

Use of Topical Rho Kinase Inhibitors in the Treatment of Fuchs Dystrophy After Descemet Stripping Only

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Purpose: Fuchs corneal dystrophy (FD) is a common cause of endothelial keratoplasty. Recently, a series of FD cases treated with Descemet stripping only (DSO) demonstrated recovery of the central endothelium without transplantation of donor cells. Ripasudil, a rho kinase inhibitor, has been shown to promote corneal endothelial wound healing in animal models. This study prospectively evaluated the use of ripasudil in patients undergoing DSO for FD.

Methods: Enrolled patients underwent DSO with or without cataract surgery, performed by 1 surgeon. On the first postoperative day, patients were assigned to topical ripasudil 0.4% (Glanatec) 4 times a day for 2 months or no ripasudil and followed up monthly for the first 6 months and then at 9 and 12 months after surgery. Endothelial cell density (ECD) and pachymetry were evaluated at each postoperative visit.

Results: Eighteen patients were enrolled, including 8 women and 1 man in each group. Overall, patients who underwent DSO with ripasudil recovered vision more quickly (4.6 vs. 6.5 weeks, $P < 0.01$). In addition, the ripasudil group had a statistically significantly higher average ECD at 3, 6, and 12 months. The patients in the DSO observation group had a 10% decrease in peripheral ECD when comparing counts before surgery with counts 12 months after surgery ($P < 0.05$). In the DSO ripasudil group, there was no significant difference between peripheral ECD at preoperative baseline versus 12 months after surgery.

Conclusions: DSO with topical rho kinase inhibitors may be an alternative treatment for patients with FD and a peripheral ECD greater than 1000 cells/mm².

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Fuchs corneal dystrophy (FD) is an increasingly common cause of corneal transplantation in the United States. Statistics from the Eye Bank Association of America reveal that almost one-third of corneal transplants performed in the United States in 2017 were due to Fuchs dystrophy.¹ FD, a genetic disorder that primarily affects women, commonly

presents in the fourth decade and requires surgical intervention decades later.² Although patients present with photophobia, glare, and or decreased vision, there is no effective surgical intervention to treat these symptoms other than replacement of the diseased endothelium.

The corneal endothelium is a monolayer of hexagonal cells that are not known to reproduce or replicate in humans and other primates.³ The cells derive from the neural ectoderm, and replication is believed to be prevented by contact inhibition.⁴ As the endothelial cells age in FD, they create excrescences (guttæ) on underlying Descemet membrane. The guttæ are initially present in the central cornea and increase in density and numbers, spreading to the midperiphery as the disease progresses.⁴ As the density of the guttæ increases and endothelial cell density (ECD) decreases, the overlying cornea becomes edematous because of influx of aqueous into the corneal stroma. Corneal edema results in further vision loss and development of microcystic corneal edema and eventually development of frank bullous keratopathy.⁵

Surgical management of FD aims at replacing diseased Descemet membrane and endothelial cells to restore clarity of the cornea and restore vision to the patient. Over the past 2 decades, there has been significant advancement of these surgical techniques.⁶ In the past, the entire cornea was replaced with full-thickness penetrating keratoplasty. This technique has been replaced with Descemet stripping endothelial keratoplasty (DSEK), which involves removal of Descemet membrane and replacement with Descemet membrane and endothelial cells on a thin stromal carrier, leaving the host stromal and epithelial tissue intact. Subsequently, this technique was refined to replace stripped Descemet membrane with donor Descemet membrane and endothelial cells. Although technically more challenging, Descemet membrane endothelial keratoplasty (DMEK) improved the recovery time for patients and further decreased the risk of corneal transplant rejection.⁵ In each of these procedures, the use of donor tissue requires prolonged application of steroid drops to prevent rejection of the transplanted tissue. The associated risk of increased intraocular pressure and cataract formation with prolonged steroid use persists.

