

## Advances in the Surgical Management of Glaucoma—The Role of the EX-PRESS® Glaucoma Filtration Device

A report on the satellite symposium 'Advances in glaucoma surgery: new evidence in filtration surgery' chaired by Ivan Goldberg and held at the World Glaucoma Congress, June 30, 2011, Paris, France

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### Abstract

Ivan Goldberg

By reducing intraocular pressure (IOP), we aim to arrest the glaucomatous process. Our strategies include medical, laser, and surgical techniques. Trabeculectomy is the gold standard drainage surgery to achieve this; as there can be a high degree of variability in the procedure and its success depends on bleb creation, with the challenges of wound healing modulation, results remain unpredictable. Several devices are being assessed to try to achieve 'minimally invasive glaucoma surgery'. While results will take some years to evaluate rigorously, it seems IOP levels by these means lie in the mid-teens. These minimally invasive glaucoma surgery techniques therefore would appear to be destined for patients whose glaucomatous damage is relatively mild to moderate and whose target IOPs fall into this range. To simultaneously achieve lower IOPs for patients with more advanced visual loss, efforts have been made to 'fine-tune' trabeculectomy. Use of the EX-PRESS® Glaucoma Filtration Device (GFD) under a scleral flap is one such approach. How does the EX-PRESS® GFD benefit the conventional trabeculectomy procedure? What tips and tricks contribute to its success? How safe is it? Is the additional cost to our health systems justifiable? This symposium, sponsored by Alcon, set out to try to answer these questions.

### Keywords

Aqueous outflow, filtration surgery, glaucoma, intraocular pressure, trabeculectomy

**Disclosure:** David Cope is a medical writer at Touch Briefings. Ivan Goldberg is an advisory board member for Alcon, Allergan, Merck, and Pfizer, a consultant for Alcon, ForSight, and Merck, and receives research support from Alcon and Allergan.

**Received:** September 16, 2011 **Accepted:** August 20, 2012 **Citation:** *US Ophthalmic Review*, 2012;5(2):81–6 DOI: 10.17925/USOR.2012.05.02.81

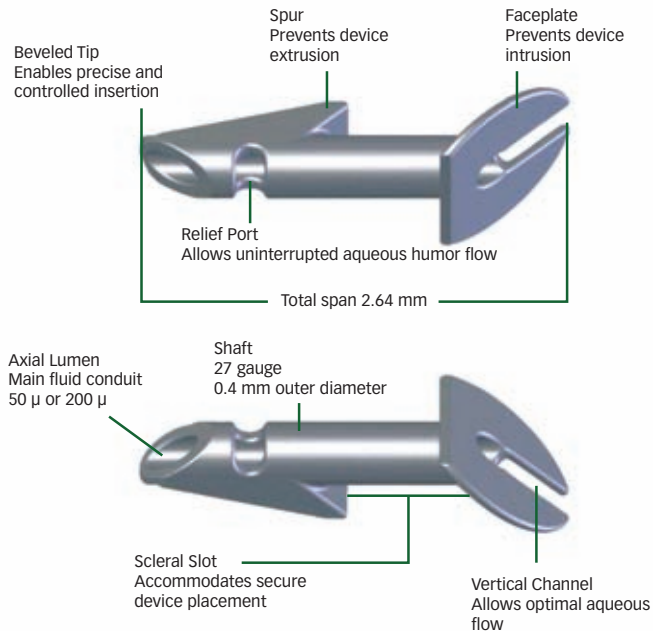
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**Support:** The editorial support for, and publication of, this article was funded by Alcon.

