Aqueous Shunts and Stents for Glaucoma

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Description:

Glaucoma is a group of eye diseases traditionally characterized by elevated intraocular pressure (IOP). However, glaucoma is more accurately described as disease affecting the optic nerve rather than a disease of high pressure. It is the second leading cause of blindness and can damage vision so gradually one may not notice any loss of vision until the disease is at an advanced stage. Standard therapy involves either topical medications or surgical intervention. The most commonly performed surgeries are laser trabeculoplasty, tube shunts such as the Baerveldt or Ahmed valve, micro-shunts, or iridectomies, depending upon the severity and type of glaucoma. There is an increasing use of Micro-invasive or minimally invasive glaucoma surgery (MIGS). These are a group of newer surgical procedures which are done via an ab interno approach resulting in less trauma to ocular structures. While MIGS are less effective in lowering IOP than trabeculectomy and aqueous shunt surgery, MIGS may have an improved safety profile in the short term and are routinely combined with phacoemulsification. Examples of MIGS include iStent® Inject and the Hydrus® Microstent.

When laser trabeculoplasty or iridectomy is unsuccessful, some patients undergo shunting procedures to help the fluid in the eye drain to reduce the pressure on the optic nerve. These can be simple silicone tubes or more complex devices. One such device is the Excessive Pressure Regulation Shunt System (EX-PRESS®) Mini Glaucoma Shunt (Alcon Laboratories, Inc., Ft. Worth, TX). This is a miniature drainage device designed to regulate intraocular pressure in eyes suffering from glaucoma. The concept behind the EX-PRESS is to divert aqueous humor (the liquid in the front portion of the eye that gives it its shape) through the implant from the anterior chamber to an intrascleral space (the space between layers of the eyeball). The EX-

PRESS glaucoma implant is manufactured from implantable stainless steel. It consists of a 2-3 mm long and 0.4 mm diameter tube, which connects the anterior chamber to the intrascleral space. Special features of this device include a cannula for draining aqueous humor from the anterior chamber to the intrascleral space, a plate to prevent excessive penetration, a spur to prevent extrusion of the EX-PRESS from the eye, and a reserve orifices near the distal end, which constitute an alternative conduit for aqueous humor drainage in case of occlusion of the primary (axial) opening of the cannula by the iris.

The iStent Trabecular Micro-Bypass stent is designed to improve aqueous outflow in patients with glaucoma. iStent improves outflow by creating a patent bypass between the anterior chamber and Schlemm's canal (SC). iStent is inserted through the phaco incision and can be performed under topical anesthesia. It is only approved in the US for implantation in association with cataract surgery. The second-generation iStent inject (iStent inject® W) is a small trabecular device that occupies less than 0.5 mm in diameter. The design allows ease of surgical use utilizing a standard implantation of 2 stents, targeting improved IOP reduction.

Another stent approved by the FDA in November 2016 is the Xen™45 Gel Stent. This device creates a permanent channel through the sclera allowing flow of the aqueous humor from the anterior chamber into the subconjunctival space. This stent is inserted using a Xen injector through a small corneal incision. The gel stent is designed to minimally swell, soften, and become flexible when hydrated. The stent's design also aids in retention of its intended location after surgical implantation.

Glaucoma surgery is intended to reduce intraocular pressure (IOP) when the target IOP cannot be reached with medications. Due to complications with established surgical approaches such as trabeculectomy, a variety of devices, including aqueous shunts are being evaluated as alternative surgical treatments for patients with inadequately controlled glaucoma.

Stents and tensioning devices are only able to reduce intraocular pressure (IOP) to the mid-teens, and may be inadequate when very low IOP is needed to reduce glaucoma damage. Micro-stents are also being evaluated in patients with mild to moderate open-angle glaucoma currently treated with ocular hypotensive medication.

Canaloplasty, which evolved from viscocanalostomy, is a surgical procedure in which tissue flaps are cut in the conjunctiva and the sclera to expose the drainage area (Schlemm's canal). The entire length of the SC is dilated with a suture loop between the canal and the trabecular meshwork using the specialized iTrack™ illuminated microcatheter device. This procedure is intended to restore the natural drainage of fluid from the eye, thus reducing IOP in persons with glaucoma. The difference between viscocanalostomy and canaloplasty is that canaloplasty attempts to open the entire length of the SC, rather than one section of it.

Phacocanaloplasty combines phacoemulsification (phaco), which is the standard care extraction and intraocular lens surgical treatment for cataracts, with canaloplasty (CP). Phacocanaloplasty utilizes a specially designed microcatheter to dilate aqueous humor collector channels to reduce IOP. The microcatheter alleviates obstructions in the SC by physically pushing through them and by injecting high-molecular-weight viscoelastic to viscodilate the SC. At the end of the procedure, a tensioning suture is placed to stent the canal open.

Policy Statement and Criteria

1. Commercial Plans/CHIP

U of U Health Plans covers internal aqueous shunting procedures with/without stent devices, including the EX-PRESS™ Mini Glaucoma Shunt, traditional trabeculectomy and the Xen™ 45 Gel Stent in members who meet ALL of the following criteria:

A. Patient has open-angle glaucoma; and
B. Limited to one implant per eye; and
C. Patient has not adequately responded to conservative therapy*.