Recently, several authors have described cases of inadvertent removal of Descemet membrane with spontaneous clearing of the cornea and repopulation of the removed endothelium due to presumed migration of the remaining endothelium.^{7–10} Borkar et al¹¹ published a series of FD cases treated with Descemet stripping only (DSO) and confirmed recovery of the central endothelium in 9 of 11 patients, thus alleviating the risk of rejection and the need for prolonged

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topical steroid use. Moloney subsequently reported a series of cases of DSO with good results, except for 1 patient's cornea that failed to clear. The patient was given topical rho kinase inhibitor drops, resulting in subsequent corneal clearing.¹²

Rho kinase inhibitors [rho-associated coiled-coil containing protein kinase (ROCK)] have been demonstrated to aid in repopulation of the human corneal endothelium.^{13–16} Okumura has also demonstrated penetration of topical ROCK inhibitor drops into the anterior chamber of the eye through an intact cornea.¹⁷ A selective ROCK inhibitor, ripasudil 0.4% (Glanatec; Kowa Company Ltd, Nagoya, Japan), is commercially available in Japan for treatment of glaucoma. Glanatec (Kowa Company Ltd, Nagoya, Japan) was approved as a glaucoma and ocular hypertension treatment in Japan in 2014. Ripasudil promotes corneal endothelial wound healing, supporting its development as a potential treatment for acute corneal endothelial damage due to eye surgeries, especially cataract surgery.¹⁶ In this study, we evaluate the use of topical ROCK inhibitors in patients with FD undergoing DSO by treating patients after DOS with or without topical ripasudil.

MATERIALS AND METHODS

After obtaining permission from the United States Food and Drug Administration (FDA) for the use of ripasudil 0.4% (Investigational New Drug Application [IND] 136290), registration of the study at clinicaltrials.gov and approval from our institutional review board, patients were enrolled in a prospective, non-placebo-controlled clinical trial on the use of ripasudil after DSO with data collection for the primary end points masked to the observer performing specular microscopy. The primary end points for this study were change in pachymetry (corneal thickness), ECD, and the number of weeks after surgery for vision to improve to 20/40 or greater between the 2 groups. Enrollment criteria included patients with FD with dense central guttae limited to the central 5 mm of the cornea and central corneal stromal edema with visually significant complaints attributable to their corneal pathology.

In addition, patients were required to have a clear peripheral cornea with an ECD of greater than 1000 cells/mm² (Nidek CEM 350; Nidek Inc, Fremont, CA), morning blur, central pachymetry >650 μm, best-corrected spectacle visual acuity of 20/50 or worse, and no visible subepithelial corneal haze or scarring that could limit their postoperative visual recovery. All patients were required to be beyond child-bearing age or willing to use contraception for the duration of the study. Preoperative evaluation included complete eye examination, including intraocular pressure measurement and dilated fundus examination, best spectacle-corrected visual acuity, pachymetry, and central and peripheral ECDs. The diameter of the area of central edema was measured at the slit lamp. Patients with posterior segment pathologies, history of glaucoma, current use of glaucoma medications, or history of previous ophthalmic surgery other than cataract surgery were excluded.

Patients were provided with informed consent before undergoing any study-related procedures. All patients underwent DSO with or without cataract surgery under monitored anesthesia. Any patient with significant cataract and FD with

corneal edema underwent a combined procedure of phacemulsification cataract extraction and placement of an intraocular lens and DSO. All other pseudophakic patients with posterior chamber intraocular lenses underwent DSO.

DSO was performed as follows: the area of central corneal edema was marked on the epithelium at the same diameter that was measured at the slit lamp in preoperative examination. The anterior chamber was filled with Viscoat (Alcon, Ft. Worth, TX) through a 2.2-mm self-sealing near-clear corneal incision. Using an upside-down Sinsky hook, the area of corneal edema was demarcated by gently incising Descemet membrane at 4 evenly spaced points. The irrigation/aspiration handpiece was then used to gently aspirate Descemet membrane at one of the incised points and carefully tear Descemet membrane in a circular fashion to create a descemetorhexis that connected the 4 incised points of Descemet membrane and resulted in a smooth curved edge of Descemet stripping. The rest of the viscoelastic was removed with aspiration. The wounds were then hydrated with moxifloxacin 0.1 mg/mL. All patients were given our standard postoperative cataract drop regimen of moxifloxacin 0.3 mg/mL and prednisolone acetate 1% drops 4 times daily for 1 week. Alternating patients were assigned to use ripasudil 4 times daily for 2 months, starting the first operative day, or no ripasudil drops. All patients used sodium chloride 5% ointment at bedtime for the first 2 months after surgery.

