Evaluation of Long-Term Visual Field Function in Patients Undergoing Glaucoma Drainage Device Implantation

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• PURPOSE: To determine the change in global and regional Humphrey visual fields (VF) after glaucoma drainage device (GDD) implantation over a 3-year follow-up period.

• DESIGN: Retrospective interventional case series.

• METHODS: Patients undergoing GDD placement from between 2010 and 2015 with reliable preoperative and yearly postoperative VF measurements were included. Clinical parameters were compared between preoperative and follow-up visits, including visual acuity, intraocular pressure (IOP), number of glaucoma medications, global VF metrics (mean deviation [MD]), pattern standard deviation (PSD), CIGTS (Collaborative Initial Glaucoma Treatment Study) score of total deviation probability (CIGTS_TDP) and pattern deviation probability (CIGTS_PDP), and regional metrics (regional total deviation (TD), regional pattern deviation (PD), and regional CIGTS_TDP and CIGTS_PDP). Multivariate regression analyses were performed to determine risk factors for VF worsening after GDD surgery.

• RESULTS: A total of 106 eyes from 95 patients were included. Mean IOP ± SD was reduced from 23.1 ± 8.5 mm Hg to 12.7 ± 3.1 mm Hg at 3-year follow-up ($P < .001$). MD, PSD, and global CIGTS_PDP showed no significant changes in follow-up, whereas global CIGTS_TDP showed mild progression from 10.7 to 12.8 at 3-year follow-up ($P = .01$). No regional metrics showed worsening at follow-up examinations. Defects in the superior hemifield were more common than in the inferior hemifield at baseline and follow-up examinations for all regional metrics. Pre-operative number of glaucoma medications was associated with worsening on CIGTS_TDP.

• CONCLUSIONS: Overall, GDD surgery is effective at stabilizing VF function over 3 years of follow-up. The superior hemifield is affected more than other regions. The number of pre-operative glaucoma medications is associated with mild VF progression, measured by CIGTS_TDP. (Am J Ophthalmol 2020;216:44–54. Published by Elsevier Inc.)

SINCE THE POPULARIZATION OF TRABECULECTOMY BY Cairns in 1968,[1] it has become the preferred surgical intervention for most glaucoma patients. The use of glaucoma drainage devices (GDD) was limited mostly to refractory glaucoma patients with limited vision who were often unable to undergo automated perimetry.[2–6] Recently, use of GDDs has expanded to first-line therapy in many patients, providing effective, safe, and long-term reduction of intraocular pressure (IOP) for patients with good vision.[7–10] Historically, most previous studies examining the outcomes of GDD implantation have focused on clinical parameters such as visual acuity, IOP, and surgical success rate,[11] whereas the analysis of the visual field has been very limited. However, as the use of GDDs increases, the need has arisen for better characterization of visual functional changes after GDD surgery.

Automated static perimetry, especially Humphrey visual field (HVF) analysis, has remained as the mainstay of assessing longitudinal progression of glaucoma disease.[12,13] Several HVF assessment strategies have been developed over the years to study disease progression, leveraging global, regional, and point-wise analyses to assist in detecting progression.[12,14–16] Global and regional metrics offer distinct benefits but also drawbacks in assessing glaucomatous damage, balancing sensitivity of detection of progression with susceptibility of noise from patient reliability and media opacities. Evaluation of HVF after trabeculectomy has been well studied in large clinical trials.[9,14,17–19] The recent uses of point-wise and regional analysis have also yielded new insights into glaucomatous disease, which showed trabeculectomy may slow or even reverse HVF damage.[17] To date, there have been no large

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studies examining the changes in perimetric visual function after GDD placement.

We hypothesized that GDD decreases IOP in patients with glaucoma, therefore stabilizing VF function compared to preoperative function. To test this hypothesis, a retrospective study was performed to evaluate global and regional HVF changes in glaucoma patients who underwent GDD implantation with 3-year postoperative follow-up. This study was intended to provide information that may assist in the surgical management of patients with glaucoma.

SUBJECTS AND METHODS

THIS STUDY WAS COMPLIANT WITH THE HEALTH INSURance Portability and Accountability Act and the Declaration of Helsinki for research involving human participants. Institutional Review Board approval was obtained from the University of California, San Francisco, Human Research Protection Program.

• **INCLUSION AND EXCLUSION CRITERIA:** This was a retrospective review of consecutive patients who underwent implantation of either an Ahmed (Stryker, Kalamazoo, Michigan), Baerveldt (Johnson & Johnson, New Brunswick, New Jersey), or Molteno (Molteno, Dunedin, New Zealand) GDD at the Glaucoma Clinic of the Department of Ophthalmology, University of California, San Francisco, from January 2010 to December 2015, who satisfied inclusion and exclusion criteria. GDD implantation was performed if the patient showed convincing evidence of progression of glaucomatous damage or if, in the surgeon's opinion, the IOP was at a level that would cause additional damage. Patients were excluded if they had best corrected visual acuity worse than 20/200; if they had no visual field testing data before or after surgery; if they had any other ocular or neurological comorbidities that affected their visual field or if their visual fields were not typical of glaucomatous defects; if they had unreliable visual fields at baseline or follow-up visits (defined as fixation losses, false positive or false negative responses > 33%); or if they had severe VF defect and should be appropriately evaluated by 10-2 test patterns instead of 24-2 patterns.

• **VISUAL FIELD TESTING:** All VF examinations were performed using a Humphrey VF analyzer (Carl Zeiss Ophthalmic Systems, Dublin, California) on a 24-2 or 30-2 test pattern, size III white stimulus, with a Swedish Interactive Threshold Algorithm (SITA) standard strategy. Eyelids were taped if ptosis was present during HVF testing.

