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# The gonio scratch study: methodology of a multicenter clinical trial establishing a new minimally invasive glaucoma surgery

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## ABSTRACT

There are numerous surgical procedures for glaucoma. Minimally invasive glaucoma surgery is becoming popular; however, the disadvantage is the high incidence of anterior chamber hemorrhage. Heavy bleeding can also lead to increased intraocular pressure (IOP) postoperatively. Gonio scratch is a surgical procedure that improves aqueous humor outflow by rubbing off deposits on the trabecular meshwork with a Diamond Dusted Sweeper. As the conjunctiva and trabecular meshwork are not incised, no postoperative bleeding is expected, and the IOP spike will be minimal. We designed this study to determine the efficacy and safety of gonio scratch. This is an on-going multicenter, prospective, clinical trial. Patients who are scheduled for glaucoma surgery with or without cataract surgery are being enrolled. A total of 80 eyes will be recruited in the Hiroshima University Hospital, Miyoshi Eye Clinic, Yokoyama Retina Clinic, and Kusatsu Eye Clinic. All patients will undergo gonio scratch. When combined with cataract surgery, gonio scratch is performed after the intraocular lens is inserted. The primary study endpoint is the change in IOP from baseline to 1 year after surgery. The secondary endpoints are complications, number of glaucoma medications, surgical time, and changes in visual acuity and the visual field. This study protocol was approved by the institutional review board of Hiroshima University. The trial results will be shared with the scientific community at international conferences and by publication in a peer-reviewed journal. Trial registration number is jRCTs062200003.

Keywords: glaucoma, gonio scratch, minimally invasive glaucoma surgery, multicenter clinical trial

Abbreviation:
IOP: intraocular pressure



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## INTRODUCTION

Glaucoma is the leading cause of irreversible blindness worldwide. As populations age, the incidence of glaucoma increases, and once established, visual impairment is irreversible, increasing the medical and economic burdens.[1] Glaucoma affected 60 million people worldwide in 2010, and this number is estimated to increase to an additional 80 million by 2020.[2] The standard treatment for glaucoma is laser surgery or eye drops to decrease intraocular pressure (IOP).[3] Surgical intervention is necessary when the progression of glaucoma cannot be controlled by eye drops alone. Surgery is also necessary when side effects preclude the regular use of glaucoma medications. There are numerous surgical procedures for glaucoma, and minimally invasive glaucoma surgery is becoming popular.[4,5]

The mechanism of IOP elevation in open-angle glaucoma remains unclear. The greatest resistance to aqueous humor outflow occurs in the juxtacanalicular tissue and the inner wall of Schlemm's canal. In the meshwork of glaucoma patients, there is an accumulation of extracellular matrix and a substance called plaque material in the juxtacanalicular tissue.[6-8] This is thought to result in increased resistance to outflow through the meshwork. Therefore, ab interno trabeculotomy using a Tanito hook, Trabectome, or Kahook Dual Blade can decrease IOP.[9-13] Trabecular aspiration can remove debris on the trabecular meshwork using a trabecular aspirator to apply suction against the trabecular meshwork.[14-17] Trabecular aspiration also lowers IOP after the surgery.

We hypothesized that the removal of extracellular matrix and plaque material on the meshwork may lower IOP. In this study, we scratched the meshwork with a Diamond Dusted Sweeper (DORC, Zuidland, Netherlands). The Diamond Dusted Sweeper is a diamond-dusted silicone-tipped manipulator. It was developed by Tano et al in 1997 to remove the epiretinal membrane during vitrectomy.[18] We designed this study to determine the efficacy and safety of the new minimally invasive glaucoma procedure, gonio scratch.

## MATERIALS AND METHODS

A synopsis of the study is provided in Table 1. This is an on-going multicenter clinical trial that is being performed at the Department of Ophthalmology of Hiroshima University Hospital, Miyoshi Eye Clinic, Yokoyama Retina Clinic, and Kusatsu Eye Clinic. The institutional review board of Hiroshima University examined the protocol for all institutes and approved the study protocol before recruitment began at all institutes. This study is registered with the Japan Registry of clinical trials (jRCTs062200003; date of access and registration, 25 May 2020). Written informed consent will be obtained from all patients before participation in the study. This study is being conducted in accordance with the tenets of the Declaration of Helsinki. Patient enrolment began in May 2020 and will end in 2024.