U of U Health Plans considers aqueous shunt revisions, for the Express, Xen, traditional trabeculectomy, and valve surgeries (such as Baerveldt and other valve devices), medically necessary for the following primary indications:

A. Bleb leak;
B. Insufficient function due to scar tissue;
C. Device exposure.

U of U Health Plans covers the iStent and the iStent injector only if ALL the following criteria are met:

A. The procedure is combined with cataract surgery (can NOT be a stand-alone procedure); and
B. Patient has open-angle glaucoma; and
C. Limited to two implants per eye; and
D. Patient has not adequately responded to conservative therapy*.

U of U Health Plans covers the Hydrus® Microstent only if ALL the following criteria are met:

A. The procedure is combined with cataract surgery (can NOT be a stand-alone procedure); and
B. Patient has open-angle glaucoma; and
C. Limited to one implant per eye; and
D. Patient has not adequately responded to conservative therapy*.

** Failure of conservative therapy is defined as progression of optic nerve changes by optical coherence tomography (OCT), Heidelberg retinal tomography (HRT), automated perimetry, or scanning laser polarimetry on maximally tolerated medical therapy over a 6 month period.*

Maximally tolerated medical therapy is defined as a minimum of 3 topical glaucoma medications, unless there is documented intolerance such that less than 3 topical glaucoma medication classes are available to be used.

U of U Health Plans does NOT cover implantation of the following intraocular devices as evidence is either insufficient to determine clinical efficacy and safety or meets the plans definition of investigational/experimental (not an all-inclusive list):

A. InnFocus Microshunt
B. iStent supra Micro-Bypass Stent
C. SOLX Gold Shunt

U of U Health Plans does NOT cover viscocanalostomy and/or canaloplasty as it is considered investigational and not medically necessary for all indications, including but not limited to the treatment of primary open-angle glaucoma (POAG).

U of U Health Plans does NOT cover combined phacoemulsification and viscocanalostomy with Ologen implant for co-existing cataract and POAG as it is considered experimental and investigational because the effectiveness of this approach has not been established.

2. **Medicaid Plans**
   Coverage is determined by the State of Utah Medicaid program; if Utah State Medicaid has no published coverage position and InterQual criteria are not available, the U of U Health Plans Commercial criteria will apply. For the most up-to-date Medicaid policies and coverage, please visit their website at: https://medicaid.utah.gov/utah-medicaid-official-publications/ or the Utah Medicaid code Look-Up tool

   CPT/HCPCS codes covered by Utah State Medicaid may still require further evaluation to determine medical necessity for coverage.

Clinical Rationale

EX-PRESS Shunt

A review of literature performed in December 2009 identified 9 primary literature papers but no systematic reviews related to internal aqueous devices, including the EX-PRESS device. Of the 9 papers, a total of 744 eyes were treated in studies examining EX-PRESS, trabeculectomy vs. EX-PRESS and a variety of other mixed study designs. The mean follow-up time following the procedure was between 7.5 and 36.9 months.

The majority of the papers referenced a statistically significant decrease in intraocular pressure following the EX-PRESS procedure. Primary post-operative endpoints were generally >5 mmHg and <18-20 mmHg IOP (the accepted IOP is generally between 10-21 mmHg).

The published literature is, however, conflicted with regards to complications. For instance, Rivier et al. remarked that implantation of the shunt under the conjunctiva was associated with a complication rate approaching 30% despite good IOP control. Fewer complications, such as erosion of the conjunctiva and hypotony, were observed when EX-PRESS was placed under a sclera flap. Maris et al. and Reinthal et al. reported that when the device was implanted under a sclera flap, it had similar IOP-lowering efficacy with a lower complication rate than with trabeculectomy.

Of the 4 papers that compared Ex-PRESS to trabeculectomy, 3 reported higher success rates with the EX-PRESS device. The fourth only remarked that the implant was equally as safe and effective as the standard of care. None of the 9 papers compared the EX-PRESS device to pharmacologic solutions.

The review concluded, though some data is lacking related to long term efficacy and complications, the preponderance of evidence demonstrates internal aqueous shunts, such as the EX-PRESS device to be equally effective and safe in the treatment of glaucoma.

A 2014 U.S. multicenter randomized trial (Netland et al) compared trabeculectomy with EXPRESS implantation in 120 eyes of 120 patients. Comparator groups were similar at baseline, with a pre-operative IOP of 25.1 mm Hg on a mean of 3.1 medications for the EX-PRESS group and 26.4 mm Hg on a mean of 3.1 medications in the trabeculectomy group. Throughout 2-year postsurgical follow-up, average IOP and number of medications were similar between groups: mean IOP was 14.7 mm Hg on 0.9 medications in the EX-PRESS group and 14.6 mm Hg on 0.7 medications in the trabeculectomy group. Surgical success was 90% and 87% at 1 year and 83% and 79% at 3 years in the EX-PRESS and trabeculectomy groups, respectively. Visual acuity returned to near baseline levels at 1 month after EX-PRESS implantation (median, 0.7 months) and at 3 months after trabeculectomy (median, 2.2 months; p=0.041). Postoperative complications were higher after trabeculectomy (41%) than after EX-PRESS implantation (18.6%).

Two additional small RCTs were published (Wagschal et al, 2015) (Gonzalez-Rodriguez et al, 2016) and both trials corroborated the results of the earlier RCTs. Reporting no differences between trabeculectomy and Ex-PRESS shunt groups on outcomes for mean IOP, success rates, number of medications used, or complication rates.