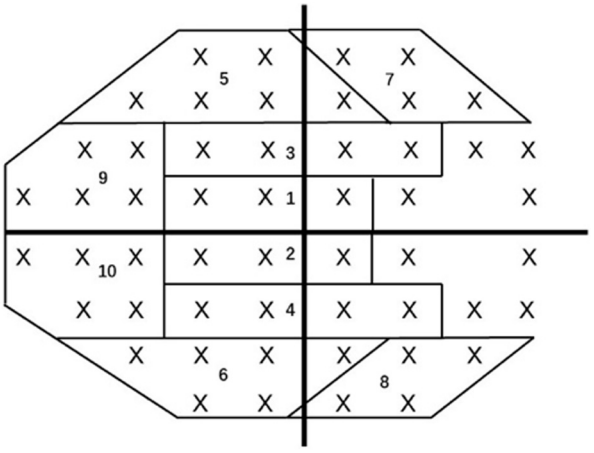

FIGURE 1. Humphrey VF 24-2 pattern. Each VF pattern was divided into 10 subfields (5 per hemifield) based on the characteristics of glaucomatous VF defect. Regions were outlined as superior central (1) or inferior central (2); superior paracentral (3) or inferior paracentral (4); superior arcuate 1 (5) or inferior arcuate 1 (6); superior arcuate 2 (7) or inferior arcuate 2 (8); and superior nasal (9) or inferior nasal (10). Regional analyses of the subfields were performed using total deviation (TD), total deviation probability (TDP), pattern deviation (PD), and pattern deviation probability (PDP).

• **SURGICAL PROCEDURES FOR TUBE SHUNT IMPLANTATION:** Standard GDD implantation surgery was performed based on each surgeon's preference. The conjunctiva and Tenon's layer were dissected from sclera in either the superior temporal or superior nasal quadrant, where the plate of the tube shunt was sutured on the sclera. A limbus- or fornix-based incision was used based on the surgeon's preference. Prior to implantation, Ahmed implants were primed using balanced saline solution through a 27-gauge cannula, and the Baerveldt and Molteno implants were ligated with a dissolvable suture for temporary restriction of flow. The tube was inserted into either the anterior chamber or the sulcus and covered by scleral flap or scleral patch allograft. Conjunctiva was closed with either interrupted or continuous sutures based on the surgeon's preference. For some patients, intraoperative antifibrotic agents (mitomycin-C, 0.4 mg/ml, or 5-fluorouracil, 50mg/ml) was injected into the subconjunctival space over the plate based on the surgeon's discretion. Postoperative care included use of a topical antibiotic for 1 week and topical prednisolone 1% ophthalmic suspension for multiple weeks followed by a tapering dosage.

• **DATA COLLECTION:** For each patient, demographic data were collected, including age, sex, race, glaucoma diagnosis, history of glaucoma laser and surgery, systemic health condition (ie, diabetes mellitus and hypertension), and lens status. Clinical data collection at preoperative visit and annual postoperative follow-up visits included IOP, the number of glaucoma medications, best-corrected visual

acuity, and intraoperative and postoperative application of antifibrosis agents.

Global HVF data, including mean deviation (MD), pattern standard deviation (PSD), VF index, global hemifield test, and point-wise VF data, such as total deviation (TD), total deviation probability (TDP), pattern deviation (PD), and pattern deviation probability (PDP) at each testing location were collected at preoperative visits (within 4 months of GDD implantation surgery) and postoperative 1-, 2-, and 3-year follow-ups. When point-wise data were recorded, VFs of all left eyes were flipped to the right-eye format. For the 30-2 VF test, only the test points falling within 24-2 VF testing points were collected. For data analysis, the VF defects were classified according to a system that was adopted and modified from the Ocular Hypertension Treatment Study classification system.[15,20] At each VF hemifield, 5 subfields based on the characteristics of glaucomatous VF defect were outlined as central, paracentral, nasal, arcuate 1, and arcuate 2 (Figure 1).

• **CALCULATION OF COLLABORATIVE INITIAL GLAUCOMA TREATMENT STUDY VF SCORE:** The CIGTS (Calculation of Collaborative Initial Glaucoma Treatment Study) score was developed as a measurement to evaluate the extent and depth of HVF loss over the region of the 24-2 test, and the calculation methodology is described in full by the CIGTS study group.[14] In the present study, the CIGTS score was applied to both the total deviation probability (TDP) and the pattern deviation probability (PDP) to calculate global metrics CIGTS_TDP and CIGTS_PDP, respectively. Additionally, regional CIGTS scores were calculated by applying the methodology to points located within each subfield described in Figure 1.

• **STATISTICAL ANALYSIS:** Global VF analysis was performed for MD, PSD, global CIGTS_TDP and global CIGTS_PDP. Regional VF analysis was performed for average TD, PD, and regional CIGTS_TDP and regional CIGTS_PDP for each subfield. Analysis of each metric (from preoperative and follow-up visits) was performed using a generalized linear regression model with a generalized estimating equation, which accounted for the intereye correlation between 2 eyes of a subject for those who contributed 2 eyes in the study as well as longitudinal correlation among repeated measurements of the same eye taken at baseline and follow-up visits. Each visit was modeled as a categorical variable to avoid assuming a linear relationship between VF measurements and time. Additionally, cross-sectional comparisons among different regions at each time point were performed to determine the worst region. To determine which baseline characteristics were risk factors for changes in VF at 3-years' follow-up compared to preoperative VF, each baseline characteristic was evaluated using a univariate linear regression model. All risk factors with univariate analysis P value $<.20$ were then included in a multivariate linear regression model. The multivariate regression models then went through with a subsequent backward variable selection to keep the significant risk factors with P values $<.05$ in the final model. This methodology is standard statistical practice to avoid missing any potentially significant risk factors and