**Table 1** Gonio scratch study synopsis

| Purpose | To compare the efficacy and safety of gonio scratch surgery |
|---|---|
| Patient eligibility | |
| Inclusion criteria | ≥20 years of age |
| | Patients who are scheduled to undergo glaucoma surgery |
| | Patients who can complete outpatient visits within 1 year after the surgery |
| | Written informed consent |

| | |
|---|---|
| Exclusion criteria | Pregnant or nursing women |
| | Patients who underwent an intraocular surgery within the previous 6 months |
| | Patients who cannot measure intraocular pressure with a Goldmann applanation tonometer |
| | Neovascular glaucoma patients |
| | Patients with an intraorbital tumor behind the eye, thyroid eye disease, Sturge–Weber syndrome, or other diseases that increase superior scleral venous pressure |
| | Patients who are allergic to nitinol |
| | Patients recognized by the physician as inappropriate for this study |
| Follow-up examination | 1 day, 1 week, 1 month, 3 months, 6 months, and 1 year after surgery |
| Outcome measures | Intraocular pressure |
| | Surgical time |
| | Number of glaucoma medications |
| | Visual acuity |
| | Visual fields |
| Enrollment | 80 eyes |
| Study centers and committees | Four clinical eye centers: |
| | Hiroshima University Hospital |
| | Miyoshi Eye Clinic |
| | Yokoyama Retina Clinic |
| | Kusatsu Eye Clinic |

*Patients and inclusion criteria*

Patients aged ≥20 years with open-angle glaucoma with or without cataracts in whom glaucoma surgery is planned are currently being enrolled. When necessary, combined cataract surgery will be performed. The exclusion criteria are pregnant or lactating women, patients within 6 months of ocular surgery, patients with difficulty measuring IOP with a Goldmann applanation tonometer, patients with neovascular glaucoma, patients with tumors behind the eye, thyroid eye disease, Sturge–Weber syndrome, or any other disease that increase superior scleral venous pressure, and patients who are allergic to nitinol.

*Outcome measures*

The primary endpoint is the change in IOP from baseline (preoperative) to 1 year after surgery. We will document the IOP at each patient visit for 1 year.

The secondary endpoints are complications, number of glaucoma medications, surgical time and changes in visual acuity and visual field.

*Surgical procedure*

The surgical procedure and postoperative management are similar in each case. Anesthesia includes subconjunctival 2% lidocaine injection. The specific method involves placing a gonioscope on the cornea and identifying the trabecular meshwork. The Diamond Dusted Sweeper (23 gauge/0.6 mm) is inserted through the corneal incision and guided across the anterior chamber

to the trabecular meshwork. The Diamond Dusted Sweeper is then used to scratch the trabecular meshwork to remove deposits. This is performed over the trabecular meshwork in 120 degrees, and the trabecular meshwork is scrubbed two to three times. When combined with cataract surgery, this procedure is performed after intraocular lens insertion. All patients receive a similar topical medical regimen, postoperatively, comprising newer generation quinolone antibacterial eye drops 3 times a day. Corticosteroid eye drops are used as needed. Patients who undergo combined gonio scratch and cataract surgery also receive non-steroidal anti-inflammatory eye drops for 3 months. The doses of the newer generation quinolone antibacterial eye drops and corticosteroid eye drops are tapered at the surgeon's discretion.

*Study measurements*

A list of study measurements for the scheduled follow-up visits is presented in Table 2. The date of informed consent is the study entry date. All follow-up visits will be calculated from the date of surgery. Enrolled patients will complete follow-up visits 1 day, 1 week, 1 month, 3 months, 6 months, and 1 year postoperatively.

**Table 2** Study measures at baseline and scheduled gonio scratch follow-up visits

| | Baseline | 1 Day | 1 Week | 1 Month | 3 Months | 6 Months | 1 Year |
|---|---|---|---|---|---|---|---|
| Range | | +1 Day | ±3 Days | ±14 Days | ±21 Days | ±1 Month | ±2 Months |
| Informed consent | ○ | | | | | | |
| Refractometry | ○ | ○ | | | | ○ | ○ |
| Visual acuity | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Tonometry | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Slit-lamp biomicroscopy | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Gonioscopy | ○ | | ○ | | | ○ | ○ |
| Ophthalmoscopy | ○ | | | ○ | | ○ | ○ |
| Perimetry | ○ | | | | | ○ | ○ |
| Corneal endothelial cell measurement | ○ | | | | | ○ | ○ |

**Visual Acuity.** Distance visual acuity will be measured with decimal visual acuity and will be converted to logMAR visual acuity. Visual acuity will be measured at the baseline examination and every follow-up visit. Refraction will be performed prior to the measurement of visual acuity at the baseline examination and on day 1, 6 months, and 1 year after the surgery.