A 2015 Cochrane review (Wang et al) evaluated the efficacy of adjunctive procedures for trabeculectomy. Three RCTs were included and compared trabeculectomy alone with trabeculectomy plus EX-PRESS Mini Shunt. These trials were rated as having high or unclear risk of bias using the Cochrane risk of bias tool. None of the RCTs reported a significant improvement for the EX-PRESS group. In pooled analysis, IOP was slightly lower in the combination group than in the trabeculectomy alone group (weighted mean difference, -1.58; 95% confidence interval [CI], -2.74 to 0.42). Pooled analysis also showed that subsequent cataract surgery was less frequent in the combination group than in trabeculectomy alone (relative risk, 0.34; 95% CI, 0.14 to 0.74). The combination group had a lower rate of some complications (e.g., hyphema, needling).

A report of published literature on the use of the EX-PRESS™ Glaucoma Filtration Device (EGFD) (Hayes et al, 2017) for the treatment of IOP in patients with OAG yielded 7 RCTs reported in 10 publications with participants ranging from 15120 patients. They concluded that a moderate-quality body of evidence suggested that EGFD results in similar outcomes when compared with trabeculectomy (the current standard of care), citing few differences between the 2 procedures relative to reduction of IOP, medication use, and the return of visual acuity in both the short and long term (up to 5 years).

XEN45 Gel Stent

This stent was FDA approved in July 2016. A recent review of the published evidence identified 2 systematic reviews and 8 primary studies which evaluated the efficacy, safety and durability of the

XEN45 gel stent. Regarding safety, several case reports included in this review (Fea et al. and Fernandez-Garcia) identify unique adverse events, the large prospective study by Schlenker et al perhaps best identifies safety issues with the XEN45 stent. This European study compares XEN45 to trabeculectomy. This is relevant as the XEN45 has been available in Europe for a number of years and thus provider experience better represents what might be expected long-term in the U.S. Comparison to trabeculectomy is also relevant as this is a much more invasive procedure considered the most definitive but also has significant potential adverse effects. This study showed no statistical difference in failure or safety concerns though numerically XEN45 appeared to have a better profile. Most notably the study by Sheybani et al. assessing flow dynamics demonstrated the risk of hypotony is low with the XEN45 stent.

With regard to efficacy, the systematic reviews by Manasses et al. in 2016 and Vinod in 2017 describe the comparative outcomes of the XEN device to other stents/shunts for the treatment of glaucoma. In the Manasses study it was noted IOP lowering reached normal levels of IOP form >20 mm Hg to ~13 mm and med reduction average 1.8 meds from 2.7 preoperative to 0.9 with no reported complications. This was noted to be comparable or superior to other stents/shunts available including the Cypass stent and iStent with a lower complication rate especially as it relates to hypotony. Vinod et al. identified similar outcomes with reduction in medications by ~1.8 meds over a two year time period and complete success (defined as sustained IOP reduction <18 mm Hg) achieved in 47% of patients studied. This systematic review also noted a low level of complications including transient hypotony (13%) and choroidal effusion (8.7%) though these also resolved spontaneously unlike what has been seen with Cypass.

A 2017 prospective, single-arm, open-label, multicenter clinical study (Grover et al), sponsored by the manufacturer (Allergan, Irvine, CA), evaluated the performance and safety of the XEN® 45 Gel Stent for the treatment of refractory glaucoma. Selection criteria included individuals with refractory glaucoma, defined as prior failure of a filtering or cilioablative procedure and/or uncontrolled IOP on maximally tolerated medical therapy. A total of 65 patients 45 years of age and older were implanted. No intraoperative complications or unexpected postoperative AEs were reported. During the 1 year of follow up, most AEs were considered mild/moderate and resolved with no sequelae. The authors concluded that the gel stent safely reduced both IOP and medication use and offer a less invasive surgical option for this subset of patients. Potential study limitations include the absence of comparator and open-label study design, which could have impacted the outcomes.

A 2017 review of published literature (Kerr et al) concluded that a growing body of evidence suggests that primary minimally invasive glaucoma surgery (including but not limited to the XEN® Glaucoma Treatment System) may be a viable initial treatment option to non-surgical intervention. However, further investigator-initiated randomized trials of sufficient size and duration are necessary to better evaluate efficacy.

Lastly, a study by De Gregorio et al from 2017 showed 80.7% complete response rate at 12 months with similar reduction in medication use post procedure. It noted no significant complications. Similarly studies by Galal et al. and Perez-Torregrosa demonstrated high levels of efficacy in patients who had failed medical therapy. Galal et al noted complete success in 42% at 12 months with greater than 12 mm Hg IOP decrease and a reduction in medication use by approximately 1.6 meds per patient on average at 12 months. Perez-Torregrosa identified improvement IOP of nearly 30% at 12 months with over 97% reduction in medication use.

Hayes performed an annual review of the XEN Glaucoma Treatment System (Allergan) for Treatment of Open-Angle Glaucoma in 2021. The authors found that implantation of the XEN Gel Stent generally resulted in positive effects on the reduction of IOP and medication burden, however, the degree of this impact varied across studies. “Results suggest that XEN implantation led to a variable rate of treatment success across studies, ranging from 47% to 77% in measures of success by achieving a target IOP or reduction in IOP without medication. In general, evidence comparing XEN implantation with trabeculectomy is insufficient to determine whether XEN implantation is equivalent or superior to trabeculectomy. In general, comparisons evaluating XEN implantation as a stand-alone treatment or in combination with cataract surgery did not identify differences between groups. Evidence evaluating whether diagnosis had an impact on the effectiveness of treatment with a XEN Gel Stent was insufficient to make definitive conclusions, although results from 2 studies generally demonstrated no difference between POAG and PEX. Finally, evidence from 1 study evaluating the effect of prior incisional surgical procedures is insufficient to draw any conclusions." The authors concluded that "although use of the XEN Gel Stent may not lead to complete elimination of ocular hypotensive medications in all patients, a reduction in the medication burden may improve patient compliance and lessen side effects of medications".