Patients were seen monthly for the first 6 months and then at 9 and 12 months postoperatively. At each visit, Snellen best spectacle-corrected visual acuity and intraocular pressure were recorded. Central corneal thickness was determined by averaging 3 ultrasonic pachymetry readings (Pachette 4; DGH Technology, Exton, PA). Central and peripheral ECDs were measured by specular microscopy, using the average from 3 images (Nidek CEM 350; Nidek Inc), performed by a single masked technician. The Nidek noncontact specular microscope was used because of its ability to obtain peripheral ECD. Central ECD was imaged while the patient fixated straight ahead on the light in the specular microscope. Peripheral ECD was obtained of the inferior cornea as the patient looked superiorly. Results were analyzed using a paired 2-tailed *t* test in Excel (Microsoft Inc, Redmond, WA).

RESULTS

Eighteen eyes of 18 patients were enrolled, with 9 patients assigned to the no ripasudil (observation) group and 9 patients assigned to the ripasudil group after DSO. Each group included 8 women and 1 man for a total of 16 women (average age 73 years) and 2 men (average age 72 years) enrolled. One patient in the ripasudil group developed severe abdominal pain and constipation within 3 days of starting ripasudil drops. The patient discontinued ripasudil, and constipation resolved; however, after resuming ripasudil drops, the symptoms recurred, so the patient was moved to the observation group. As a result, there were 10 patients in the observation group and 8 in the ripasudil treatment group.

In the observation group, 9 patients recovered 20/40 vision or better by 3 months, whereas 1 patient achieved this vision by 6 months after DSO (Table 1). The average pachymetry measurement in the observation group was

TABLE 1. DSO Observation Group

VA	Preoperative		3 Months Postoperative			6 Months Postoperative			12 Months Postoperative			Weeks to 20/40	
	CCT (μ)	ECD Periphery (cells/mm ²)	VA	CCT (μ)	ECD Central (cells/mm ²)	VA	CCT (μ)	ECD Central (cells/mm ²)	VA	CCT (μ)	ECD Central (cells/mm ²)		ECD Periphery (cells/mm ²)
20/50	697	1246	20/30	619	606	20/25	609	662	20/25	598	720	1125	8
20/50	670	1324	20/30	606	601	20/20	600	683	20/20	602	765	1209	6
20/60	710	1184	20/40	598	545	20/25	584	602	20/25	575	686	1120	8
20/60	700	1254	20/40	623	612	20/20	584	684	20/20	565	790	1134	8
20/70	656	1285	20/30	620	671	20/25	597	734	20/25	587	821	1137	5
20/50	675	1147	20/30	590	659	20/25	589	712	20/20	576	802	1085	6
20/50	686	1436	20/25	608	651	20/20	610	710	20/20	588	750	1325	5
20/50	692	1327	20/20	621	588	20/20	618	685	20/20	577	734	1278	5
20/60	668	1232	20/25	612	590	20/20	603	664	20/20	593	680	1186	8
20/70	703	1139	20/60	790	NA	20/40	610	548	20/30	609	612	827	26
Mean	686	1257	Mean	629	614	Mean	600	668	Mean	587	736	1143	8.5
SD	17.7	90.9	SD	57.7	40.1	SD	11.8	55.4	SD	13.8	63.9	134.1	6.3

CCT, central corneal thickness; NA, not acquired; VA, best spectacle-corrected visual acuity.

686 μm preoperatively and averaged 606, 600, and 587 μm at 3, 6, and 12 months postoperatively, respectively. The average postoperative central ECD measurement in the observation group was 552, 672, and 736 cells/mm² at 3, 6, and 12 months, respectively (Fig. 1). The average peripheral ECD was 1257 cells/mm² preoperatively and 1142 cells/mm² postoperatively. The average number of weeks to vision of 20/40 was 6.5 (Table 2).