TABLE 1. Baseline Patient and Ocular Characteristics

	Total (95 Patients and 106 Eyes)
Age (at time of surgery)[a]	
Mean ± SD	65.9 (15.9)
Gender	
Males	46.3% (44)
Females	53.7% (51)
Diabetes	
No	90.5% (86)
Yes	9.5% (9)
Systemic hypertension	
No	64.2% (61)
Yes	35.8% (34)
Number of eyes in study	88.4% (84)
1	11.6% (11)
2	
Diagnosis	
Primary open angle glaucoma	81.1% (86)
Mixed mechanism glaucoma	1.9% (2)
Primary angle closure/glaucoma	3.8% (4)
Pseudoexfoliative syndrome	2.8% (3)
Pigmentary glaucoma	1.9% (2)
Uveitic glaucoma	1.9% (2)
Aphakic glaucoma	1.9% (2)
Congenital glaucoma	0.9% (1)
Steroid-induced glaucoma	2.8% (3)
Others	0.9% (1)
Prior glaucoma surgery	
None	85.8% (91)
Trabeculectomy	2.8% (3)
Tube-shunt	5.7% (6)
Tube-shunt and endocyclophotocoagulation	0.9% (1)
Express shunt placement	4.7% (5)
Prior cataract surgery	
No	36.8% (39)
Yes	63.2% (67)
Type of tube-shunt	
Ahmed glaucoma implant	88.7% (94)
Baerveldt glaucoma implant	4.7% (5)
Molteno glaucoma implant	6.6% (7)
Intraoperative mitomycin-C	
No	24.5% (26)
Yes	75.5% (80)
Intraoperative 5- fluorouracil	
No	95.3% (101)
Yes	4.7% (5)

[a]For the 11 patients with both eyes included in the study, their ages at surgery can differ from 0 to 5 years.

TABLE 2. IOP, Visual Acuity, and Number of Glaucoma Medications Over Time

	Baseline (N = 106)	1 Year (n = 106)	2 Years (n = 95)	3 Years (n = 81)	*P* Value[a]
IOP					<.001
Mean (SD)	23.1 (8.5)	13.1 (4.0)	12.7 (3.9)	12.7 (3.1)	
BCVA (LogMAR)					.84
Mean (SD)	0.2 (0.4)	0.2 (0.2)	0.2 (0.3)	0.2 (0.3)	
Number of glaucoma medications					<.001
Mean (SD)	2.7 (0.8)	1.2 (1.1)	1.4 (1.0)	1.5 (1.2)	

BCVA = best corrected visual acuity; IOP = intraocular pressure; SD = standard deviation.

[a]Linear model with Generalized Estimating Equation (GEE) method for comparison of any difference across time points (baseline, 1, 2, and 3 years.

overfitting the data by including all candidate risk factors into a multivariate regression model.[21] Statistical analyses were performed using SAS version 9.4 software (Cary, North Carolina). *P* values <.05 were considered statistically significant for all analyses except for the comparisons by regions, where Bonferroni corrections for multiple comparisons were performed.

RESULTS

A TOTAL OF 242 EYES WERE SCREENED, AND 136 EYES WERE excluded, with 94 eyes having pre-operative best-corrected visual acuity worse than 20/200, 23 eyes with only 10-2 VF, 10 eyes with unreliable VF, and 9 eyes with other reasons. A total of 106 eyes from 95 patients were included in the final data analysis. The baseline demographic and clinical characteristics are listed in Table 1. Eleven patients (11.6%) required GDD implantation surgery performed in both eyes. The most common diagnosis was primary open-angle glaucoma (81.1%). The most common type of implant used was the Ahmed glaucoma drainage device (88.6%). Ninety-one patients (85.8%) had no prior glaucoma surgery. A majority of patients received antifibrotic agents, with most receiving mitomycin-C (80 eyes, 75.5%). Sixty-seven eyes (63.2%) had previously undergone cataract extraction before preoperative HVF tests (Table 1); according to the latest follow-up, 88.9% of eyes had undergone cataract extraction. The number of eyes included at 1-, 2-, and 3-year follow-up examinations was 103 (97%), 95 (90%) and 81 (76%), respectively. The reasons for the loss to follow-up included missed clinic visits or failure to obtain reliable VF tests. The average number of HVF tests performed per patient during the study period was 4.6 ± 1.1 in this cohort.

IOP was significantly reduced after GDD implantation surgery, with IOP decreasing from a mean 23.1 ± 8.5 SD mm Hg at the preoperative visit to 13.1 ± 4.0 mm Hg, 12.7 ± 3.9 mm Hg, and 12.7 ± 3.1 mm Hg at postoperative-1, -2 and -3 years, respectively ($P < .001$) (Table 2). The number of glaucoma medications decreased from 2.7 ± 0.8 before the surgery to 1.5 ± 1.2 at the third year after surgery ($P < .001$). The best-corrected visual acuity did not change significantly over time ($P = .84$).

• **GLOBAL HVF CHANGES OVER 3 YEARS:** Changes in global HVF index, including MD, PD, VF index, global hemifield test, and global CIGTS VF score were summarized in Table 3. MD, PD, and global CIGTS_PDP were not significantly changed over the 3-year follow-up examinations, whereas the mean CIGTS_TDP score increased from 10.7 ± 6.9 to 12.8 ± 6.2 at postoperative year 3 ($P = .01$).

• **LOCAL HVF CHANGES OVER 3 YEARS:** Changes over time in regional VF index, such as TD, PD, TPD, PDP, CIGTS_TPD, and CIGTS_PDP are shown in Table 4. There were no significant changes in any region using index of PD and CIGTS_PDP over the time period. For index TD, only the inferior arcuate 1 region showed gradually decreased TD over 3 years ($P = .03$). For index CIGITS_TDP, 7 of 10 regions showed increased scores over the follow-up with a *P* value ranging from .03 to .008 at corresponding locations. However, if the multiple comparisons using Bonferroni corrections are accounted for, none of these *P* values was significant (as there were 10 tests for each index, only raw *P* value ≤ .005 were considered statistically significant).

