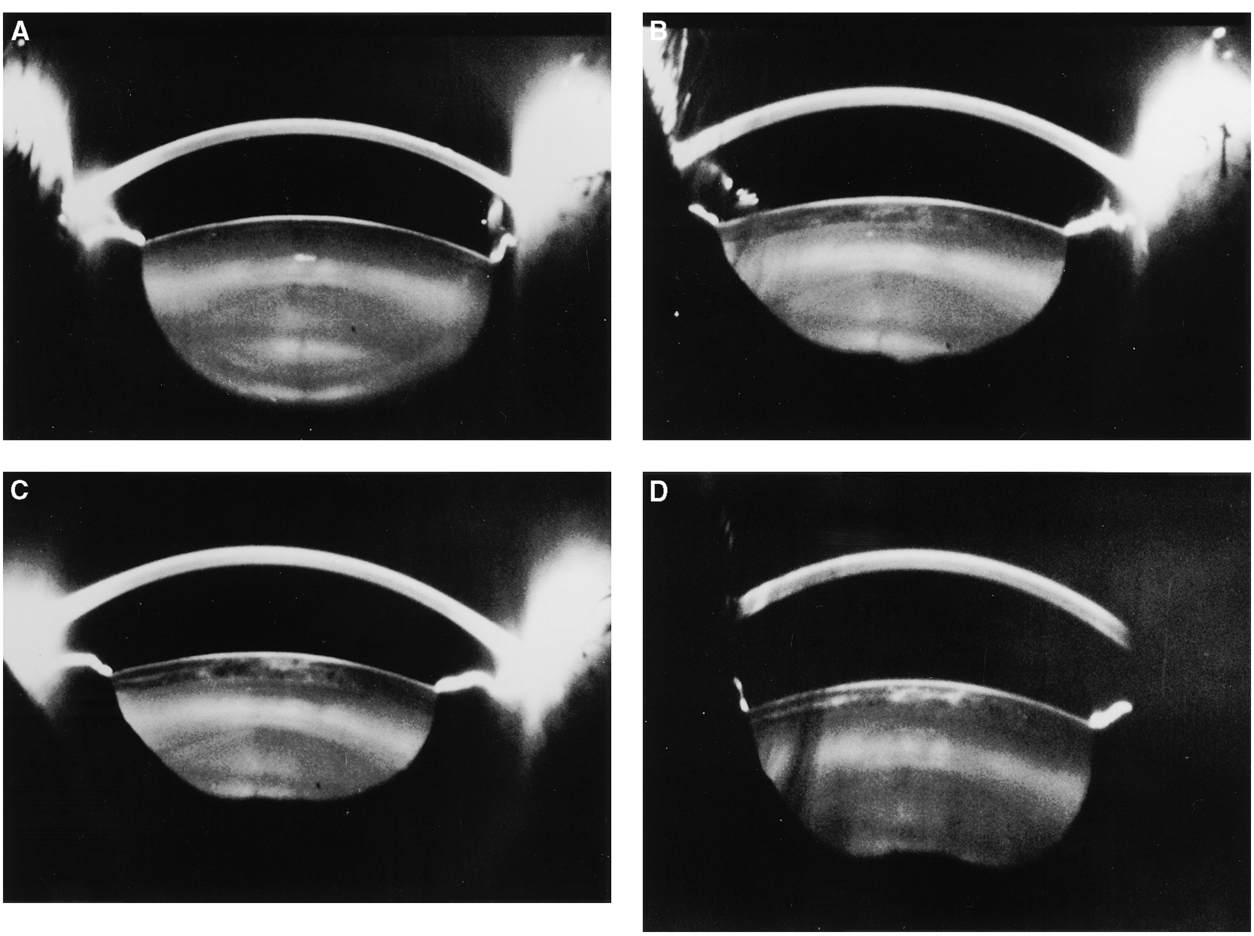


**Figure 1.** Slit-image Scheimpflug photos in a 73-year-old patient. (**A**) Crystalline lens before trabeculectomy (0° meridian). (**B**) Crystalline lens 1 month after surgery. (**C**) Crystalline lens 3 months after surgery. (**D**) Crystalline lens 12 months after surgery.

**Table 1.** Changes in Mean Light Scattering Intensity*

| Lens Zone | Preoperative | 1 Month Postop. | 3 Months Postop. | 12 Months Postop. |
|---|---|---|---|---|
| Anterior 10 pixels | 61.5 ± 14.2 | 65.4 ± 21.7 | 66.5 ± 14.0 | 76.5 ± 19.5 |
| Anterior cortical | 68.8 ± 14.9 | 72.4 ± 17.0 | 73.4 ± 18.1 | 78.0 ± 17.1 |
| Nuclear | 70.8 ± 23.1 | 72.1 ± 24.9 | 72.9 ± 27.6 | 79.6 ± 31.6 |

Unit: *cct*.
*Number of eyes: 40. One eye was excluded because of cataract surgery.