In the DSO ripasudil group, all 8 patients recovered 20/40 vision by 2 months (Table 3). The average pachymetry measurement in the treatment group was 701 μm preoperatively and averaged 611, 586, and 584 μm at 3, 6, and 12 months post-DSO, respectively. The average postoperative central ECD in the ripasudil group was 860, 934, and 1086 cells/mm² at 3, 6, and 12 months, respectively (Fig. 2). The average peripheral ECD in the ripasudil group was 1239 cells/mm² preoperatively and 1233 cells/mm² postoperatively. Vision improvement to 20/40 or greater took an average of

4.6 weeks (Table 2). One patient in the ripasudil group did well at the 3- and 6-month postoperative visits with vision of 20/40; however, when the patient returned for the 1-year visit, her vision had decreased to 20/200, and she had no detectable endothelial cells in the central cornea by specular microscopy and pachymetry measured more than 700 μm. The patient elected to undergo DMEK surgery, resulting in vision improvement to 20/25 at 3 months after surgery.

No patients experienced any change in their posterior pole examination. No intraocular pressure elevations were observed because all intraocular pressure measurements remained below 21 mm Hg throughout the follow-up period.

Patients who underwent DSO with ripasudil recovered vision more quickly (4.6 vs. 6.5 weeks, *P* < 0.01). In addition, the ripasudil group had a higher average ECD than the observation group at 3 months (859 vs. 552, *P* < 0.01), 6 months (934 vs. 672, *P* < 0.01), and 12 months (1086, vs. 736, *P* < 0.01) (Table 2).

ECD Without Ripasudil

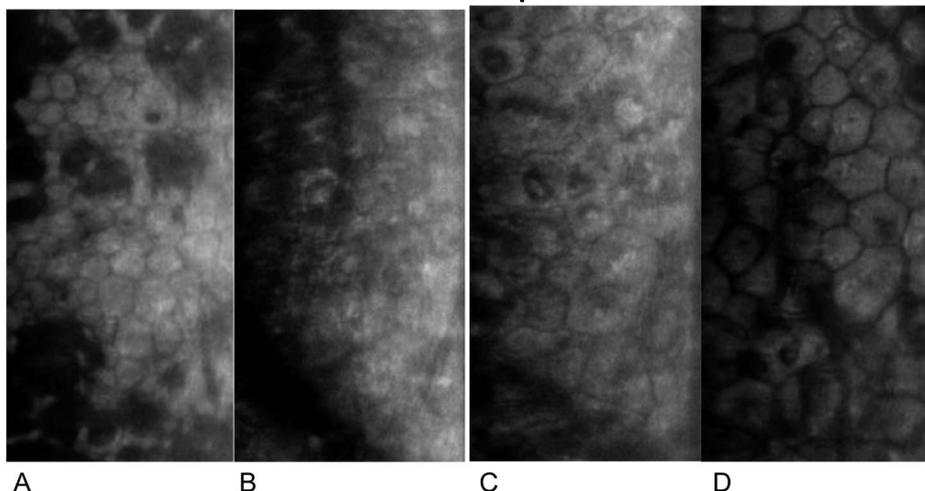


FIGURE 1. Specular micrographs of the corneal endothelium: the peripheral endothelium before Decemet stripping (A) and the central endothelium at 3 (B), 6 (C), and 12 months (D) after DSO not treated with topical ripasudil.

TABLE 2. DSO Observation Group Versus DSO Ripasudil Group Pachymetry and Endothelial Cell Count

	Preoperative		3 Months Postoperative		6 Months Postoperative		12 Months Postoperative			Weeks to 20/40
	CCT (μ)	ECD Periphery (cells/mm ²)	CCT (μ)	ECD Central (cells/mm ²)	CCT (μ)	ECD Central (cells/mm ²)	CCT (μ)	ECD Central (cells/mm ²)	ECD Periphery (cells/mm ²)	
DSO observation	686	1257	629	614*	600	668*	587	736*	1143	6.5
DSO ripasudil	701	1240	611	860*	586	934*	584	1086*	1233	4.6

**P* < 0.05 between the DSO observation and ripasudil groups.
CCT, central corneal thickness.

In comparing peripheral ECD at baseline with ECD at 12 months after surgery, the DSO observation group had a statistically significant reduction in ECD (1257 vs. 1142 cells/mm², *P* < 0.01). In the DSO ripasudil group, the peripheral ECD did not change significantly from baseline to 12 months postoperatively (1239 vs. 1233 cells/mm², *P* > 0.1).