• **IDENTIFICATION OF THE REGION WITH THE MOST HVF LOSS AND ITS CHANGE OVER TIME:** At baseline and each year of follow-up, which of the local regions had the worst HVF function for each index was identified and compared and whether the pattern of VF defect remained the same during the follow-up visits (Table 5). At baseline, for TD and PD, the superior nasal region had the worst VF function; for CIGTS_TDP, the superior paracentral region had the worst VF function; for CIGTS_PDP, both the superior nasal and superior paracentral regions had the worst VF functions (Figure 2). This pattern of VF defect was maintained during the course of the 3-year follow-up examinations.

TABLE 3. Global Visual Field Change Over Time

	Baseline (N = 106 eyes)	1 Year (n = 103 eyes)	2 Years (n = 95 eyes)	3 Years (n = 81 eyes)	*P* Value[a]
VFI					.43
Mean (SD)	0.7 (0.3)	0.7 (0.2)	0.7 (0.2)	0.7 (0.2)	
GHT					.07
Normal	12 (11.3%)	6 (5.9%)	3 (3.2%)	6 (7.4%)	
Abnormal	91 (85.8%)	94 (92.2%)	90 (94.7%)	75 (92.6%)	
Borderline	3 (2.8%)	2 (2.0%)	2 (2.1%)	0 (0.0%)	
MD					.14
Mean (SD)	−9.9 (8.4)	−11.4 (7.2)	−11.2 (7.5)	−11.7 (7.8)	
PSD					.33
Mean (SD)	7.5 (4.1)	8.0 (3.8)	7.8 (3.8)	7.8 (3.8)	
CIGTS_TDP					.01
Mean (SD)	10.7 (6.9)	12.4 (6.1)	12.3 (6.2)	12.8 (6.2)	
CIGTS_PDP					.27
Mean ± SD	7.0 (5.8)	7.8 (5.6)	8.1 (5.9)	8.2 (6.0)	

CIGTS_PDP: Collaborative Initial Glaucoma Treatment Study score on pattern deviation probability; CIGTS_TDP = Collaborative Initial Glaucoma Treatment Study score on total deviation probability; GHT = global hemifield test; MD = mean deviation; PSD = pattern standard deviation; SD = standard deviation; VFI = visual field index.

[a]Linear model with GEE method for comparison of any difference across time points (baseline, 1, 2, and 3 years).

• **RISK FACTORS ASSOCIATED WITH GLOBAL HVF CHANGES:** The risk factors associated with HVF changes at the 3-year follow-up after GDD implantation were studied. Because only global CIGTS_TDP showed significant changes over time, the analysis was based upon comparisons of CIGTS_TDP indexes between baseline and postoperative year 3. In the univariate analysis for baseline characteristics (age, sex, diabetes, hypertension (HTN), diagnosis, prior glaucoma surgery/laser, prior cataract surgery, preoperative IOP, postoperative maximal IOP, mitomycin use, and preoperative number of glaucoma medication), age ($P = .04$) and number of glaucoma medications before operation ($P = .01$) were found to be the significant risk factors for CIGTS_TDP changes. In the multivariate analysis model that included age and number of medications, only the number of preoperative glaucoma medications remained statistically significant ($P = .03$). Specifically, every increase in glaucoma medication was associated with an increase of 1.31 on global CIGTS_TDP scores (Table 6).

DISCUSSION

RECENTLY, GDDS HAVE BEEN IMPLANTED NOT ONLY IN PAtients with refractory glaucoma but also as a first-line therapy in patients with good vision, to provide effective, safe, and long-term IOP reduction. As the use of GDDs increases, there is a need for better characterization of visual functional changes after the surgery in addition to commonly observed vision, IOP, and success rate. This retrospective study examined the change in HVF after GDD implantation over a 3-year follow-up. Analysis found that GDD implantation conferred stable, well-controlled IOP with stable HVF function on regional and global analyses.

There are several studies that have examined the perimetric changes after trabeculectomy.[6,20,22,23] The Advanced Glaucoma Intervention Study (AGIS) study demonstrated that, whereas early trabeculectomy yielded better IOP control in most patients, white patients had better preservation of their global VF function than African-American patients.[24] Additionally, post hoc analysis of the AGIS study showed a correlation between the proportion of visits with IOP >18 mm Hg and VF progression and revealed a dose-response relationship between IOP control and glaucomatous progression. This helped establish the fact that the IOP control provided by trabeculectomy was critical in VF preservation and also demonstrated the variable benefit of VF preservation in patients undergoing trabeculectomy. The CIGTS further helped elucidate this variable benefit, showing that initial surgical intervention may provide better long-term outcomes in patients with moderate to advanced field loss[14]; and their discussion also suggested that control of not only the mean IOP but also IOP diurnal variations was a factor in VF preservation and that surgical intervention offered a way to achieve control over diurnal variations.[25] These landmark studies, while supporting the optic nerve-protective effect of trabeculectomy, focused only on global VF metrics, which limited their ability to characterize the effect and benefit of treatment in preventing VF progression. Caprioli and associates[17] used a point-wise analysis of VF function and showed that trabeculectomy not only preserved VF function in some areas but may also improve localized function