The studies appear to demonstrate the XEN45 stent to be safe and effective in lowering IOP in patients inadequately responsive to medical management. Evidence suggests potential reduced side effects compared to some MIGS devices. The volume of evidence remains limited despite the availability of this device in Europe for several years and the lack of more head to head comparison to other MIGS devices.

iStent

Based on a 2015 iStent study group, a notation was made that the devices have a good safety profile (Wellik et al). The most common complication across studies was early postoperative stent occlusion and malposition, which was observed in 2.6% to 18.0% of study subjects. Across all studies, malposition and occlusion necessitated surgical intervention (neodymium-doped yttrium aluminum garnet laser, recombinant tissue plasminogen activator, or stent revision) in a range of 4.5% to 11.3% of study subjects. This review also noted the occurrence of hyphema ranged from 2.3% to 70.0%, however, specific definitions of what constituted normal bleeding versus complicated bleeding were not given. Other adverse events were rare.

Multiple studies assessed the impact of iStent implant (in addition to cataract surgery which itself can lower IOP) on medication usage post-procedure. The evidence from the studies suggests a post-procedure reduction in medication use ranging from 0.48 to 1.7 medications in time periods as long as 3 years post procedure.

The evidence tends to identify the longer the measurement period after the procedure, the more likely the patient may once again need medication to control their intraocular hypertension. Whether this represents a loss of durability of the iStent or a natural progression of the disease is not identified in the studies.

The systematic reviews as a whole support the efficacy of the iStent device as measured in intraocular pressure (IOP) lowering in patients undergoing simultaneous cataract surgery. The two reviews by Malvankar-Mehta et al., from 2015 also support efficacy of iStent in lowering IOP as a standalone procedure. The Hayes review from 2016 which was updated in 2017 also focuses on the use of multiple stents, a practice reported to occur not uncommonly, and notes the body of evidence is of very low quality limiting that ability to make a statement as to the efficacy and safety of this approach.

The published studies also support efficacy of iStent in lowering IOP though many of the studies are of small size, lack randomization and are of short duration with outcomes typically measured to 12 months or less. Two studies, Arriola-Villalobos et al. (2012) Tan et al. (2016) looked at outcomes out to 54 months and 30 months respectively. These studies support the durability of the effect in lowering IOP in patients though both studies only assessed iStent in patients with associated cataract surgery.

In 2016 a search of all available PubMed publications for ab interno trabeculectomy (AIT) with the Trabectome device to determine the reduction in intra-ocular pressure (IOP) and medications following the procedure was conducted. For IOP outcomes, another search through PubMed retrieved all available papers for “trabectome”, “ab interno trabeculotomy” and “ab interno trabeculectomy”. This meta-analysis by Kaplowitz et al used a random-effects model to achieve conservative estimates and assess statistical heterogeneity. To investigate complications, these researchers included all abstracts from the American Glaucoma Society, AAO, American Society of Cataract and Refractive Surgery and the Association for Research in Vision and Ophthalmology. The overall arithmetic mean baseline IOP for stand-alone Trabectome was 26.71 ± 1.34 mm Hg and decreased by 10.5 ± 1.9 mm Hg (39 % decrease) on 0.99 ± 0.54 fewer medications.

Defining success as IOP less than or equal to 21 with a 20 % decrease while avoiding re-operation, the overall average success rate after 2 years was 46 ± 34 %. For combined phacoemulsification-Trabectome, the baseline IOP of 21 ± 1.31 mm Hg decreased by 6.24 ± 1.98 mm Hg (27 % decrease) on 0.76 ± 0.35 fewer medications. The success rate using the same definition at 2 years was 85 ± 7%. The weighted mean IOP difference from baseline to study end-point was 9.77 mm Hg (95 % CI: 8.90 to 10.64) stand-alone and 6.04 mm Hg (95 % CI: 4.95 to 7.13) for combined cases. Despite heterogeneity, meta-analysis showed significant and consistent decrease in IOP and medications from baseline to end-point in AIT and phaco-AIT. The rate of visually threatening complications was less than 1 %. On average, trabectome lowered the IOP by approximately 31 % to a final IOP near 15 mm Hg while decreasing the number of medications by less than 1, with a low rate of serious complications. After 2 years, the overall average success rate is 66 %.

A 2017 search of published literature identified 4 systematic reviews including a Hayes Brief report and 18 primary studies. These studies included more than 1305 patients dating from 2009 to 2016. As these devices have been approved in Europe for several years, many of the older studies are of European origin. Though several of the studies were larger randomized prospective studies most studies suffered from methodological weaknesses in that they were smaller case series without comparative arms and often were retrospective in their analyses. Nearly all studies focus on the first generation iStent leading to limitations to conclusions regarding the iStent injector.