DISCUSSION

Corneal endothelial cells (CECs) show poor regenerative ability in humans, and noncompensatory damage of CECs in FD causes corneal edema and bullous keratopathy. Although corneal transplantation provides considerable clinical benefits, allograft rejection, primary graft failure, and the shortage of donor corneas are persistent problems. One potential solution is DSO in patients with FD because it offers a lower cost, less complex procedure for these patients. However, the response of individual patients to this treatment remains unpredictable. DSO offers advantages of an easier surgery while eliminating the risk of tissue rejection with the DMEK/DSEK techniques.¹⁷ Yet, in some patients, DSO does not result in corneal clearing, leading investigators to search for a molecule that will promote corneal endothelial proliferation.¹¹

In our study, application of topical ripasudil in patients undergoing DSO resulted in more rapid visual recovery (4.6 vs. 6.5 weeks, *P* < 0.01), a higher central ECD at 1 year (1086 vs. 736 cells/mm², *P* < 0.01), and less loss of peripheral ECD (1142 vs. 1233 cells/mm², *P* < 0.01) Table

2. One patient was intolerant to topical ripasudil drops because of constipation during use. From our review, this has not been reported as a known side effect of ripasudil and is not in package labeling. However, this may be due to systemic absorption of ripasudil, resulting in an effect on the smooth muscle of the bowel. One patient experienced late endothelial failure at 1-year post-DSO, despite treatment with ripasudil, and required DMEK to recover vision and corneal deturgescence. In our study, patients who underwent DSO with or without ripasudil did well. In the observation group, 1 patient was a slow healer as described by Borkar et al and took 26 weeks to clear.

The advantages of DSO with or without the use of topical rho kinase inhibitors represent an exciting alternative treatment for patients with FD. These risks include disease transmission, infectious keratitis, and lifelong application of corticosteroid drops to reduce the chance of rejection of the transplanted tissue. Hence, the risk of increased intraocular pressure and cataract formation from the long-term use of topical corticosteroids is avoided. In addition, DSO with topical rho kinase inhibitors may improve the visual outcomes and reduce other known complications of endothelial keratoplasty. Restoration of the corneal endothelium without donor tissue may reduce the higher-order aberrations and light scatter that are known to reduce visual acuity after DSAEK and remove any scatter caused by the donor–host interface.^{18,19} Our patients recovered good visual acuity, yet, in general, some patients with prolonged corneal edema may

TABLE 3. DSO Ripasudil Group

	Preoperative		3 Months Postoperative			6 Months Postoperative			12 Months Postoperative			Weeks to 20/40	
	CCT (μ)	ECD Periphery (cells/mm ²)	VA	CCT (μ)	ECD Central (cells/mm ²)	VA	CCT (μ)	ECD Central (cells/mm ²)	VA	CCT (μ)	ECD Central (cells/mm ²)		ECD Periphery (cells/mm ²)
20/60	753	1124	20/40	622	676	20/40	624	688	20/200	712	NA	575	6
20/70	685	1135	20/40	598	986	20/30	556	1020	20/25	545	1102	1086	4
20/50	676	1249	20/30	602	848	20/20	585	986	20/20	557	1098	1196	4
20/50	710	1324	20/30	612	953	20/20	589	1048	20/20	568	1112	1297	5
20/50	700	1284	20/25	617	894	20/20	575	902	20/20	564	1005	1246	4
20/60	690	1245	20/25	622	784	20/20	596	942	20/20	581	1132	1231	5
20/50	693	1382	20/30	599	942	20/25	587	1002	20/25	575	1152	1345	5
20/60	698	1173	20/30	613	794	20/25	576	884	20/20	567	1002	1232	4
Mean	701	1240	Mean	611	860	Mean	586	934	Mean	584	1086	1233	4.6
SD	23.5	91.2	SD	9.8	104.6	SD	19.6	114.5	SD	53.0	59.4	244.6	0.7

CCT, central corneal thickness; VA, best spectacle-corrected visual acuity.