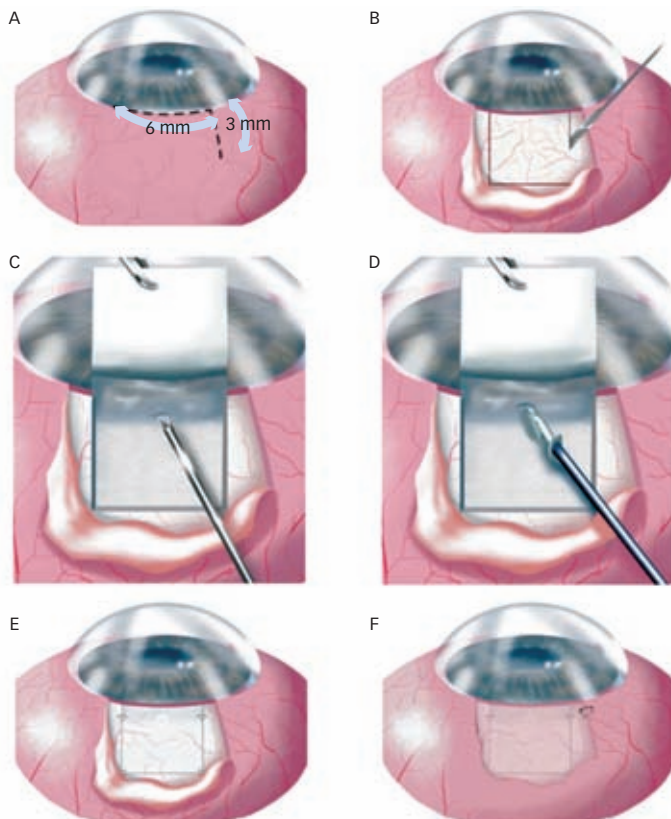
Although for open-angle glaucoma the level of intraocular pressure (IOP) is no longer recognized as a defining criterion, it is a major risk factor for the development and progression of the disease.<sup>1–6</sup> Medical, laser, and surgical therapies therefore reduce IOP to attempt to modify disease progression.<sup>7,8</sup> Trabeculectomy is the current gold standard of filtration surgery in the management of primary open-angle glaucoma following the failure of IOP-lowering medications or non-invasive surgery such as laser trabeculoplasty.<sup>9–11</sup> Trabeculectomy can effectively control IOP,<sup>12–15</sup> even in the long term,<sup>16–20</sup> but published

success rates can vary, in part due to the lack of standard definitions of success.<sup>21</sup> Moreover, trabeculectomy is associated with significant complications including early post-operative hypotony, bleb leak, blebitis and bleb failure, choroidal effusions, endophthalmitis, hyphema, shallowing of the anterior chamber, and accelerated cataract progression.<sup>9</sup> Patients who fail to respond to trabeculectomy may require additional surgery, in some instances a second trabeculectomy, or implantation of a drainage device.<sup>22</sup> As a result, some studies have suggested that the risks of trabeculectomy outweigh the benefits.<sup>18,23</sup>

**Figure 1: The P Series EX-PRESS® Glaucoma Filtration Device**



**Figure 2: Implantation of the EX-PRESS® Glaucoma Filtration Device**



A: A fornix-based conjunctival flap is created in the upper quadrant. B: A 50% depth limbus-based scleral flap is created. C: The anterior chamber is penetrated under the scleral flap with a 25–27 gauge needle entering through the blue-gray transition zone between the sclera and the clear cornea. D: The EX-PRESS® Glaucoma Filtration Device is inserted. E: The scleral flap is sutured. F: The conjunctival flap is sutured watertight. Reproduced from Dahan and Carmichael, 2005.<sup>34</sup>

Incremental improvements in trabeculectomy have proved valuable in refining the technique and include the use of a traction suture to control the position of the eye, appropriate and optimal wound healing techniques to prevent fibrosis and scarring, use of a fornix-based conjunctival flap, creation of a large scleral flap to maximize posterior aqueous flow and enable the development of a diffuse bleb, adjustable sutures to control aqueous flow, and a standardized trabeculectomy aperture.<sup>24,25</sup> Such refinements can improve patient outcomes.<sup>26,27</sup>

