NCT04468633

PROJECT TITLE: The Baerveldt versus ClearPath Comparison Study

SHORT TITLE: Baerveldt vs. ClearPath (BVC)

IDENTIFYING WORDS: Baerveldt, ClearPath, IOP, complications, outcomes, ripcord

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PRIMARY STUDY COORDINATOR:

PRIMARY REGULATORY COORDINATOR:

PROJECT USES IONIZING RADIATION: No

PROJECT INVOLVES USE OF DURABLE POWER OF ATTORNEY: No

MULTI-INSTITUTIONAL PROJECT: No

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1.0 LIST OF ABBREVIATIONS

Abbreviation	Term
IOP	Intraocular pressure
ICH	International Conference on Harmonisation
IRB	Internal review board
ITT	Intention to treat
GCP	Good Clinical Practice
LH	Leon Herndon
LOCF	Last Observation Carried Forward
mm Hg	Millimeters Mercury
POD	Post-operative day
POW	Post-operative week
POM	Post-operative month

2.0 STUDY FLOW CHART

			Study Day					
	Screening / Baseline visit	Post-Op Day 1 ± 1 day	Post-Op Week 1 ± 5 days	Post-Op Week 4 ± 1 week	Post-Op Week 6 ± 1 week	Post-Op Month 3 ± 1 week	Post-Op Month 6 ± 2 weeks	Post-Op Year 1 ± 1 month
Informed Consent	X							
Review inclusion and exclusion criteria	X							
Visual acuity assessment	X	X	X	X	X	X	X	X
Slit-lamp biomicrosopy	X	X	X	X	X	X	X	X
Applanation Tonometry	X	X	X	X	X	X	X	X
Subjective diplopia		X	X	X	X	X	X	X
Pachymetry	X							X
Direct fundus exam	X							X
Humphrey visual field	X							X
Optical coherence tomography	X							X
Self-report dysesthesia scale	X							X
Motility history and exam	X							X
Quality of life questionnaires								X

X procedure performed at the time of clinic visit

3.0 INTRODUCTION

3.1 Background

Implanting aqueous drainage devices has become an increasingly common surgical treatment for glaucoma. Medicare data between 1995 and 2004 demonstrated a steady increase in the use of these devices.[1,2] Even with the advent of minimally invasive glaucoma surgery (MIGS), aqueous drainage devices is still a mainstay of treatment for uncontrolled intraocular pressure (IOP).[3] Currently, one of the most common aqueous drainage devices used is the Baerveldt implant (Johnson & Johnson, Vision, Jacksonville, Florida) (Figures 1&2).

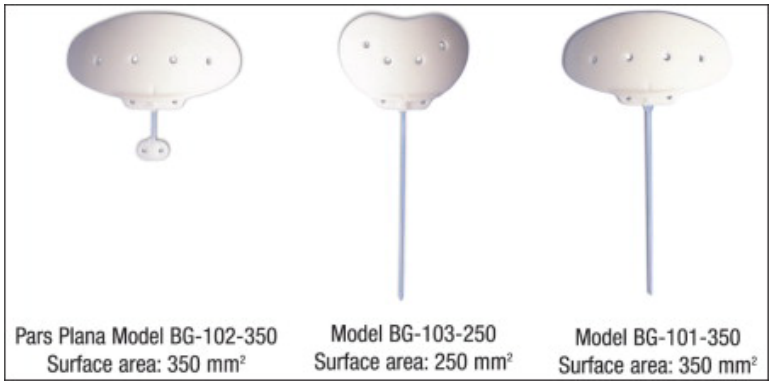

Figure 1. Schematic of the different Baerveldt Implant Models available. On the far most right is the Baerveldt 101-350 model that will be utilized in this study.

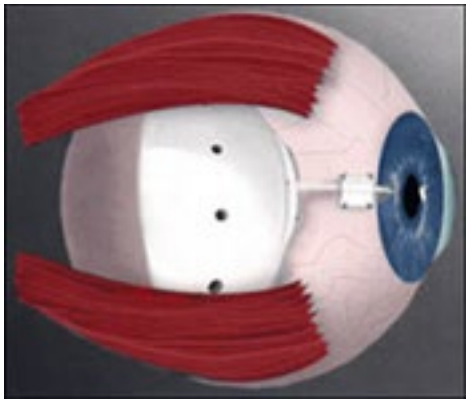

Figure 2. Depiction of typical Baerveldt implant once positioned and implanted on the eye. (www.towerclockeyecenter.com)

The Baerveldt implant is an FDA-approved silicone, non-valved implant. This device comes in 3 variants: a single 250 mm^2 model and two 350 mm^2 models (Figures 1&2). For the purposes of this study, we will be focusing on the Model BG-101-350, (Figures 1&2) which will be the only variant of the Baerveldt evaluated in this study. As it is non-valved, it needs early restriction of fluid flow to minimize hypotony while the eye forms a fibrous capsule around the implant. One common way of restricting fluid flow is by ligating or tying off the Baerveldt tube with an absorbable suture that dissolves by post-operative week 4 to 6. For better control of the tube opening and intraocular pressure reduction during the post-operative

period, many surgeons place a suture within the lumen of the implant, called a ripcord, at the time of surgery. This ripcord suture is accessible at the slit lamp in clinic.