TABLE 4. Local Visual Field Change Over Time

	Baseline Mean (SD) (N = 106)	1 Year Mean (SD) (n = 103)	2 Years Mean (SD) (n = 95)	3 Years Mean (SD) (n = 81)	*P* Value[a]
TD superior central	−11.5 (10.9)	−12.0 (10.7)	−12.1 (10.7)	−14.2 (11.8)	.13
TD superior paracentral	−12.5 (11.1)	−13.5 (10.2)	−12.9 (10.6)	−13.7 (11.3)	.52
TD superior nasal	−14.0 (12.1)	−15.7 (10.7)	−15.0 (11.5)	−15.9 (11.2)	.21
TD superior arcuate 1	−11.5 (10.8)	−13.3 (9.8)	−13.0 (10.0)	−13.1 (10.5)	.21
TD superior arcuate 2	−9.9 (9.5)	−11.0 (8.9)	−10.6 (8.7)	−11.4 (9.5)	.42
TD inferior central	−6.8 (8.1)	−7.7 (7.3)	−8.8 (7.9)	−9.3 (8.2)	.048
TD inferior paracentral	−9.5 (10.3)	−10.7 (9.4)	−10.8 (9.3)	−10.8 (9.6)	.22
TD inferior nasal	−11.4 (11.2)	−13.4 (10.4)	−13.1 (10.0)	−13.6 (10.4)	.09
TD inferior arcuate 1	−8.8 (9.8)	−11.1 (9.1)	−10.9 (8.9)	−11.0 (9.3)	.03
TD inferior arcuate 2	−7.1 (9.1)	−8.8 (8.7)	−8.7 (9.0)	−8.8 (8.0)	.10
PD superior central	−9.5 (10.3)	−9.5 (11.2)	−9.6 (10.1)	−11.7 (11.3)	.13
PD superior paracentral	−10.3 (10.0)	−11.0 (10.3)	−10.5 (10.2)	−11.1 (10.8)	.78
PD superior nasal	−12.1 (11.0)	−13.2 (10.8)	−12.5 (10.5)	−13.3 (10.4)	.42
PD superior arcuate 1	−9.6 (9.5)	−10.5 (9.2)	−10.7 (9.3)	−10.5 (9.6)	.67
PD superior arcuate 2	−8.0 (8.4)	−8.1 (8.5)	−8.1 (8.3)	−8.7 (8.9)	.86
PD inferior central	−4.7 (7.0)	−5.3 (7.4)	−6.4 (7.6)	−6.6 (8.3)	.13
PD inferior paracentral	−7.6 (9.6)	−8.7 (10.1)	−8.4 (9.3)	−8.1 (9.7)	.42
PD inferior nasal	−9.5 (10.2)	−11.2 (10.8)	−10.8 (10.3)	−11.0 (10.5)	.17
PD inferior arcuate 1	−7.0 (8.9)	−8.9 (9.5)	−8.5 (8.9)	−8.4 (9.3)	.08
PD inferior arcuate 2	−5.2 (8.0)	−6.6 (8.9)	−6.2 (8.8)	−6.1 (8.1)	.16
TDP superior central	2.5 (1.6)	2.7 (1.6)	2.6 (1.6)	2.8 (1.6)	.26
TDP superior paracentral	2.6 (1.6)	3.0 (1.5)	2.9 (1.5)	2.9 (1.5)	.048
TDP superior nasal	2.5 (1.6)	2.9 (1.4)	2.7 (1.5)	2.9 (1.5)	.03
TDP superior arcuate 1	2.3 (1.6)	2.7 (1.5)	2.6 (1.5)	2.6 (1.6)	.008
TDP superior arcuate 2	1.9 (1.7)	2.2 (1.5)	2.1 (1.6)	2.3 (1.6)	.02
TDP inferior central	2.0 (1.6)	2.2 (1.5)	2.5 (1.5)	2.4 (1.5)	.02
TDP inferior paracentral	2.4 (1.6)	2.8 (1.5)	2.9 (1.5)	2.8 (1.5)	.02
TDP inferior nasal	2.4 (1.7)	2.7 (1.4)	2.7 (1.5)	2.8 (1.4)	.06
TDP inferior arcuate 1	2.2 (1.6)	2.7 (1.4)	2.6 (1.4)	2.7 (1.4)	.007
TDP inferior arcuate 2	1.7 (1.6)	2.2 (1.6)	2.1 (1.6)	2.3 (1.6)	.008
PDP superior central	1.7 (1.7)	1.6 (1.7)	1.8 (1.7)	2.0 (1.8)	.14
PDP superior paracentral	2.0 (1.7)	2.2 (1.7)	2.1 (1.6)	2.1 (1.7)	.63
PDP superior nasal	2.0 (1.8)	2.2 (1.7)	2.1 (1.7)	2.3 (1.7)	.15
PDP superior arcuate 1	1.7 (1.7)	2.0 (1.7)	1.9 (1.6)	2.0 (1.7)	.18
PDP superior arcuate 2	1.4 (1.6)	1.5 (1.6)	1.5 (1.6)	1.6 (1.6)	.52
PDP inferior central	1.0 (1.3)	1.1 (1.5)	1.3 (1.5)	1.2 (1.5)	.42
PDP inferior paracentral	1.4 (1.5)	1.5 (1.6)	1.8 (1.6)	1.6 (1.6)	.15
PDP inferior nasal	1.6 (1.7)	1.7 (1.8)	1.8 (1.7)	1.8 (1.8)	.48
PDP inferior arcuate 1	1.3 (1.5)	1.6 (1.6)	1.6 (1.6)	1.5 (1.6)	.15
PDP inferior arcuate 2	0.9 (1.4)	1.1 (1.6)	1.2 (1.6)	1.2 (1.6)	.11

PD = pattern deviation; PDP = pattern deviation probability; SD = standard deviation; TD = total deviation; TDP = total deviation probability.
[a]Linear model with Generalized Estimating Equation (GEE) method for comparison of any difference across time points (baseline, 1, 2, and 3 years).

in patients with glaucomatous damage. This variable response of different regions within the VF indicates that a localized analysis of VF function is critical in understanding the benefit of different treatments.