One such incremental advance has been the development of the EX-PRESS® Glaucoma Filtration Device (GFD), an attempt to standardize trabeculectomy and enable predictable aqueous flow.<sup>28</sup> In the US, EX-PRESS® GFD implantation is currently indicated for patients who have failed to respond to both medications and surgeries such as laser trabeculoplasty.<sup>29</sup> The satellite symposium ‘Advances in glaucoma surgery: new evidence in filtration surgery’ at the World Glaucoma Congress 2011 examined some of the recent findings evaluating the performance of the EX-PRESS® GFD and the role it can play in improving conventional trabeculectomy surgery. This article documents some of these findings, specifically in relation to glaucoma surgery in the US.

## A Historical Perspective on the EX-PRESS® Glaucoma Filtration Device

*A report on the presentation ‘What is the EX-PRESS® GFD and how is it different than a traditional trabeculectomy?’ by Robert Fechtner*

Dr Fechtner’s presentation provided a broad overview of the EX-PRESS® GFD and began by describing the EX-PRESS® GFD and its properties. The EX-PRESS® GFD is a <3 mm long implant made from 316L medical grade stainless steel that is fully biocompatible with the eye (see Figure 1).<sup>28,30</sup> The device comes with a spur to prevent extrusion and an end plate to prevent intrusion into the anterior chamber. It is non-valved and designed to divert aqueous away from the anterior chamber to the subconjunctival space, in a similar manner to a traditional trabeculectomy, with the flow being controlled by the diameter of the lumen.<sup>28</sup> In addition, a vertical slot in the end plate is designed to facilitate the generation of a diffuse bleb.<sup>28</sup> The P series EX-PRESS® GFD is available with a lumen size of 50 or 200 μm. Standardization of the lumen therefore makes one step of the trabeculectomy procedure more predictable.

Initial versions of the EX-PRESS® GFD were implanted directly under the conjunctiva, but this led to excessive post-operative complications, including sustained hypotony, due to the lack of resistance to aqueous flow, subconjunctival scar tissue formation, endophthalmitis, and conjunctival erosions.<sup>31–33</sup> In 2005, the procedure was improved by implanting the EX-PRESS® GFD under a half-thickness scleral flap.<sup>34</sup> In the initial description of the new procedure, IOP was well controlled at 24 months with few complications, transient hypotony being the most common.<sup>34</sup> Like a traditional trabeculectomy, the current EX-PRESS® GFD implantation technique is therefore a guarded procedure. In 2007, the first study comparing guarded EX-PRESS® GFD implantation with traditional trabeculectomy was published.<sup>35</sup> Following EX-PRESS® GFD implantation in 50 eyes of 49 patients and trabeculectomy in 50 eyes of 47 patients, IOP reduction from baseline

was similar in both groups after 12 months (39.9 % and 42.1 %, respectively) with fewer incidences of early post-operative hypotony and choroidal effusion in those implanted with the EX-PRESS® GFD.<sup>35</sup> This initial study therefore demonstrated EX-PRESS® GFD implantation was as effective as traditional trabeculectomy in controlling IOP, with fewer post-operative complications.

Dr Fechtner then described the standard procedure for implantation of the EX-PRESS® GFD (see *Figure 2*).<sup>34</sup> A fornix-based conjunctival flap is created in the nasal or temporal upper quadrant, as in trabeculectomy, leaving sufficient room for additional surgery if later required. Appropriate wound healing techniques are applied to the sclera to prevent potential scarring and fibrosis. A limbus-based scleral flap of approximately half thickness is dissected up to the clear cornea, as in trabeculectomy, of sufficient size to cover the device end plate. At this point a paracentesis can be created and the chamber deepened before the anterior chamber is entered with a 25–27 gauge needle under the scleral flap posterior to the blue-gray transition zone between the sclera and cornea. The EX-PRESS® GFD is inserted through the perforation using the EX-PRESS® GFD delivery system (EDS) (see *Figure 2*). The device comes loaded onto the wire of the EX-PRESS® GFD and is released, once in position, by depression of a button on the EX-PRESS® GFD that withdraws the guide wire. Finally, as in trabeculectomy, the scleral flap is sutured with releasable or adjustable sutures and the conjunctival flap sutured watertight. Post-operative care with anti-inflammatories and antibiotics is also similar to trabeculectomy.