The Ahmed ClearPath is a newly developed non-valved glaucoma drainage device that entered United States markets in late 2019 (New World Medical, Inc., Rancho Cucamonga, CA) (Figure 2). This device comes in two sizes: a 250 mm^2 model (Figure 3A) and a 350 mm^2 model (Figure 3B). We will be focusing on the 350 mm^2 model which will be the only variant of the ClearPath evaluated in this study. There are several features of the ClearPath that are advertised as advantageous compared to the Baerveldt. For instance, the 350 mm^2 model features a posteriorly positioned plate in order to avoid intraocular muscle attachment points upon insertion. It has a flexible, contoured design and anteriorly positioned suture points which are intended to optimize the process of device implantation for the surgeon, though this has not yet been confirmed. As it is non-valved implant, it also requires early restriction for the same reasons mentioned for the Baerveldt. However, the ClearPath device comes packaged with a pre-threaded 4-0 polypropylene ripcord though some surgeons do replace this with sutures of differing materials or size per preference.

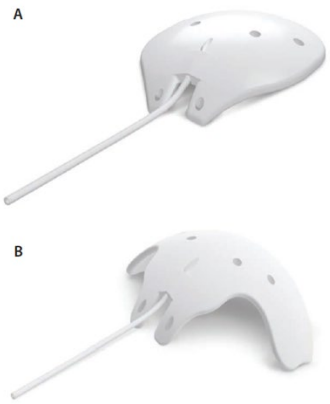

Figure 3. The Ahmed ClearPath 250mm^2 (A) and 350 mm^2 (B) (www.newworldmedical.com).

3.2 Rationale

Previous studies have compared the efficacy of the Baerveldt to the older, valved Ahmed FP7 glaucoma drainage device (Ahmed Glaucoma Valve; New World Medical, Inc., Rancho Cucamonga, CA). These studies have yielded mixed results, and many surgeons will opt to use either a Baerveldt or an Ahmed FP7 depending on a number of patient-dependent factors. However, there is currently no data published comparing the Baerveldt to the new, non-valved Ahmed ClearPath. We are interested in performing a head-to-head trial in order to compare overall efficacy and failure rates of the Baerveldt as compared to the ClearPath. Criteria for device failure includes: IOP >18 mmHg or not reduced by 20% less than baseline on two consecutive visits after three months, IOP < 6 mmHg on two consecutive visits after three months, need for additional glaucoma surgery or device removal, and the loss of light perception vision. Given the similarities in design, in particular the equal sizes of the implant plate, we hypothesize that there is no difference in the efficacy of IOP reduction or complication rates in patients who undergo Baerveldt implant versus those who undergo ClearPath implants. However, this cannot be verified without sufficient investigation. The results of this study will provide important data for surgeons to select the most appropriate device to achieve favorable outcomes while minimizing complications.

4.0 OBJECTIVE

To compare the post-operative surgical outcomes and complication rates in patients with a Baerveldt 350 aqueous drainage device (model 101-350; Johnson & Johnson, Vision) vs the Ahmed ClearPath implant (350 mm2; New World Medical, Inc., Rancho Cucamonga, CA).

5.0 STUDY DESIGN AND METHODS

5.1 Experimental Design
This is a randomized prospective study of post-operative surgical outcomes and complication rates in patients with a Baerveldt 350 implant vs the Ahmed ClearPath implant. Each subject will be randomized to the Baerveldt group or ClearPath group at the time of consent for the study. A baseline eye exam will be conducted as per the study flowchart (Section 2). Surgeons will include

- Pratap Challa, MD
- Jiaxi Ding, MD
- Sharon Freedman, MD
- Divakar Gupta, MD
- Leon W. Herndon Jr, MD
- Thomas G. L. Hunter, MD
- Stuart J. McKinnon, MD, PhD
- Filipe Medeiros, MD, PhD
- Frank J. Moya, MD
- Kelly Muir, MD
- Jullia Rosdahl, MD
- Henry Tseng, MD, PhD
- Molly Walsh, MD
- Joanne Wen, MD

It will not be possible for the surgeon to be masked given that s/he will be implanting the device. The subject will then be seen on post-operative day 1 (±1 day), week 1 (±5 days), week 4 (±1 week), week 6 (±1 week), month 3 (±1 week), month 6 (±2 weeks) and year 1(±1 month) as per the standard-of-care post-operative schedule. At each of these post operative visits, ophthalmic exams will be conducted, collecting data such to be in accordance with the study flowchart (Section 2).