66.5 ± 14.0 *cct* (10.8 ± 13.1% increase) at 3 months, and 76.5 ± 19.5 *cct* (26.9 ± 30.4% increase) at 12 months in the anterior 10-pixel zone of the lens. The average light scattering intensity increased from 68.8 ± 14.9 to 72.4 ± 17.0 *cct* (5.0 ± 6.4% increase) at 1 month, to 73.4 ± 18.1 *cct* (5.9 ± 6.9% increase) at 3 months, and to 78.0 ± 17.1 *cct* (13.4 ± 12.6% increase) at 12 months in the anterior cortical zone of the lens; and from 70.8 ± 23.1 to 72.1 ± 24.9 *cct* (2.1 ± 3.6% increase) at 1 month, to 72.9 ± 27.6 *cct* (3.2 ± 4.9% increase) at 3 months, and to 79.6 ± 31.6 *cct* (10.9 ± 12.9% increase) at 12 months in the nuclear zone of the lens. Table 1 demonstrates the change in light scattering intensity of the lens in 40 cases during the 12-month follow-up period, and Figure 2 demonstrates percentage of changes in light scattering intensity of the lens during the follow-up. Table 2 demonstrates the number of new cases in which the light scattering intensity had increased more than 10%.

The results of the multiple regression analysis are given in Tables 3–5. It was demonstrated that the mean of postoperative IOP, history of a shallow anterior chamber, bleb revision, diabetes mellitus, or long use of pilocarpine were associated with increased light scattering intensity in the most anterior 10 pixels of the lens at the 12-month follow-up. Postoperative IOP, age, and history of systemic hypertension were significant for increased light scattering intensity in the anterior cortical zone, and the level of preoperative light scattering intensity, postoperative IOP, and history of systemic hypertension were associated with increased light scattering intensity in the nuclear zone of the lens.

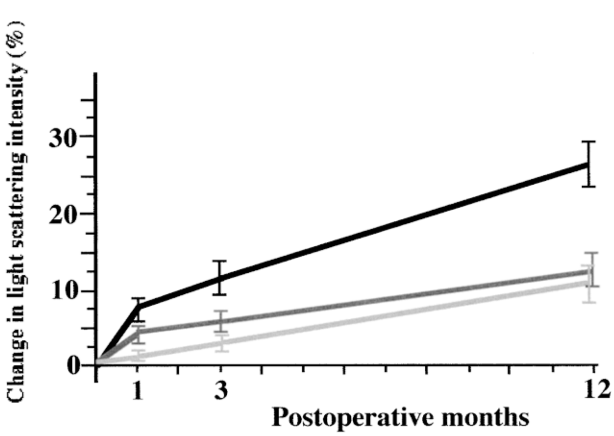


**Figure 2.** Mean percent changes in light scattering intensity in most anterior 10-pixel zone of lens, anterior cortical and nuclear zones during 12-month follow-up. Black line: anterior 10-pixel zone; dark gray: anterior cortical; and light gray: nuclear zone.

## Discussion

In the current 12-month study, we found that some cataractous changes developed as early as 1 month postoperatively and progressed during the next 11 months in a substantial number of cases after trabeculectomy with mitomycin C, although they were not necessarily accompanied by subjective visual impairment. The current study also demonstrated that the most prominent increase in light scattering intensity occurs in the anterior part of the lens, especially in the anterior subcapsular region during the early postoperative period. Later, development of new cases is noticed with increased light intensity in the deeper lenticular regions, too. In other studies on the late complications after filtration surgeries, which followed patients beyond 6 months, most of them for several years, investigators discussed cases composed of advanced cataracts with severe visual impairment and/or cases requiring cataract extraction.[1–7] The definition of and the method to detect cataract development after filtration surgery vary among these reports. When cataract pro-

**Table 2.** Number of New Cases in Which Light Scattering Intensity Increased by ≥10% Compared with Preoperative Data

| Lens Zone | 1 Month | 3 Months | 12 Months |
|---|---|---|---|
| Anterior 10 pixel | 12 | 5 | 5 |
| Anterior cortical | 9 | 2 | 8 |
| Nuclear | 3 | 3 | 13 |

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**Table 3.** Results of Stepwise Regression Analysis of Anterior 10-Pixel Zone

| Factors Identified | Parameter Estimate | *P* Value |
|---|---|---|
| Diabetes mellitus | 0.12 | .0397 |
| Period of pilocarpine use (y) | 2.29 | .0646 |
| Shallow anterior chamber | 31.60 | .0725 |
| Bleb revision | 20.51 | .1236 |
| Postoperative IOP | −2.42 | .1259 |
| Difference in pre- and postoperative IOP | | NS |
| Hypotony | | NS |
| Refraction | | NS |
| Preoperative light scattering intensity | | NS |
| Gender | | NS |
| Age (y) | | NS |
| Systemic hypertension | | NS |

IOP: intraocular pressure; NS: not significant.