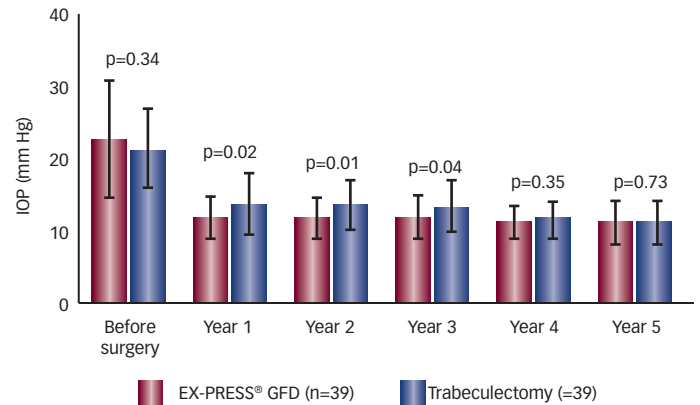
As well as providing good control of IOP,<sup>34,35</sup> EX-PRESS® GFD implantation has several advantages compared with traditional trabeculectomy. Implantation of the EX-PRESS® GFD is not a great leap in surgical skill; the skills required are the same as for trabeculectomy. Intra-operatively, there is no requirement for iridectomy so there is less inflammation and less potential for bleeding. It standardizes the sclerectomy step in the trabeculectomy procedure enabling predictable aqueous outflow. Finally, as already indicated, the incidence of post-operative complications is smaller compared with trabeculectomy.<sup>35</sup> Some eyes that might be candidates for trabeculectomy may not necessarily be candidates for EX-PRESS® GFD implantation. There must be sufficient conjunctiva and sclera to create the appropriately sized flap. In the setting of extensive prior surgery or scarring there may not be enough room for an EX-PRESS® GFD. Similarly, there should be enough room in the angle to accommodate the device. When there is not enough room for an EX-PRESS® GFD it still may be possible to perform trabeculectomy. The device has a financial cost. Dr Fechtner finished his presentation by saying that this cost may be offset, however, by potentially reduced lifetime costs to the healthcare system.

### Long-term Evaluation of the EX-PRESS® Glaucoma Filtration Device

*A report on the presentation ‘Improving the efficacy and predictability of filtration surgery with the EX-PRESS® GFD—new 5 year study results comparing EX-PRESS® GFD versus trabeculectomy’ by Leo de Jong*

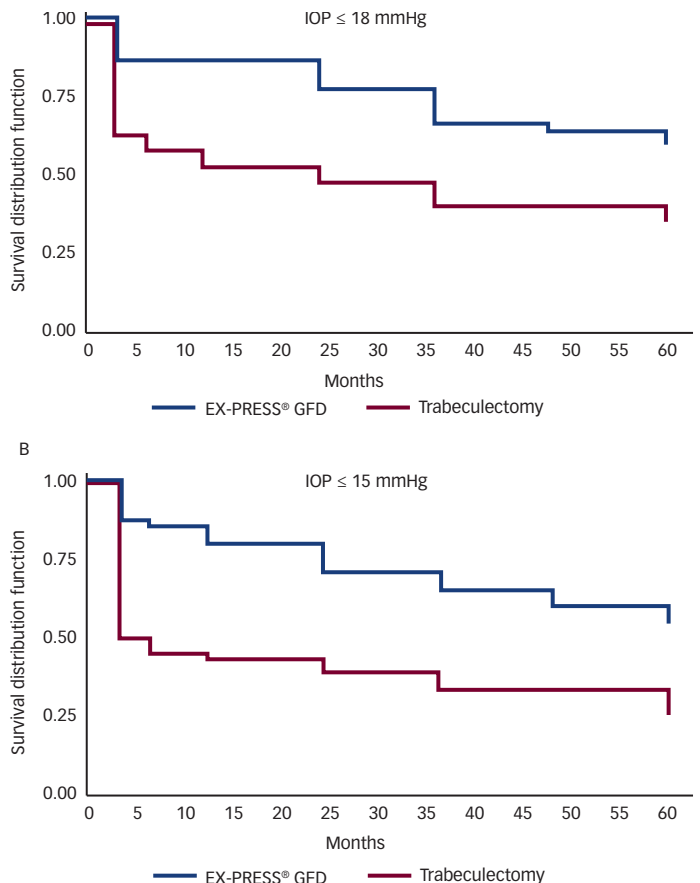
As glaucoma is a lifelong disease, long-term studies evaluating IOP control with the EX-PRESS® GFD versus traditional trabeculectomy are needed. In his presentation, Dr de Jong presented the recent findings