5.2 Subject Selection
Subjects will be identified from patients presenting for ophthalmologic consultation at the Duke Eye Center and/or one of its satellite clinical locations. Individuals with uncontrolled glaucoma are routinely available from this clinic and will be the primary study group. A care provider known to the patient will introduce the study and his/her ophthalmologist will be asked for prior approval to enroll the patient. The target enrollment will be approximately 304 subjects. Subjects will not be compensated for participation. All adults meeting study criteria (as detailed in Section 6.0) will be asked to participate.
Informed consent will be obtained for each patient. The surgeon or his/her study staff will initially approach potential subjects for consent. During the consent process, the person obtaining consent will inform the potential subject of all elements of informed consent and shall discuss the nature of the study, its requirements and its restrictions. Adequate time will be allowed for the potential subject to ask questions prior to deciding whether to participate in the study.

5.3 Sample Size
Approximately 152 subjects will be enrolled in each treatment group for a total of approximately 304 subjects. This sample size was based on a power analysis aimed at detecting a 2 mmHg difference in IOP between the Baerveldt and ClearPath groups with 80% power, using the mean post-op year 1 Baerveldt IOP of 13.6±5.9 mmHg from the pooled AVB and ABC data.[4] The results were adjusted for an expected 10% drop out rate at 1 year.

5.4 Baseline Evaluation
The initial evaluation for glaucoma and need for surgical intervention will include a standard-of-care ophthalmic examination that is performed by a licensed ophthalmologist. Collection of all data will be under the supervision of a licensed ophthalmologist

5.5 Study Evaluation
If the potential subject meets the criteria for study-inclusion and consents to participate following full explanation of the research, the subject will be randomly assigned to either group. The subject's baseline exam findings will be documented, including: age, sex, race, glaucoma diagnosis and cause, ocular history (including prior treatments and procedures), best-corrected Snellen visual acuity, IOP by Goldmann applanation tonometry (masked, 2-person), glaucoma medications, slit lamp findings, external exam findings, motility exam, Humphrey Visual Field, Optical Coherence Tomography, and a patient reported-reported dysesthesia scale.

5.6 Randomization and Masking
At the time of consent, subjects will be randomized to receive either the Baerveldt or ClearPath according to a computer-generated randomization code. Study subjects will be masked as to which implant they will receive. In the patient chart, the device will be noted at a glaucoma drainage device (GDD).

5.7 Duration of Subject Participation
Each subject will participate in the study for approximately 1 year. Participation will include an initial evaluation where the decision to undergo implantation of Baerveldt or ClearPath implant is made and a baseline visit. Following surgery, the patient will be evaluated per study schedule (detailed in **Section 2.0**)

5.8 Duration of Study
The clinical portion of the study will last approximately 1 year for each patient enrolled. Study recruitment is anticipated to occur over the course of 2 years with 1 year follow up for each patient enrolled. Therefore, we anticipate a total study duration of 3 years.

6.0 INCLUSION/EXCLUSION CRITERIA

6.1 Inclusion Criteria
- Men or women with age at screening $\geq$ 18 years and $\leq$ 90 years
- Inadequately controlled glaucoma
- Valve-less aqueous shunt as the planned surgical procedure
- Patients with primary glaucomas or pseudoexfoliation, pigmentary and traumatic glaucoma with a previous failed trabeculectomy or other intraocular surgery included.
- Primary tubes included
- Investigators to recruit consecutively all eligible patients from their clinics.
- Superotemporal or inferonasal placement of the tube
- Capable and willing to provide consent

6.2 Exclusion Criteria

- NLP
- Unable/unwilling to provide informed consent
- Unavailable for regular follow up
- Previous cyclodestructive procedure
- Prior scleral buckling procedure or other external impediment to supratemporal drainage device implantation
- Presence of silicone oil
- Vitreous in the anterior chamber sufficient to require a vitrectomy
- Uveitic glaucoma
- Neovascular glaucoma
- Nanophthalmos
- Sturge-Weber syndrome or other conditions associated with elevated episcleral venous pressure
- Procedure combined with other surgery
- Any abnormality other than glaucoma in the study eye that could affect tonometry.

7.0 STUDY SCHEDULE (see Flowchart)

All study procedures are performed as standard of care for the condition.

7.1 Surgical Procedure

The patient will undergo standard superotemporal or inferonasal placement of either a Baerveldt or ClearPath implant, which may include placement of a suture ripcord as per the surgeon's preference. The methods utilized to place the tube will vary based on surgeon preference to enhance the generalizability of the results.