Although GDDs offer similar long-term IOP control, they may not lower IOP as much as trabeculectomy.[26] It is important to study how well visual function has been preserved after GDD placement. To date, there is limited information in the ophthalmic literature examining the long-term perimetric outcomes after tube shunt surgery. A few previous studies published long-term perimetric follow-up data for patients undergoing Molteno aqueous tube shunt implantation, showing a VF loss progression of 12%-18%.[27,28] However, these studies had several limitations in their VF analysis, as they relied on several different perimetry platforms (including Humphrey, Goldmann, and Medmont platforms) within their patient cohort. These studies of VF function scoring

TABLE 5. Cross-Sectional Analysis of Local Visual Field (Which Region Was the Worst)

	Inferior Arcuate 1	Inferior Arcuate 2	Inferior Central	Inferior Nasal	Inferior Paracentral	Superior Arcuate 1	Superior Arcuate 2	Superior Central	Superior Nasal	Superior Paracentral	*P* Value[a]
Baseline											
TD											<0.001
N	106	106	106	106	106	106	106	106	106	106	
Mean (SD)	−8.8 (9.8)	−7.1 (9.1)	−6.8 (8.1)	−11.4 (11.2)	−9.5 (10.3)	−11.5 (10.8)	−9.9 (9.5)	−11.5 (10.9)	**−14.0 (12.1)**	−12.5 (11.1)	
PD											<0.001
N	106	106	106	106	106	106	106	106	106	106	
Mean (SD)	−7.0 (8.9)	−5.2 (8.0)	−4.7 (7.0)	−9.5 (10.2)	−7.6 (9.6)	−9.6 (9.5)	−8.0 (8.4)	−9.5 (10.3)	**−12.1 (11.0)**	−10.3 (10.0)	
TDP											<0.001
N	106	106	106	106	106	106	106	106	106	106	
Mean (SD)	2.2 (1.6)	1.7 (1.6)	2.0 (1.6)	2.4 (1.7)	2.4 (1.6)	2.3 (1.6)	1.9 (1.7)	2.5 (1.6)	2.5 (1.6)	**2.6 (1.6)**	
PDP											<0.001
N	106	106	106	106	106	106	106	106	106	106	
Mean (SD)	1.3 (1.5)	0.9 (1.4)	1.0 (1.3)	1.6 (1.7)	1.4 (1.5)	1.7 (1.7)	1.4 (1.6)	1.7 (1.7)	**2.0 (1.8)**	**2.0 (1.7)**	
1 Year											
TD											<0.001
N	103	103	103	103	103	103	103	103	103	103	
Mean (SD)	−11.1 (9.1)	−8.8 (8.7)	−7.7 (7.3)	−13.4 (10.4)	−10.7 (9.4)	−13.3 (9.8)	−11.0 (8.9)	−12.0 (10.7)	**−15.7 (10.7)**	−13.5 (10.2)	
PD											<0.001
N	103	103	103	103	103	103	103	103	103	103	
Mean (SD)	−8.9 (9.5)	−6.6 (8.9)	−5.3 (7.4)	−11.2 (10.8)	−8.7 (10.1)	−10.5 (9.2)	−8.1 (8.5)	−9.5 (11.2)	**−13.2 (10.8)**	−11.0 (10.3)	
TDP											<0.001
N	103	103	103	103	103	103	103	103	103	103	
Mean (SD)	2.7 (1.4)	2.2 (1.6)	2.2 (1.5)	2.7 (1.4)	2.8 (1.5)	2.7 (1.5)	2.2 (1.5)	2.7 (1.6)	2.9 (1.4)	**3.0 (1.5)**	
PDP											<0.001
N	103	103	103	103	103	103	103	103	103	103	
Mean (SD)	1.6 (1.6)	1.1 (1.6)	1.1 (1.5)	1.7 (1.8)	1.5 (1.6)	2.0 (1.7)	1.5 (1.6)	1.6 (1.7)	**2.2 (1.7)**	**2.2 (1.7)**	
2 years											
TD											<0.001
N	95	95	95	95	95	95	95	95	95	95	
Mean (SD)	−10.9 (8.9)	−8.7 (9.0)	−8.8 (7.9)	−13.1 (10.0)	−10.8 (9.3)	−13.0 (10.0)	−10.6 (8.7)	−12.1 (10.7)	**−15.0 (11.5)**	−12.9 (10.6)	
PD											<0.001
N	95	95	95	95	95	95	95	95	95	95	
Mean (SD)	−8.5 (8.9)	−6.2 (8.8)	−6.4 (7.6)	−10.8 (10.3)	−8.4 (9.3)	−10.7 (9.3)	−8.1 (8.3)	−9.6 (10.1)	**−12.5 (10.5)**	−10.5 (10.2)	
TDP											<0.001
N	95	95	95	95	95	95	95	95	95	95	
Mean (SD)	2.6 (1.4)	2.1 (1.6)	2.5 (1.5)	2.7 (1.5)	2.9 (1.5)	2.6 (1.5)	2.1 (1.6)	2.6 (1.6)	2.7 (1.5)	**2.9 (1.5)**	
PDP											<0.001
N	95	95	95	95	95	95	95	95	95	95	
Mean (SD)	1.6 (1.6)	1.2 (1.6)	1.3 (1.5)	1.8 (1.7)	1.8 (1.6)	1.9 (1.6)	1.5 (1.6)	1.8 (1.7)	**2.1 (1.7)**	**2.1 (1.6)**	
3 Years											

Continued on next page

TABLE 5. Cross-Sectional Analysis of Local Visual Field (Which Region Was the Worst) (*Continued*)