**Figure 3: Intraocular Pressure Control over Five Years Follow-up after EX-PRESS® Glaucoma Filtration Device (GFD) Implantation or Trabeculectomy**



Data are presented as mean ± standard deviation. IOP = intraocular pressure; n = number of patients in each group. Adapted from de Jong et al., 2011.<sup>37</sup>

**Figure 4: Kaplan–Meier Survival Curves Comparing EX-PRESS® Glaucoma Filtration Device (GFD) Implantation with Trabeculectomy for Target IOPs of ≤18 or ≤15 mmHg without Additional Medications or Glaucoma Surgery**



A: Survival curves for target intraocular pressure ≤18 mmHg. B: survival curves for target intraocular pressure ≤15 mmHg. IOP = intraocular pressure. Adapted from de Jong et al., 2011.<sup>37</sup>

**Table 1: Complete Success Rates for Defined Target Intraocular Pressures over Five Years following EX-PRESS® Glaucoma Filtration Device (GFD) Implantation or Trabeculectomy**

Year	IOP ≤18 mmHg			IOP ≤15 mmHg		
	EX-PRESS® GFD (%)	Trabeculectomy (%)	P-value	EX-PRESS® GFD (%)	Trabeculectomy (%)	P-value
1	86.8	61.5	0.01	80.0	51.3	0.01
2	76.3	51.3	0.02	71.1	48.7	0.046
3	66.7	41.0	0.02	66.7	38.5	0.01
4	64.1	46.2	0.11	61.5	46.2	0.17
5	59.0	46.2	0.25	59.0	46.2	0.26

Number of patients in the EX-PRESS® GFD implantation group = 39. Number of patients in the trabeculectomy group = 39. IOP = intraocular pressure. Adapted from de Jong et al., 2011.<sup>37</sup>

**Table 2: Movement, Force, and Temperature Change of the EX-PRESS® Glaucoma Filtration Device in Various Strength Magnetic Fields**

MRI Strength (T)	Rotation (°)	Displacement (mm)	Angular Deflection (°)	Force (dyn)	ΔT (°C)
1.5	0	0	5.0	0.2	+0.1
3.0	0	0	11.0	0.4	0.0
4.7	n/a	>40	40.0	1.8	0.0

ΔT = change in temperature; MRI = magnetic resonance imaging; n/a = unable to detect. Adapted from Seibold et al., 2011.<sup>38</sup>

from his prospective five-year study comparing EX-PRESS® GFD implantation with trabeculectomy that extended previous results from 12 months of follow-up.<sup>36</sup>