**Table 5.** Results of Stepwise Regression Analysis of Nuclear Zone

| Factors Identified | Parameter Estimate | *P* Value |
|---|---|---|
| Preoperative light scattering intensity | 0.22 | .0252 |
| Systemic hypertension | 7.13 | .0976 |
| Postoperative IOP | −1.12 | .1089 |
| Difference in pre- and postoperative IOP | | NS |
| Refraction | | NS |
| Shallow anterior chamber | | NS |
| Hypotony | | NS |
| Period of pilocarpine use (y) | | NS |
| Age (y) | | NS |
| Bleb revision | | NS |
| Gender | | NS |
| Diabetes mellitus | | NS |

IOP: intraocular pressure; NS: not significant.

gression was defined by a decrease in visual acuity of two or more lines, our study found that 35% of operated eyes had a decrease in visual acuity at 12 months after filtration surgery; this does not differ from other reports.[1–7] Because visual acuity decreases after trabeculectomy from various causes other than cataract, we used a system that enabled us to do densitometric analysis of Scheimpflug photographs in the current study.

The incidence and the morphology of cataract after mitomycin C trabeculectomy were quite similar to those after nonantiproliferative surgery.[13,15,23,24] There were, however, no reports on developing anterior subcapsular opacities as in the current study. The slight and early cataractous changes in the anterior part of the lens found in this study might be attributed to the toxicity of mitomycin C to the lens epithelium and superficial fiber cells.

**Table 4.** Results of Stepwise Regression Analysis of Anterior Cortical Zone

| Factors Identified | Parameter Estimate | *P* Value |
|---|---|---|
| Systemic hypertension | 7.51 | .0925 |
| Postoperative IOP | −1.28 | .1254 |
| Age (y) | 0.19 | .1320 |
| Preoperative light scattering intensity | | NS |
| Refraction | | NS |
| Shallow anterior chamber | | NS |
| Hypotony | | NS |
| Period of pilocarpine use (y) | | NS |
| Difference in pre- and postoperative IOP | | NS |
| Bleb revision | | NS |
| Gender | | NS |
| Diabetes mellitus | | NS |

IOP: intraocular pressure; NS: not significant.

Our regression analyses revealed that different risk factors are associated with the lens change for each lens area. Some factors have been discussed previously.[25] As for the anterior subcapsular area, we found association between increase in light scatter and some factors directly affecting this area, such as long-lasting hypotony,[1–3,6] shallow anterior chamber,[1,2,13,15] or bleb revision. It is not surprising that these postoperative complications are associated with cataract development in the anterior lenticular area, possibly resulting from alterations in aqueous humor circulation and the influence on lens metabolism, or minor mechanical trauma to the lens. Our analysis demonstrates association of increase in light scattering intensity and long-term use of pilocarpine. It is known that pilocarpine has a toxic effect on the ciliary body and other anterior segment structures and can cause characteristic anterior and posterior subcapsular lens opacity,[20,22,23] the same pattern as that seen in the anterior lens area in our study. Diabetes mellitus is a strong risk factor for cataract development, especially for the development of nuclear sclerosis, posterior subcapsular or mature cataract.[17,21,24] Our study demonstrates that this systemic disease influences the transparency of the lens in the anterior area. Decreased preoperative lens transparency could be followed by further cataract progression after trabeculectomy, especially in elderly patients.[2,3,5,7]

In summary, slight cataractous changes developed after trabeculectomy with mitomycin C as early as 1 month postoperatively, and they increased in extent and in intensity during the next 11 months. During the first postoperative month the most remarkable change occurred primarily in the anterior part of the lens, especially in the anterior subcapsular region, although later, deeper lenticular structures started to show increase in light scatter. Related factors and mechanisms of this change are not clear, but it is highly probable that some intraocular and systemic factors influence the physiologic metabolism of the lens to cause cataractous changes. The presently used quantitative method operating on the Scheimpflug principle for detecting lens opacification is very helpful to find even slight increased light scattering intensity as we found in the anterior part of the lens. Further prospective study is needed by applying the same method to compare lenticular change after trabeculectomy without antiproliferatives with the present results.

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