In a 2019 study, Hayes assessed the iStent Inject Trabecular Micro-Bypass Stent as a standalone open-angle glaucoma procedure. Seven studies were found, 1 RTC, 1 cohort and 5 pre-test/post-test studies. The RTC study was of fair quality, the other 6 were of very poor quality. The literature generally reflected a reduction rate in intraocular pressure, although, results varied greatly between studies. Currently, the body of evidence is insufficient to fully evaluate the safety and efficacy of this procedure. Larger comparative studies are needed, with adequate follow-up duration, to establish better patient outcomes to the current routine treatments.

Hydrus® Microstent

The COMPARE study demonstrated the effectiveness of the Hydrus implant when compared with other MIGS procedures. In a standalone procedure, this prospective study affirmed the moderate pressure-lowering effect of the implant. The authors note that at 12 months, the Hydrus had a better rate of complete surgical success ($P < 0.001$) with reduced medication use. More Hydrus subjects were found to be medication free at 12 months. Similar findings by Laspas et al. were reported in the 3-year findings of the Hydrus II prospective study. The authors noted in this randomized control trial that a greater benefit was seen at the end of the follow-up for the Hydrus plus cataract surgery group compared with the control cataract surgery (CS) group. Thirty-six months after surgery, diurnal IOP averaged 18.3 mmHg in the Hydrus plus CS group and 20.6 mmHg in the CS control group. The number of medications needed also was lower significantly in the Hydrus plus CS group compared with the CS control group. Moreover, the proportion of patients without medication was significantly higher in the Hydrus plus CS group compared with the CS control group. They concluded that the Hydrus implant was a safe and effective method for lowering IOP and reducing medication in patients with glaucoma. The pressure lowering effect was maintained for 3 years.

Comparative of shunts effectiveness

Five-year results of 2 RCTs comparing the Ahmed and Baerveldt shunts have been published by Budenz et al in 2015 and 2016. The Ahmed Baerveldt Comparison (ABC) study was a multicenter international RCT evaluating the comparative safety and efficacy of the Ahmed Glaucoma Valve FP7 and Baerveldt Glaucoma Implant BG 101-350 (1:1 ratio) in 276 adults with previous incisional eye surgery or refractory glaucoma. ABC was funded by National Eye Institute, Research to Prevent Blindness and New World Medical. Mean IOP was 14.7 mm Hg in the Ahmed group and 12.7 mm Hg in the Baerveldt group at 5 years (p=0.01). The number of glaucoma medications in use at 5 years, cumulative probability of failure at 5 years, and visual acuity at 5 years did not differ statistically significantly between the 2 groups. The number of patients with inadequately controlled IOP or reoperation for glaucoma was 46 (80%) with the Ahmed shunt and 25 (53%) with the Baerveldt shunt (p=0.003). The 5-year cumulative reoperation rate for glaucoma was 21% in the Ahmed group versus 9% in the Baerveldt group (p=0.01). Late complications were defined as those developing after 3 months. Late complications occurred in 56 (47%) patients in the Ahmed group and 67 (56%) patients in the Baerveldt group during 5 years of follow-up (p=08). The cumulative incidences of serious complications at 5 years were 16% and 25% in the Ahmed and Baerveldt groups, respectively (p=0.03).

The Ahmed Versus Baerveldt (AVB) study (Christakis et al) was a 2016 international, multicenter RCT enrolling 238 patients with uncontrolled glaucoma despite maximum tolerated medical therapy. AVB is funded by the Glaucoma Research Society of Canada. Patients were randomized in a 1:1 ratio to the Ahmed FP7 implant and the Baerveldt 350 implant. Failure of the shunt implant was the primary outcome or was defined as any one of the following: IOP of less than 5 mm Hg or more than 18 mm Hg or less than a 20% reduction from baseline for 2 consecutive visits after 3 months; de novo glaucoma surgery required; removal of the implant; severe vision loss related to the surgery; or progression to no light perception for any reason. The cumulative failure rate was 53% in the Ahmed group and 40% in the Baerveldt group at 5 years (p=0.04). In the Ahmed and Baerveldt shunts, the mean percent reduction in IOP was 47% and 57% (p=0.001) and mean percent reduction in medication use was 44% and 61% (p=0.03), all respectively. Hypotony was reported in 5 (4%) patients in the Baerveldt group but not in the Ahmed group (p=0.02).

The comparative effectiveness of the Ahmed vs Baerveldt has been addressed in two trials, the Ahmed versus Baerveldt (AVB) trial and the Ahmed Baerveldt Comparison (ABC) trial. The trials had similar results. Both of the devices lowered IOP. There was a small difference in reduction in IOP favoring Baerveldt (1.2 – 1.3 mmHg lower) and patients with Baerveldt required slightly fewer medications. The Baerveldt also had a higher rate of serious hypotony related complications.

In conclusion, there is a moderate sized body of literature of low to moderate quality that demonstrates implantation of the first generation iStent device is safe and likely effective in lowering IOP and improving intraocular pressure control post-cataract surgery in patients with glaucoma. Evidence is less robust for the iStent injector with most studies using the first generation iStent device. Additionally, the effectiveness of iStent is suggested as a standalone treatment but the evidence is inadequate to draw conclusions in this setting.