7.2 Post-operative interval visits

The subject will be evaluated at post-operative day 1 (±1 day), week 1 (±5 days), week 4 (±1 week), week 6 (±1 week), month 3 (±1 week1), month 6 (±2 weeks), and year 1 (±1 month) as described in **Section 2.0**. Additional appointments may be made as deemed necessary per standard-of-care. The subject will undergo a standard of care post-operative evaluation including assessment of visual acuity, slit lamp biomicroscopy, and tonometry at each interval visit. Addition of glaucoma medications will be at the surgeon's discretion throughout the post-operative period in addition to standard post-operative eye drops, which includes an antibiotic eye drop, a steroid eye drop, and an antibiotic ointment. Ripcord removal and additional glaucoma surgery will be at the surgeon's discretion throughout the post-operative period.

7.3 Post-operative visit year 1 (± 1 month)

The subject will undergo a standard of care post-operative assessment of visual acuity, slit lamp biomicroscopy, and tonometry. At the year 1 post-operative visit, subjects will also undergo visual field testing, optical coherence tomography, pachymetry, and motility testing. Subjects will also complete self-report questionnaires pertaining to dysesthesia and quality of life.

8.0 SUBJECT MONITORING AND DATA COLLECTION PLAN

Clinically indicated care will be provided to all subjects as required. Descriptive statistics will be applied to safety assessments.

8.1 Statistical Considerations

8.1.1 Analysis Plan
The Intent-To-Treat (ITT) population includes all randomized subjects who had at least one post-op assessment. The primary efficacy analysis will be performed on the ITT population with Last Observation Carried Forward (LOCF). If a subject is deemed to have a failed surgery and undergoes a rescue procedure, the last observation collected prior to the intervention will be used for efficacy analyses at all later timepoints.

8.1.2 Study hypotheses
The analysis will be based on the following null hypothesis: there is no difference in IOP or complication rates in patients who undergo Baerveldt implant vs those who undergo ClearPath implants.

8.1.3 Sample Size Considerations
With a 2-sided significance level of 0.05, a sample size of 152 in each group would be required to detect a 2 mm difference in IOP with 80% power (accounting for a 10% drop out rate). The total planned enrollment for this pilot study is approximately 304 subjects

8.1.4 Statistical Methods
Descriptive statistical analysis of patient characteristics across the 2 treatment groups will be performed. Snellen VA measurements will be converted to logMAR equivalents for the purpose of data analysis. Student t test for continuous variables, Fisher exact test, and the $\chi 2$ test, or exact permutation $\chi 2$ test for categorical variables will be utilized. All tests will be 2-sided in accordance with our hypothesis. A P-value of 0.05 will be considered statistically significant.

9.0 HUMAN SUBJECT PROTECTION

9.1 Safety and Confidentiality
No long-term safety concerns are anticipated as a result of study interventions as both devices are FDA approved. The surgeon and his/her study staff will monitor safety events on a regular basis. After-hours contact information will be provided to all study participants in case of an adverse event. Subject records will be maintained on a password-protected computer or in a locked file, and a study-assigned identification number will be used in lieu of the subject's name or personal identifiers on data summary sheets.

9.2 Subject Consent:
A consent form has been developed that describes the nature of the research, the risk/benefit ratio, and the voluntary nature of subject involvement. Consent will be obtained directly from the participant in a private location within the clinic by the study PI, study coordinator, or other study staff. Potential subjects will be given a verbal explanation of the research and then will be granted ample time to read the consent form or have the consent read to them if necessary, and permitted to ask questions. Subjects unwilling to provide signed consent will not be enrolled.

9.3 Risks and Benefits:
As both arms of this study are consistent with current standard-of-care practices, we do not anticipate any increase in rates of complication compared to the reported rates in published literature.

9.4 Discomforts and Inconveniences:
The expected discomforts and inconveniences are related to the placement of a Baerveldt or ClearPath implant and the time required in the standard-of-care post-operative follow up. Participation in this study is not expected to add any significant discomfort and/or inconvenience to the subject as the study interventions and follow-up schedule are utilized in current standard of care post-operative management.

9.5 Discontinuation of Treatment and Withdrawal of Subjects
The reasons why a subject may discontinue or be withdrawn from the study include, but are not limited to, adverse effects, subject request, investigator request, protocol violation and lost to follow-up.

10.0 ETHICS

This study will not commence without approval of the study protocol, protocol amendments, informed consent forms, and other relevant documents from the Duke IRB. The study will be performed in accordance with the protocol, International Conference on Harmonization Good Clinical Practice guidelines, and applicable local regulatory requirements and laws. Additionally, the study will be conducted accordance with the Declaration of Helsinki.

11.0 CHANGES TO THE PROTOCOL

Changes or additions to this protocol will only be made after approval of a written protocol amendment by the Duke IRB.

12.0 REFERENCES

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