**Slit-lamp biomicroscopy.** Examination of the anterior segment with slit-lamp biomicroscopy will be performed at the baseline examination to document the preoperative condition of the eye, and at every follow-up visit to detect any changes in ocular status.

**Tonometry.** Goldmann applanation tonometry (Haag Streit, Koeniz, Switzerland) will be used to measure IOP.

**Gonioscopy.** Gonioscopy will be performed at the baseline examination to establish the type of glaucoma using a Goldmann 2-mirror lens. We will also observe changes after gonio scratch.

**Ophthalmoscopy.** A fundus examination will be performed to detect posterior segment complications, such as serous choroidal effusions, suprachoroidal hemorrhage, or hypotony maculopathy.

**Perimetry.** Quantitative automated perimetry will be performed before the surgery, and 6- and 12 months postoperatively. A Humphrey field analyzer will be used to conduct a Swedish Interactive Thresholding Algorithm Standard 24–2 threshold test with a size III white stimulus in all patients.

*Statistical analyses*

All statistical analyses will be performed using JMP software, version 16 (SAS Institute Inc, Cary, NC, USA). Preoperative and postoperative IOP at 3, 6, 9, and 12 months will be analyzed using the Mann–Whitney nonparametric test at a significance level of 5% (two-sided). Bonferroni correction will be applied when repetitive analyses are performed. Results will be presented as mean ± standard deviation. All statistical tests are two-sided, and P-values <0.05 are considered statistically significant. A total of 80 eyes will be enrolled in this study. Because this is an exploratory study, the target number of patients was set with consideration of the feasibility to obtain the minimum information necessary for the next study.

## DISCUSSION

The primary aim of this study is the change in IOP from preoperative baseline to postoperative 3, 6, 9, and 12 months to establish the efficacy of the minimally invasive glaucoma surgery, gonio scratch. In Japan, the Trabectome (NeoMedix Corp, Tustin, CA, USA), iStent Trabecular Micro-Bypass Stent System (Glaukos, San Clemente, CA, USA), microhook ab interno trabeculotomy (Tanito microhook: M-2215 s; Inami & Co, Ltd, Tokyo, Japan), Kahook Dual Blade (New World Medical, Inc, Rancho Cucamonga, CA, USA), and iStent Inject Trabecular Micro-Bypass Stent System (Glaukos) were approved in 2011, 2016, 2016, 2016, and 2019, respectively. Trabeculotomy ab interno has become popular, recently.[19]

Smith reported the principle of trabeculotomy in 1960.[20] The first procedure was the prototype of the current basic procedure. Schlemm's canal was identified by creating a scleral flap, and a trabeculotome was used to incise the trabecular meshwork. Trabeculotomy has the advantages of fewer complications owing to the resulting low IOP and no bleb-related complications, such as bleb infection and bleb leak. However, trabeculotomy is inferior to trabeculectomy for lowering IOP, and bleeding into the anterior chamber is inevitable.[21] The techniques for trabeculotomy can be divided into two major categories: the original basic technique, in which a scleral flap is created from the transconjunctival membrane and a trabeculotome is inserted and rotated into the identified Schlemm's canal to incise the trabecular meshwork (ab externo trabeculotomy) and a second technique in which the trabecular meshwork is incised from the anterior chamber (ab interno trabeculotomy). Ab interno trabeculotomy involves making an incision through the anterior chamber into the trabecular meshwork,[9] and the procedure is similar to the removal of trabecular meshwork deposits that is the subject of this study. The removal of deposits on the trabecular meshwork improves aqueous humor outflow,[14-17] whereas ab interno trabeculotomy improves aqueous humor outflow by partially incising the trabecular meshwork from within the eye.[22] Ab interno trabeculotomy can achieve significant IOP reduction; however, its disadvantage is the high incidence of anterior chamber hemorrhage, which results in poor immediate postoperative visual acuity. As the bleeding resolves, visual acuity improves; however, loss of visual acuity often causes anxiety in the patient. Heavy bleeding can also lead to increased IOP.

The gonio scratch surgical technique improves aqueous humor flow by rubbing off deposits on the trabecular meshwork with a Diamond Dusted Sweeper without a conjunctival incision or an incision on the trabecular meshwork. Because the conjunctiva and trabecular meshwork are not

incised, no postoperative bleeding is expected, and the IOP spike will be minimal. As a result, we expect fewer complications and shorter operative times. We designed this study to determine the efficacy and safety of this new procedure. We expect that gonio scratch will become another glaucoma treatment option.

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## CONFLICT OF INTEREST

None.

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