	Inferior Arcuate 1	Inferior Arcuate 2	Inferior Central	Inferior Nasal	Inferior Paracentral	Superior Arcuate 1	Superior Arcuate 2	Superior Central	Superior Nasal	Superior Paracentral	*P* Value[a]
TD											<0.001
N	80	80	80	80	80	80	80	80	80	80	
Mean (SD)	−11.0 (9.3)	−8.8 (8.0)	−9.3 (8.2)	−13.6 (10.4)	−10.8 (9.6)	−13.1 (10.5)	−11.4 (9.5)	−14.2 (11.8)	**−15.9 (11.2)**	−13.7 (11.3)	
PD											<.001
N	80	80	80	80	80	80	80	80	80	80	
Mean (SD)	−8.4 (9.3)	−6.1 (8.1)	−6.6 (8.3)	−11.0 (10.5)	−8.1 (9.7)	−10.5 (9.6)	−8.7 (8.9)	−11.7 (11.3)	**−13.3 (10.4)**	−11.1 (10.8)	
TDP											<.001
N	81	81	81	81	81	81	81	81	81	81	
Mean (SD)	2.7 (1.4)	2.3 (1.6)	2.4 (1.5)	2.8 (1.4)	2.8 (1.5)	2.6 (1.6)	2.3 (1.6)	2.8 (1.6)	**2.9 (1.5)**	**2.9 (1.5)**	
PDP											<.001
N	81	81	81	81	81	81	81	81	81	81	
Mean (SD)	1.5 (1.6)	1.2 (1.6)	1.2 (1.5)	1.8 (1.8)	1.6 (1.6)	2.0 (1.7)	1.6 (1.6)	2.0 (1.8)	**2.3 (1.7)**	2.1 (1.7)	

PD = pattern deviation; PDP = pattern deviation probability; SD = standard deviation; TD = total deviation; TDP = total deviation probability.
The bolded values indicates the worst regional VF loss.
[a]Linear model with Generalized Estimating Equation (GEE) method for comparison of any difference across different regions.

relied largely on global measurements and scotoma distances from fixation and included no localized or regional VF analyses.

In the present study cohort, there were no global or regional changes in MD or PD over the 3-year follow-up period compared to the preoperative visit. This indicates a preservation of visual function after GDD placement. The average MD at baseline in this study was approximately −10 dB, indicating a moderate to severe baseline glaucoma disease. This stability of VF function was correlated with the magnitude of IOP reduction from approximately 23-13 mm Hg (40% reduction). This outcome is consistent with that of previous large clinical trials studying trabeculectomy, including AGIS and CIGTS, which showed that, when tight IOP control was achieved, HVF function was maintained even for patients with severe glaucoma.[14] Thus, our data showed that GDD implantation is able to achieve stable VF function, which supports its application in surgical management of glaucoma. In the present study, most patients received intraoperative and/or antifibrosis agents (mostly mitomycin-C), which may contribute to steady postoperative IOP control and VF stability.

We analyzed not only local raw MD and PD data but also probability data, including TDP and PDP, calculated at each location. Probability data consider variations in visual sensitivities at each testing location and may provide more information for understanding visual functional changes. It was found that global CIGTS_TDP score showed a statistically significant decline with local CIGTS_TDP score at most locations, showing a trend of decline (although this localized trend was not statistically significant), whereas global and local CIGTS_PDP did not. The authors believe the mild change in CIGTS_TDP may reflect a subtle glaucoma progression but not media opacity, as patients with significant pre-existing media opacities were excluded, and patients who developed visually significant cataracts during the follow-up period underwent prompt cataract extraction surgery. Raw MD did not show any progression over the follow-up period. On the other hand, the change in CIGTS_TDP score was small and was below the typically accepted threshold change of 3 used in evaluating clinically significant VF progression in clinical trials.[29] Thus, although statistically significant, this trend may not be clinically significant. Overall, given the stable MD, PSD, and CIGTS_PDP values, the cause for and clinical implication with slight decrease in CIGTS_TDP needs more investigation in future study.

The univariate and multivariate analyses applied to identify risk factors for worsening on HVF were performed only with regard to CIGTS_TDP as it was the only metric that showed changes over the follow-up period. Multivariate analysis showed that only the pre-operative number of glaucoma medications used was a risk factor for progression over the follow-up period. Univariate analysis also showed increasing age to be a risk factor for progression, but this association proved to be null after controlling for