In the current study, 39 eyes of patients with primary open-angle glaucoma were implanted with the EX-PRESS® GFD and 39 underwent traditional trabeculectomy.<sup>37</sup> The study evaluated not only differences in IOP levels between the two treatments, but also the need for additional IOP-lowering medications or further surgical interventions in order to maintain IOP at target pressures of ≤18 or ≤15 mmHg. At baseline, IOP values in the two treatment groups were similar, but at one, two, and three years post-operatively, IOP levels were significantly lower in individuals implanted with the EX-PRESS® GFD compared with those who underwent trabeculectomy (see *Figure 3*). IOP levels were similar in the two treatment groups at Years 4 and 5. At all time points, fewer patients implanted with the EX-PRESS® GFD required additional IOP-lowering medications and the mean number of drugs per patient was also lower. Complete success rates, defined as IOP ≤18 or ≤15 mmHg without additional medications or post-operative surgery, were significantly higher up to three years after treatment in patients implanted with the EX-PRESS® GFD but did not reach statistical significance in Years 4 and 5 (see *Table 1*). Moreover, the time to treatment failure for response criteria of complete success (see *Figure 4*) and partial success (with additional medication but no surgery) was significantly longer in patients implanted with the EX-PRESS® GFD compared with the trabeculectomy group. Time to treatment failure also favored the EX-PRESS® GFD over trabeculectomy for response criteria of marginal success (with additional medications or surgery), but not significantly. Patients who underwent trabeculectomy required more surgical interventions than those implanted with the EX-PRESS® GFD. One patient in each group required a Baerveldt implant, but more patients required bleb needling in the trabeculectomy group compared with those receiving

the EX-PRESS® GFD (nine versus three, respectively) and more patients required cataract extraction (eight versus five, respectively).<sup>37</sup>

At the end of his presentation, Dr de Jong summarized his findings: the EX-PRESS® GFD provided significantly better IOP control than trabeculectomy for the first three years of follow-up and the time to treatment failure was longer in those patients implanted with the EX-PRESS® GFD. Moreover, patients implanted with the EX-PRESS® GFD required fewer IOP-lowering medications and fewer surgical interventions than those who underwent trabeculectomy. Dr de Jong postulated that lack of a statistically significant difference in IOP control between the two treatment groups at Years 4 and 5 may be due to the increased need for additional medications or surgery to regulate inadequately controlled IOP in the trabeculectomy group.

## Compatibility of the EX-PRESS® Glaucoma Filtration Device with Magnetic Resonance Imaging

*A report on part of the presentation 'Improving patient visual recovery in filtration surgery: results from a newly published study on the EX-PRESS® GFD' by Malik Kahook*

Given its location following implantation, the safety of the EX-PRESS® GFD for patients undergoing magnetic resonance imaging (MRI) is of paramount importance. MRI of the head is permitted, however not recommended, in the first two weeks post implantation. Although the EX-PRESS® GFD is made of the highest medical grade stainless steel that is considered to be non-ferromagnetic, its compatibility with the different strength magnetic fields commonly used in MRI has yet to be fully determined. The presentation by Dr Kahook contained his recent findings that used the American Society for Testing and Materials (ASTM) guidelines for MRI compatibility to examine the movement, force, and temperature change of individual EX-PRESS® GFDs in different strength magnetic fields.<sup>38</sup>

In magnetic fields of 1.5 and 3.0 T, individual EX-PRESS® GFDs exhibited no rotation, no displacement, and minimal angular deflection (see *Table 2*). In addition, there was no apparent translational force or heating. At 4.7 T there was considerable displacement of the device, which prevented accurate measurement of the amount of rotation, more angular deflection, and a greater amount of translational force compared with magnetic fields of 1.5 and 3.0 T. However, even at 4.7 T there was no heating of the device (see *Table 2*). According to the ASTM guidelines, the EX-PRESS® GFD can therefore be considered MRI-compatible.<sup>38</sup>

Dr Kahook finished his presentation by offering some tips and pearls for success when using the EX-PRESS® GFD. Together with those provided by Dr Fechtner, they provided the perfect lead into the final talk by Dr Moster.