Canaloplasty

Bull and colleagues (2011) reported 3-year results of a European, prospective, multi-center, interventional study consisting of 109 eyes of 109 adults with open-angle glaucoma undergoing canaloplasty or combined cataract-canaloplasty surgery. Primary outcome measures included IOP, glaucoma medication usage, and adverse events. Eyes with canaloplasty showed a mean baseline IOP of 23.0 ± 4.3 mm Hg and mean glaucoma medication usage of 1.9 ± 0.7 medications, which decreased to a mean IOP of 15.1 ± 3.1 mm Hg on 0.9 ± 0.9 medications at 3 years postoperatively. Eyes with combined cataract-canaloplasty surgery showed a mean baseline IOP of 24.3 ± 6.0 mm Hg on 1.5 ± 1.2 medications, which decreased to a mean IOP of 13.8 ± 3.2 mm Hg on 0.5 ± 0.7 medications at 3 years. Intraocular pressure and medication use results for all study eyes were significantly decreased from baseline at all intervals (p<0.00001). Late postoperative complications included transient IOP elevation (1.8%) and cataracts (19.1%). The authors concluded that predictive factors for successful canaloplasty outcomes and reasons for later failure remain unclear and should be explored in future studies.

In a retrospective case series, Ayyala and colleagues (2011) compared individual outcomes through 12 months of follow-up post canaloplasty and trabeculectomy procedures. Individuals with open-angle glaucoma who underwent either canaloplasty (33 eyes of 33 subjects) or trabeculectomy with mitomycin C (46 eyes of 46 subjects) to control IOP between January 2007 and December 2008 were included. A single surgeon performed all surgeries. Primary outcome measures were: change in IOP, visual acuity, postoperative medications, failure based on IOP (> 18 or < 4 mm Hg at 1 year) or second operative procedure (any eye requiring reoperation) and complication rates at 12 months. There were no differences in demographics, previous surgery, or preoperative and postoperative visual acuity between the groups. The mean percentage of reduction in IOP from preoperative values at 12 months after surgery was 32% (± 22%) for the canaloplasty group compared with 43% (± 28%) for the trabeculectomy group. The median reduction in the number of medications at 12 months follow-up was 2 in the canaloplasty group and 3 in the trabeculectomy group. A higher percentage of those treated with canaloplasty than trabeculectomy (36% vs. 20%) required postoperative medications. Failure based on IOP (IOP >18 or <4 mm Hg at 12 months) was 12.1% (4/33 subjects) for the canaloplasty group and 4.3% (2/46 subjects) for the trabeculectomy group. Surgical failure rates for the canaloplasty group (n=5, 15%) and trabeculectomy group (n=5, 11%) were comparable. The authors concluded that these results need to be confirmed by a prospective, randomized, longitudinal study. Limitations of this study included small size and limited duration of follow-up.

Rulli and colleagues (2013) conducted a systematic review and meta-analysis of comparative studies of two or more surgical techniques (one of which had to be Trabeculectomy [TE]), including individuals with open-angle glaucoma. Comparisons were made between TE and the main types of non-penetrating surgery (NPS) (deep sclerectomy, viscocanalostomy, and canaloplasty). The primary outcome was the mean between-group difference in the reduction in diurnal IOP from baseline to the 6- or 12-month follow-up evaluation. A total of 18 articles, consisting of 20 comparisons, were analyzed. The 6-month follow-up data demonstrated that the pooled estimate of the mean between-group difference was −2.15 mm Hg (95% CI, −2.85 to −1.44) in favor of TE. There was no difference between the NPS subgroups. The absolute risk of hypotony, choroidal effusion, cataract, and flat or shallow anterior chamber was higher in the TE group than in the NPS group. The authors concluded that trabeculectomy seemed to be the most effective surgical procedure for reducing IOP in individuals with open-angle glaucoma. However, it was associated with a higher incidence of complications when compared with NPS.

Brusini and colleagues (2014) performed a 3-year follow-up from an independent series of 214 individuals treated with canaloplasty in Europe. Mean IOP was reduced from 29.4 mm Hg at baseline to 17.0 mm Hg after excluding 17 subjects (7.9%) who later underwent trabeculectomy. IOP was 21 mm Hg or lower in 86.2% of subjects, 18 mm Hg or lower in 58.6%, and 16 mm Hg or lower in 37.9%. There was a decrease in mean medication use, from 3.3 at baseline to 1.3 at follow-up. Complications, which included hyphema, Descemet membrane detachment, IOP spikes, and hypotony, were fewer than is usually seen with trabeculectomy. Disadvantages of canaloplasty that were reported included the inability to complete the procedure in 16.4% of eyes, a long and rather steep surgical learning curve, the need for specific instruments, and an average postoperative IOP level that tended to not be very low.

A small, prospective clinical trial by Matlach and colleagues (2015) consisted of 62 eyes of 62 Caucasian subjects with uncontrolled, open-angle glaucoma randomized to either a trabeculectomy (n=32) or canaloplasty (n=30). Both surgeries were performed by a single glaucoma surgeon at a single European center, and all subjects were followed for 2 years postoperatively. A significant reduction of intraocular pressure (IOP) occurred in both groups. Mean absolute IOP reduction was 10.8 ± 6.9 mm Hg in the trabeculectomy and 9.3 ± 5.7 mm Hg in the canaloplasty group after 2 years. Mean IOP was 11.5 ± 3.4 mm Hg in the trabeculectomy and 14.4 ± 4.2 mm Hg in the canaloplasty group after 2 years. Complications were more common in the trabeculectomy group and included choroidal detachment (12.5%), hypotony (37.5%), and elevated IOP (25.0%). The authors concluded that trabeculectomy allowed for a stronger decrease of IOP with less need for medication, and canaloplasty had a lower complication rate. Limitations of this study included a small sample size.