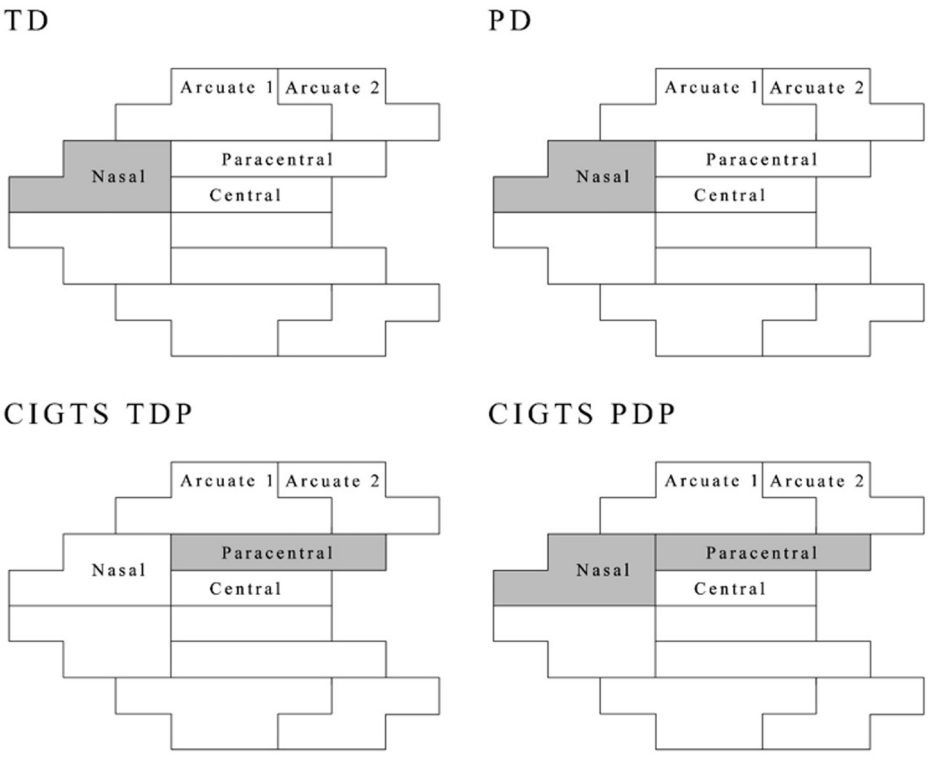

FIGURE 2. At baseline, for total deviation (TD) and pattern deviation (PD), the superior nasal region had the worst VF function. For the Collaborative Initial Glaucoma Treatment Study score of total deviation probability (CIGTS_TDP), superior paracentral region had the worst VF function. For the Collaborative Initial Glaucoma Treatment Study score on pattern deviation probability (CIGTS_PDP), both superior nasal and superior paracentral region had the worst VF function. This pattern was maintained over the 3-year follow-up. Adapted from Atalay and associates.[15]

the number of glaucoma medications. These findings overall are logical, as the preoperative number of glaucoma medication is likely a proxy for more aggressive disease or IOP that is more difficult to control. Preoperative IOP and postoperative maximal IOP were not significant factors, which may be because IOP had been tightly controlled in this cohort patients. Cataract was not a significant risk factor in univariate analysis in this study, because only 11.1% of patients were phakic at the 3-year follow-up visit (compared to 36.8% preoperatively). Visually significant cataract was corrected during the follow-ups.

The regional analysis also provides insight into the areas most vulnerable to damage in glaucoma. In this study, VF defects appeared the worst in the superior hemifield at both baseline and follow-up visits. For example, CIGTS_TDP, the superior paracentral sector was the worst, and by CIGTS_PDP, the superior nasal and superior paracentral sectors were the worst. This is consistent with previous studies. For example, Atalay and associates[15] found worse damage to the superior hemifield and nasal VF in a cohort of primary-angle closure glaucoma patients with varying disease severity. There have been several proposed mechanisms for this distribution of injury, based mostly on histopathologic anatomy observations noting the possibility vulnerabilities and higher incidences of structural defects in the inferior and inferotemporal optic nerve head tissue and lamina cribrosa.[30,31] These findings suggest a biomechanical vulnerability of the optic nerve head related to high-pressure mechanical insult, but more studies are needed to fully elucidate this.

The present study has several limitations. The study included patients with preoperative uncontrolled IOP determined by the surgeon, thus the patients may not have had definitive HVF progression prior to GDD placement. The retrospective nature of this study makes it subject to possible selection bias, although consecutive data collection helped to avoid this. Inclusion of phakic patients might have introduced noise into follow-up data as cataracts are known to have an effect on VFs. Although visually significant cataracts were promptly extracted during the follow-up period, subtle lens status changes might not have been identified. However, significant changes were

TABLE 6. Risk Factor Analysis of Change in Global Visual Field at 3 Year from Baseline (n = 81 Eyes)

	Change in CIGTS_TDP			
	Estimate (95% CI)	*P* Value	Adjusted Estimate (95% CI)	Adjusted *P* Value
Risk Factors	Univariate analysis		Multivariate analysis	
Age (every 1-year increase)	0.07 (0.00-0.13)	.04	0.06 (−0.00 to 0.12)	.06
Preoperative number of eye drops (every 1 drop increase)	1.49 (0.30-2.68)	.01	1.31 (0.10-2.52)	.03

CIGTS_TDP = Collaborative Initial Glaucoma Treatment Study (CIGTS) score on total deviation (TDP) probability.

All the risk factors with $P < 0.20$ from univariate analysis were included in the initial model. The backward variable selection was performed to get the final model, which contains risk factors listed in the table.

not found in global and local MD analyses. Mean visual acuity remained stable throughout the duration of the study, and phakic status was not found to be a statistically significant baseline risk factor for VF loss, which indicates that media opacity likely did not change significantly. Most of the GDDs used in the study were the Ahmed glaucoma valve type. More information on other types of GDDs is needed to more thoroughly evaluate the effect of tube shunt type on VF outcomes.

In summary, this is the first large study of HVF changes after GDD implantation. The study found that GDD implantation provides effective IOP control and prevents VF progression in global and regional analysis over a 3-year follow-up period. Analysis using CIGTS scoring of total deviation showed mild worsening in VF, possibly related to media opacities, with pre-operative numbers of glaucoma medications the only significant risk factor associated with this progression. In regional analysis, the superior hemifield was more severely affected in baseline and follow-up fields, consistent with prior studies.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

QIAN LIU: DATA CURATION, WRITING - ORIGINAL DRAFT, Writing - review & editing, Investigation, Validation, Methodology, Visualization. **Murtaza Saifee:** Data curation, Writing - original draft, Writing - review & editing, Investigation, Validation, Software, Visualization. **Yinxi Yu:** Methodology, Formal analysis, Data curation, Writing - review & editing. **Gui-Shuang Ying:** Methodology, Formal analysis, Data curation, Writing - review & editing. **Shuning Li:** Conceptualization, Methodology, Writing - review & editing. **Hua Zhong:** Conceptualization, Methodology, Writing - review & editing. **Steven J. Gedde:** Conceptualization, Methodology, Writing - review & editing. **Ying Han:** Conceptualization, Methodology, Validation, Investigation, Resources, Writing - review & editing, Visualization, Supervision, Project administration, Funding acquisition.

ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE FORM FOR DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST and none were reported.

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