### Real-life Experience Using the EX-PRESS® Glaucoma Filtration Device

*A report on the presentation 'The tips and pearls of using the EX-PRESS® GFD' by Marlene Moster*

Dr Moster focused on guidance for using the EX-PRESS® GFD gathered from her own clinical experiences. Dr Moster began by saying that although she initially used the EX-PRESS® GFD almost exclusively in advanced or complex glaucoma cases—i.e., patients who may have already had multiple surgeries—over time her use of the device had evolved so that she now used it more frequently in place of a standard trabeculectomy. Successful use of the EX-PRESS® GFD is in part dependent on careful patient selection, and Dr Moster, in agreement with remarks from Dr Fechtner and Dr Kahook, outlined her ideal first patient. Such an individual should be a candidate for trabeculectomy, preferably pseudophakic with primary open-angle glaucoma, wide-open angles, and a deep anterior chamber. Patients should have failed medications and non-invasive surgeries, and should have clear corneal temporal wounds, from prior cataract surgery, and no previous conjunctival surgery. In patients who have failed to respond to previous trabeculectomy or deep penetrating surgery, implantation of the EX-PRESS® GFD is still a viable option if there is sufficient room, either temporally or nasally, to insert it. The EX-PRESS® GFD is also a suitable alternative to the larger Baerveldt, Ahmed, and Molteno drainage devices, which are themselves associated with post-operative complications, including corneal decompensation, tube erosion, migration of the plate or the tube itself, failure of the corneal graft, and diplopia. However, Dr Moster emphasized that the EX-PRESS® GFD is increasingly seen as a surgical treatment for glaucoma, even in patients who have not previously undergone trabeculectomy, when medical and laser therapy has failed.

For the implantation procedure itself, Dr Moster advocated the use of a 'blitz' anesthesia regime with xylocaine 1 % non-preserved, both intracamerally and beneath the conjunctiva/Tenon's capsule, in order to produce a reservoir of anesthetic, and a traction suture to manipulate the eye. The conjunctival flap is created in the standard manner with a fornix-based incision and a half-thickness scleral flap generated; the larger the flap, the larger and more diffuse the resultant bleb, with Dr Moster advocating a 3 x 3 mm flap. Appropriate wound healing techniques are applied over the sclera and sutures pre-placed in the scleral flap before breaching the anterior chamber, in order to prevent additional astigmatism later on during the operation. As with traditional trabeculectomy, each member of the symposium faculty stressed the importance of a paracentesis during implantation, in case of intra-operative complications such as shallowing of the anterior chamber. There was also general consensus on the optimal position for device insertion beneath the scleral flap: in the blue-gray transition zone between the sclera and the clear cornea. In the first few patients, the symposium faculty also advocated breaching the anterior chamber with a 25 gauge needle for greater ease of device insertion, switching to a

26 gauge needle after gaining experience for a tighter fit of the device in the sclera. The EX-PRESS® GFD is then inserted on its side and then rotated 90° before being released from the EX-PRESS® GFD. Dr Kahook stressed the importance of holding the EX-PRESS® GFD in the correct position before inserting the device: ensuring one's finger is in the correct position over the release button so that it can be fully depressed without having to look away from the microscope, reducing the risk of incorrect insertion. For the suturing of the scleral flap, Dr Moster emphasized that releasable sutures are the most appropriate so that aqueous flow can be controlled tightly, either during the operation itself or post-operatively at the slit lamp, although laserable sutures can work as well. The conjunctival flap should be sutured watertight to prevent any wound leak—of particular importance when using proper wound healing techniques. Post-operatively, Dr Kahook underlined the importance of treating patients implanted with the EX-PRESS® GFD no differently from those who undergo traditional trabeculectomy. Wound healing must be carefully monitored, paying close attention to signs of fibrosis around either the scleral flap or the conjunctival incision.