Zhang and colleagues (2017) published a systematic review and meta-analysis on the efficacy and safety of canaloplasty compared to trabeculectomy. Using a baseline of 28 studies published before April 1, 2016, the researchers compared 1-year, post-procedure outcomes for 1498 eyes. Trabeculectomy was more efficient in IOP reduction than canaloplasty (MeD 3.61 mm Hg; 95% CI, 1.69 to 5.53). For both procedures, there was a similar reduction in the need for glaucoma medications (MeD –0.37 mm Hg; 95% CI, –0.83 to 0.08). Adverse events included hyphema (≥ 1 mm), which was higher in the canal-oplasty group (OR 9.24; 95% CI, 3.09 to 27.60), and hypotony, which was higher in the trabeculectomy group (OR 0.32; 95% CI, 0.13 to 0.80). In addition, trabeculectomy had higher incidences of choroidal effusion or detachment (OR 0.25; 95% CI, 0.06 to 0.97). Some adverse events were specific to the procedure, with incidences of Descemet membrane attachment in the canaloplasty group only (3%), and incidences of suprachoroidal hemorrhage and bleb needling in the trabeculectomy group only (2.3% and 10.9%, respectively). The researchers concluded that trabeculectomy was more effective than canal-oplasty in reducing IOP, but trabeculectomy had more complications. The researchers concluded that high-quality, randomized controlled trials are needed to verify the findings.

Liu and colleagues (2017) analyzed the safety and efficacy of canaloplasty versus trabeculectomy for the treatment of glaucoma. The researchers pooled data from 8 included studies published between 2010 and 2015, focusing on complications and intraocular pressure at 6 and 12 months post-procedure. The researchers did not find a difference in intraocular pressure at 6 months; however, at 12 months, the intraocular pressure was higher in the canaloplasty group (weighted mean difference [WMD] 1.90; 95% CI, 0.12 to 3.69; p<0.05). The canaloplasty group was more likely to have hyphema (RR 2.96; 95% CI, 1.51 to 5.83), but less likely to have hypotony (RR 0.30; 95% CI, 0.11 to 0.83) and postoperative choroid abnormalities (RR 0.24; 95% CI, 0.09 to 0.66). The researchers concluded that trabeculectomy "can significantly reduce the intraocular pressure better than canaloplasty method in glaucoma patients after operation," and "trabeculectomy leads a more marked IOP decrease than canaloplasty at the cost of a higher complication rate."

Khaimi and colleagues (2017) published 3-year outcomes following canaloplasty for the treatment of open-angle glaucoma. The researchers retrospectively reviewed charts at a single center to gather a cohort of 277 eyes treated by canaloplasty. Primary endpoints were the mean IOP and mean number of glaucoma medications at each follow-up visit and secondary endpoints were surgical and post-surgical complications. The overall baseline IOP of 19.7 mmHg was reduced to 15.2 mmHg at 3 years (p<0.001). Average medication usage was reduced from a baseline of 2.1 to 0.6 at 3 years (p<0.001). Hyphema was present postoperatively in 144 eyes (52.8%) but was resolved in 125 of those eyes in 3 months. Baseline mean visual acuity was 0.31 ± 0.35 with a mean Snellen fraction of 20/41.1. At 3 years (n=65), mean visual acuity was 0.20 ± 0.24 with a Snellen fraction of 20/31.5 (p=0.29). The authors noted that visual acuity "worsens significantly after surgery but may return to preoperative values by around 3-12 months postoperatively." The researchers concluded "the risk profile of canaloplasty was favorable and consistent with the well-documented, lower risks associated with other non-penetrating procedures." The study was limited by a retrospective design and loss to follow-up.

Canaloplasty is currently under investigation. Several trials are currently underway to further support the benefits and safety of this technique.

Phacocanaloplasty

Recently, a meta-analysis (Hayes, Inc. 2020) assessed phacocanaloplasty (P-CP) for the treatment of concomitant open-angle glaucoma (OAG) and cataract in adult patients. Nine eligible studies were found (1 RCT, 4 retrospective cohort studies, 1 multicenter prospective, un-controlled study and 3 retrospective, uncontrolled studies) that evaluated P-CP for treating OAG plus cataract. One systematic review/meta-analysis that evaluated published efficacy and safety outcomes of stand-alone glaucoma surgeries compared with the same surgery plus phaco (e.g., P-TE versus TE; P-DS versus DS; P-CP versus canaloplasty). Five studies (n=237 total patients) compared canaloplasty (CP) with P-CP. The primary comparison of interest was mean IOP reduction from baseline. When analyzing IOP reduction, the authors concluded that the pooled weighted mean difference between groups was –3.78% favoring P-CP over CP. Although, the difference was not statistically significant (P=0.11; I2=not reported). Patients receiving P-CP had glaucoma and visually significant cataract, whereas patients receiving CP may not have also had cataract in addition to glaucoma. No treatment-related mortality or serious adverse events occurred in any of the reviewed studies. The most common and serious complications included hypotony (0%-13%), Descemet's membrane detachment (0%-2.8%), microhyphema (4.03%-28.0%), hyphema (0.62%-46%), bleb formation (0%-25%), and choroidal effusion/detachment (0%-5%). In conclusion, even though OAG plus cataract patients appear to improve following P-CP, the relative efficacy of P-CP versus other surgical interventions, such as P-TE, remains uncertain. Therefore, more prospective studies are needed to prove efficacy, especially since the body of evidence found for this study was of low quality.