ECD With Ripasudil

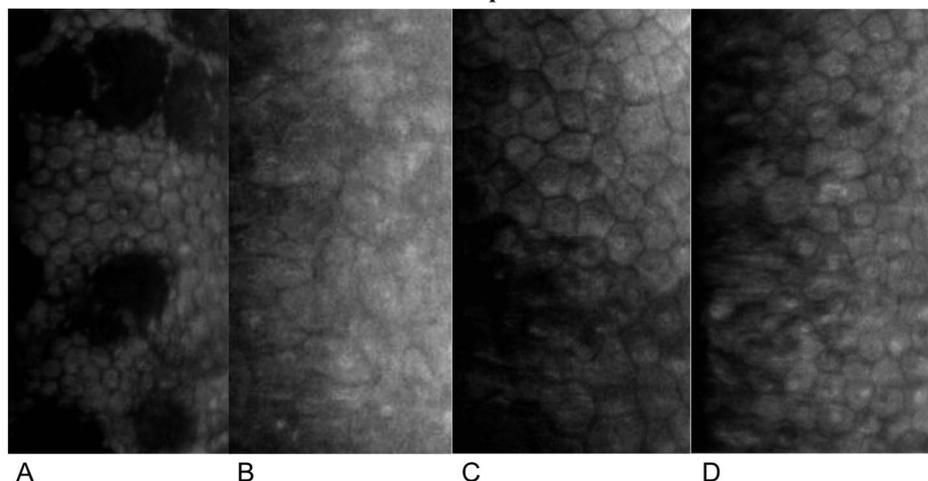


FIGURE 2. Specular micrographs of the corneal endothelium: the peripheral endothelium before Descemet stripping (A) and the central endothelium at 3 (B), 6 (C), and 12 months (D) after Descemet stripping treated with topical ripasudil.

develop anterior corneal stromal changes that are detrimental to visual recovery or result in glare from increases in anterior corneal light scatter.^{20,21}

The inability of human CECs to reproduce in response to injury or damage has been a mainstay of our understanding of corneal physiology. The densely packed monolayer of hexagonal endothelial cells exhibits strong contact inhibition. This contact inhibition seems to upregulate p27Kip1, a cyclin-dependent kinase inhibitor that prevents transition to the S-phase; as a result, the endothelial cells are arrested in the G1 phase.¹⁴

Okumura et al²² were the first to identify a specific ROCK inhibitor Y-27632 capable of promoting adhesion, survival, and proliferation of primate-derived CECs in vitro. ROCK inhibitors enhance corneal endothelial wound healing in vivo in animal models, both when injected intracamerally with a cell suspension and when applied topically as eye drops.^{23–25} In 2013, 4 patients with FD and 4 patients with bullous keratopathy underwent transcorneal freezing, creating an endothelial wound of 2-mm diameter, followed by 10- μ M ROCK inhibitor eye drops 6 times daily for 7 days. Corneal edema was reduced at 6 months, and there was no significant difference between the groups.²⁵

In 2015, the same investigators reported an adapted treatment protocol for patients who lost half ($n = 1$) or more than two-thirds ($n = 2$) of their endothelium during cataract surgery. These patients did not undergo transcorneal freezing but did receive topical ROCK inhibitors 6 times daily for 4 months and 4 times daily for the following 2 months. At 3 months after treatment, corneal edema was reduced, but the numbers remained too low to make definitive conclusions.²⁴

Moloney et al¹² reported a series of patients with FD who underwent DSO. A ROCK inhibitor was implemented as a salvage procedure when there was no corneal resolution 2 months after Descemet stripping.¹² In the first nonresponder, Y-27632 (an investigational rho kinase inhibitor) was applied topically but was replaced by another topical formulation of ripasudil, thereby effectively clearing the cornea within 10 days. Similarly, 2 other responders and an additional patient with a small edematous patch were administered ripasudil, all resulting in a transparent cornea within 14 days.