Dr Moster concluded her talk with three individual case studies. The first was a patient who presented with an IOP of 28 mmHg and -11 D of myopia. The decision was made to implant an EX-PRESS® GFD rather than perform trabeculectomy in order to prevent hypotony maculopathy. In this case study, the predictable aqueous outflow from the EX-PRESS® GFD, combined with the use of releasable sutures, enabled the precise titration of IOP to a final, stable value of approximately 15 mmHg. In the second case study, the patient presented with a sinking intraocular lens (IOL) and an IOP of 40 mmHg with pseudoexfoliation. Having performed minimally invasive surgery to suture the IOL haptic to the sclera, thus preventing further sinking, the patient still presented with an excessively high IOP. Here, the EX-PRESS® GFD was used, rather than trabeculectomy, to reduce the incidence of post-operative complications. Using the tips and pearls outlined above, IOP was well controlled at the desired level. In her final case study, Dr Moster highlighted the need to remain flexible during the intra-operative period. The patient was earmarked for implantation of the EX-PRESS® GFD but, after having created the scleral flap, a thin section of the scleral bed near the insertion point ruptured, causing the iris to prolapse. As a result, implantation of the EX-PRESS® GFD had to be abandoned and the operation continued as a standard trabeculectomy, including peripheral iridectomy. Use of the EX-PRESS® GFD therefore provides a great deal of comfort for the operating surgeon, enabling the right decisions to be made at the right times.

### Conclusions

The EX-PRESS® GFD is a valuable addition to the armamentarium of the glaucoma surgeon, allowing one variable of the trabeculectomy procedure, aqueous flow, to be more predictable. Both retrospective and prospective studies indicate the EX-PRESS® GFD controls IOP levels as well as, if not better than, traditional trabeculectomy, and is associated with fewer post-operative complications.<sup>35,37</sup> Moreover, studies indicate the EX-PRESS® GFD is associated with a need for fewer additional IOP-lowering medications and post-operative surgical interventions, leading to higher complete success rates and longer times to treatment

failure compared with traditional trabeculectomy.<sup>37</sup> In line with previous findings,<sup>39</sup> and as defined by stringent ASTM criteria, the EX-PRESS® GFD is MRI-compatible<sup>38</sup> and does not compromise neurological scans, although it may affect MRI of the optic nerve.<sup>40</sup> Implantation of the EX-PRESS® GFD can be successfully combined with other procedures, for

instance cataract phacoemulsification,<sup>41</sup> or in cases where previous trabeculectomy surgical intervention has failed.<sup>42</sup> The EX-PRESS® GFD is a viable alternative to primary trabeculectomy, can be used by any glaucoma surgeon skilled in trabeculectomy, and provides additional management options for the treatment of glaucoma. ■

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## EX-PRESS® Glaucoma Filtration Device Brief Statement

**CAUTION:** Federal (USA) law restricts this device to sale by, or on the order of, a physician.

**INDICATION:** The EX-PRESS® Glaucoma Filtration Device is intended to reduce intraocular pressure in glaucoma patients where medical and conventional surgical treatments have failed.

### GUIDANCE REGARDING THE SELECTION OF THE APPROPRIATE VERSION:

Prior clinical studies were not designed to compare between the various versions of the EX-PRESS® Glaucoma Filtration Device. The selection of the appropriate version is according to the doctor's discretion.

**CONTRAINDICATIONS:** The use of this device is contraindicated if one or more of the following conditions exist:

- Presence of ocular disease such as uveitis, ocular infection, severe dry eye, severe blepharitis.
- Pre-existing ocular or systemic pathology that, in the opinion of

the surgeon, is likely to cause postoperative complications following implantation of the device.

- Patients diagnosed with angle closure glaucoma.

### WARNINGS/PRECAUTIONS:

- The surgeon should be familiar with the instructions for use.
- The integrity of the package should be examined prior to use and the device should not be used if the package is damaged and sterility is compromised.
- This device is for single use only.
- MRI of the head is permitted, however not recommended, in the first two weeks post implantation.

**ATTENTION:** Reference the Directions for Use labeling for a complete listing of indications, warnings, precautions, complications, and adverse events.

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