Combined Phacoemulsification and Viscocanalostomy with Ologen Implant

In a prospective, interventional, randomized clinical study, Gad and colleagues (2019) examined the efficacy of the biodegradable collagen implant Ologen as an adjuvant in phaco-viscocanalostomy in patients with co-existing cataract and POAG. This trial entailed patients with co-existing cataract and glaucoma who were randomized to receive either phaco-viscocanalostomy (Phacovisco group) (39 eyes) or phaco-viscocanalostomy with Ologen implant (OloPhacovisco group) (40 eyes). Follow-up period was 2 years; Nd:YAG laser gonio-puncture was performed in cases where the IOP was elevated above 21 mmHg after discontinuation of corticosteroid eye drops at any follow-up visit. No significant operative or post-operative complications (other than failure) were encountered in either group. At 2 years follow-up, the mean IOP level was statistically significantly decreased in the OloPhacovisco group (p = 0.02) and complete success occurred in 23 eyes (59.0 %) in the Phacovisco group and in 32 eyes (80.0 %) in the OloPhacovisco group. There was a statistically significant higher success rate regarding complete success in patients that received Ologen implant (p = 0.04). The authors concluded that Ologen implant improved the success rate of phaco-viscocanalostomy. Moreover, these researchers stated that larger studies with longer follow-up periods are needed to confirm the safety and efficacy of this device in viscocanalostomy. The main drawbacks of this study were the relatively small sample size (40 eyes in the OloPhacovisco group) and short follow-up period (2 years).

Revisions
Indications for revisions are based on the risk of sight-threatening complications due to inadequate IOP control or infection, which can result from bleb leaks, scar-induced malfunction, or device exposure. Revision in these cases helps to maintain therapeutic effectiveness, reduce complications, and support optimal long-term management of glaucoma.

Applicable Coding

CPT Codes

Possibly covered

0449T	Insertion of aqueous drainage device, without extraocular reservoir, internal approach, into the subconjunctival space; initial device **[XEN45 Gel Stent and XEN Injector]**
0450T	Insertion of aqueous drainage device, without extraocular reservoir, internal approach, into the subconjunctival space; each additional device (List separately in addition to code for primary procedure) **[XEN45 Gel Stent and XEN Injector]**
0671T	Insertion of anterior segment aqueous drainage device into the trabecular meshwork, without external reservoir, and without concomitant cataract removal, one or more
66179	Aqueous shunt to extraocular equatorial plate reservoir, external approach; without graft
66180	Aqueous shunt to extraocular equatorial plate reservoir, external approach; with graft
66183	Insertion of anterior segment aqueous drainage device, without extraocular reservoir, external approach **[(For Ex-PRESS Mini Glaucoma Shunt ONLY), InnFocus Micro-shunt and SOLX Gold Shunt are NOT covered]**
66184	Revision of aqueous shunt to extraocular equatorial plate reservoir; without graft
66185	Revision of aqueous shunt to extraocular equatorial plate reservoir; with graft
66989	Extracapsular cataract removal with insertion of intraocular lens prosthesis (1-stage procedure), manual or mechanical technique (eg, irrigation and aspiration or phacoemulsification), complex, requiring devices or techniques not generally used in routine cataract surgery (eg, iris expansion device, suture support for intraocular lens, or primary posterior capsulorrhexis) or performed on patients in the amblyogenic developmental stage; with insertion of intraocular (eg, trabecular meshwork, supraciliary, suprachoroidal) anterior segment aqueous drainage device, without extraocular reservoir, internal approach, one or more
66991	Extracapsular cataract removal with insertion of intraocular lens prosthesis (1 stage procedure), manual or mechanical technique (eg, irrigation and aspiration or phacoemulsification); with insertion of intraocular (eg, trabecular meshwork,

supraciliary, suprachoroidal) anterior segment aqueous drainage device, without extraocular reservoir, internal approach, one or more

66250 Revision or repair of operative wound of anterior segment, any type, early or late, major or minor procedure

HCPCS Codes

Possibly covered

C1783 Ocular implant, aqueous drainage assist device

L8612 Aqueous shunt

Non-covered codes

0253T Insertion of anterior segment aqueous drainage device, without extraocular reservoir, internal approach, into the suprachoroidal space **[iStent G3 Supra]**

0474T Insertion of anterior segment aqueous drainage device, with creation of intraocular reservoir, internal approach, into the supraciliary space

0660T Implantation of anterior segment intraocular non-biodegradable drug-eluting system, internal approach

0661T Removal and reimplantation of anterior segment intraocular non-biodegradable drug-eluting implant

66174 Transluminal dilation of aqueous outflow canal; without retention of device or stent

66982 Extracapsular cataract removal with insertion of intraocular lens prosthesis (1-stage procedure), manual or mechanical technique (e.g., irrigation and aspiration or phacoemulsification), complex, requiring devices or techniques not generally used in routine cataract surgery (e.g., iris expansion device, suture support for intraocular lens, or primary posterior capsulorrhexis) or performed on patients in the amblyogenic developmental stage; without endoscopic cyclophoto-coagulation **[phacoemulsification and viscocanalostomy with Ologen implant]**

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