In previous safety studies of topical ripasudil induced transient guttae-like findings in humans, most likely due to protrusion formation along intercellular borders caused by the reduction in actomyosin contractility of the CECs.¹⁴ Transient morphological changes of CECs such as indistinct cell borders with pseudoguttas were observed by noncontact specular microscopy in healthy subjects after ripasudil administration. Corneal edema was not observed, and corneal ECD did not decrease after 1-week repetitive administration.¹⁴ These morphological changes were reversible, and CEC morphology returned to normal before the next administration.¹⁵

Our study patients were assigned to receive ripasudil, a selective rho-associated coiled-coil containing protein kinase (ROCK) inhibitor, to promote corneal endothelial wound healing after DSO. In the observation DSO group, corneal edema resolved in 9 of 10 patients within 8 weeks, whereas 1 patient's edema resolved at 26 weeks. All patients in this group had a peripheral ECD greater than 1000 cell/ mm^2 before DSO. When the peripheral ECDs were repeated 1 year post-DSO, all patients had a decrease in their peripheral ECD. The average preoperative peripheral ECD was 1257 in this group, and it decreased to 1143 at 1 year, a 10% decrease in peripheral ECC ($P < 0.01$) Table 2.

If the central 5 mm of Descemet membrane is stripped from a 12-mm cornea, approximately 17% of the endothelial cells are removed, assuming the same ECD in the central and peripheral corneas. Hence, a decrease of 10% in the peripheral cornea after DSO would be expected when there is migration of the peripheral endothelial cells to cover the central area of stripped Descemet membrane. The lack of decrease in the peripheral ECD in the DSO group treated with ripasudil may support the concept of endothelial cell proliferation in this group, as opposed to endothelial cell migration in the DSO group. Hence, the size of the descemetorhexis may limit the ability of the endothelium to recover in a timely manner. In addition, the smooth edge of the descemetorhexis and the undisrupted underlying stromal fibers seem to improve the ability of the endothelial cell to migrate over the denuded area. Therefore, we believe that it is critical to remove only the central portion of Descemet membrane and the endothelium,

leaving a smooth descemetorhexis edge and no disruption of the underlying stromal fibers. We found that this was best accomplished using slow, steady aspiration of incised Descemet membrane with the irrigation and aspiration handpiece of the phacoemulsification unit, while tearing Descemet membrane in a curvilinear pattern much like the lens capsule in capsulorhexis formation.

There are many remaining questions about this procedure. We do not know how long the corneas will remain clear. In the DSO and topical ripasudil group, 1 patient experienced endothelial decompensation at 1 year despite good vision at 6 months. It remains unclear as to why some patients heal more quickly than others, and in DSO, the overall recovery time is longer than traditional endothelial keratoplasty (DSEK or DMEK). The limitations of our study include the small sample size and the failure to use a standardized central image analysis reading center for ECD determination. The small sample size limits our ability to recommend the broad use of ripasudil with DSO in patients with FD. In addition, it is possible that moving the patient who was intolerant to ripasudil because of constipation may have resulted in some bias of our results. Last, our limited ability to image the peripheral endothelium may have excluded potentially qualified candidates for DSO, but we were not able to adequately image or assess their peripheral ECD with our current technology. Additional unanswered questions include appropriate patient selection, drug dosage and duration, and long-term stability of ECD. In the future, treatment of FD will require a personalized approach based on clinical appearance, genetics, and peripheral ECD. For example, patients with FD with no symptoms will be treated with observation, whereas patients with a peripheral ECD greater than 1000 cells/mm² may be treated with DSO and topical ripasudil. DSO with topical ripasudil may be the treatment of choice early in the disease process, reserving DMEK for patient who present with more advanced disease states.

From a societal perspective, DSO with topical rho kinase inhibitors may decrease the cost of visual rehabilitation for both individual patient and society as a whole. The cost of an EK procedure was estimated to be between \$16,000 and \$21,000 in 2015.²⁶ The projected lifetime benefit of corneal transplantation was, on average, \$118,000, including direct and indirect medical costs.²⁶ DSO is cheaper than conventional therapies as a result of not requiring donor corneal tissue resulting in lower medical costs. In patients treated with ripasudil, the cost of the medication was \$400. However, in both the DSO group and patients treated with a ROCK inhibitor, there may be a need for surgical intervention in the distant future. However, by elimination of rejection, decreased corticosteroid use, and potentially fewer related side effects, the long-term medical care should be less, assuming that the CECs do not decompensate.¹⁸ This potential for a cheaper less complex surgical procedure with no risk of graft rejection should prompt a larger multicenter trial to evaluate the efficacy of this procedure.

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