

Refractive Changes after Descemet Stripping Endothelial Keratoplasty: A Simplified Mathematical Model

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PURPOSE. To develop a mathematical model that can predict refractive changes after Descemet stripping endothelial keratoplasty (DSEK).

METHODS. A mathematical formula based on the Gullstrand eye model was generated to estimate the change in refractive power of the eye after DSEK. This model was applied to four DSEK cases retrospectively, to compare measured and predicted refractive changes after DSEK.

RESULTS. The refractive change after DSEK is determined by calculating the difference in the power of the eye before and after DSEK surgery. The power of the eye post-DSEK surgery can be calculated with modified Gullstrand eye model equations that incorporate the change in the posterior radius of curvature and change in the distance between the principal planes of the cornea and lens after DSEK. Analysis of this model suggests that the ratio of central to peripheral graft thickness (CP ratio) and central thickness can have significant effect on refractive change where smaller CP ratios and larger graft thicknesses result in larger hyperopic shifts. This model was applied to four patients, and the average predicted hyperopic shift in the overall power of the eye was calculated to be 0.83 D. This change reflected in a mean of 93% (range, 75%–110%) of patients' measured refractive shifts.

CONCLUSIONS. This simplified DSEK mathematical model can be used as a first step for estimating the hyperopic shift after DSEK. Further studies are necessary to refine the validity of this model. (*Invest Ophthalmol Vis Sci.* 2011;52:1043–1054) DOI: 10.1167/jovs.10-5839

Descemet stripping endothelial keratoplasty (DSEK)^{1–3} and Descemet stripping automated endothelial keratoplasty (DSAEK)⁴ are lamellar corneal surgical techniques used to replace abnormal corneal endothelium in patients with endothelial diseases, such as Fuchs' corneal endothelial dystrophy and pseudophakic bullous keratopathy. The abnormal corneal endothelium is removed and replaced with donor posterior lamellae of cornea containing healthy endo-

thelium. DSEK offers several advantages over traditional penetrating keratoplasty, including faster visual recovery and less postoperative astigmatism, because the structural integrity of the eye is largely maintained.

Initially, DSEK was thought to be a relatively neutral procedure regarding changes in refractive error. However, there is now evidence that these grafts produce a hyperopic shift in the recipient cornea.^{4–6} This shift should be considered during preoperative planning, in particular when choosing the power of the intraocular lens in combination surgery of DSEK along with phacoemulsification and intraocular lens placement. However, no quantitative model exists to explain or predict the hyperopic shift that results after placement of the donor graft. Because DSEK is largely a posterior corneal procedure, studies have suggested that the hyperopic shift occurs because of a change in the posterior corneal curvature.⁷ In a previous study, Yoo et al.⁸ demonstrated a linear correlation between the ratio of central to peripheral thickness (CP ratio) of the donor graft and the resulting postsurgical hyperopic shift. However, the mathematical reason for such a correlation is not well understood.

We developed a mathematical model based on donor graft corneal central thickness and donor CP ratio to predict changes in the posterior curvature of the cornea and thus the overall refractive changes of the recipient eye after DSEK surgery. Perhaps this model can be the first step in developing a tool for preoperative estimation of the hyperopic shift that will occur after DSEK surgery.

METHODS

Mathematical Model

In the Gullstrand eye model, which mathematically describes the refractive power of the eye, the primary components that contribute to refraction are the anterior surface of the cornea, the posterior surface of the cornea, and the lens, which are illustrated in Figure 1. Table 1 lists common variables used in the Gullstrand eye model. Because DSEK surgery involves replacing posterior stroma and the endothelium of the cornea, we assumed that there would be minimal changes affecting the power of the anterior corneal surface, the power of the lens, and the index of refraction of the aqueous humor and cornea. Mathematical and geometric models were generated to estimate the refractive change after DSEK surgery by modeling the change in curvature of the posterior corneal surface: Figure 2 shows the ideal shape of a corneal graft; Figure 3 illustrates how a graft with a thicker periphery affects the posterior corneal curvature; Figure 4 explains the derivation of the optical sagitta (sag) equation; Figure 5 illustrates how measurements were taken from the corneal grafts; Figures 6, 7, and 8 and the Appendix include the mathematical derivation of the post-DSEK posterior corneal radius of curvature and example calculations using the DSEK mathematical model. Figures 2 to 8 will be discussed in more detail below.

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Presented at the World Cornea Congress VI, Boston, Massachusetts, April 2010.

Supported by Research to Prevent Blindness.

Submitted for publication May 6, 2010; revised August 13, 2010; accepted September 4, 2010.

Disclosure: **R.Y. Hwang**, None; **D.J. Gauthier**, None; **D. Wallace**, None; **N.A. Afshari**, None

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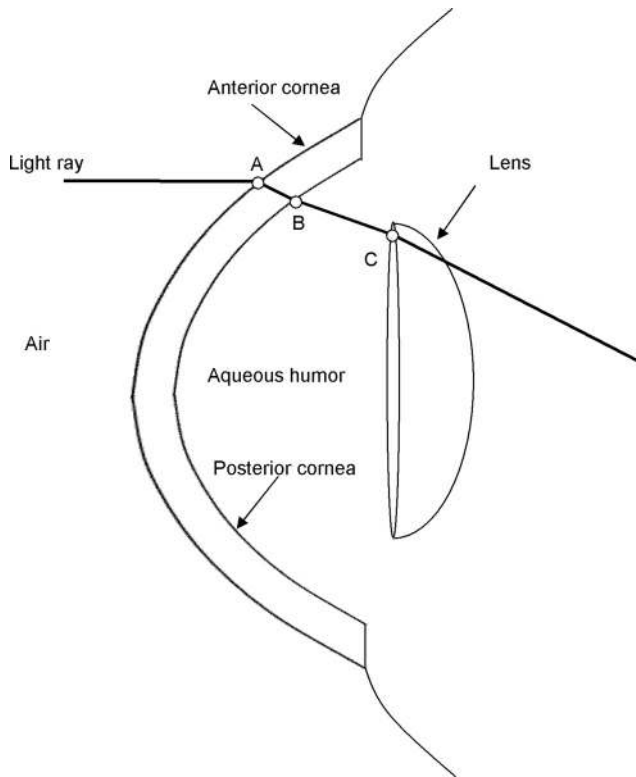


FIGURE 1. Gullstrand eye model divides the refractive power of the eye into three main components: anterior cornea (point A), posterior cornea (point B), and lens (point C).

The following assumptions were made in the development of our mathematical model:

1. The shape of the anterior curvature of the recipient cornea does not change after surgery.

2. The shape of the posterior curvature (excluding the corneal graft) of the recipient cornea does not change after surgery.
3. The thickness of the recipient cornea does not change after endothelial stripping (i.e., removal of endothelium does not affect recipient corneal thickness).
4. The corneal graft's radius of curvature can be estimated at a distance $b' = 1.5$ mm from the visual axis. The visual axis is defined as the axis that passes through the geometric center or vertex of the cornea.
5. Calculations using the radius of curvature, sagittal depth, and chord length (sag equation) assume that the sag is much less than the radius of curvature.
6. The recipient cornea and donor graft are symmetric around the visual axis.
7. The variation in thickness of the transplant is symmetrical around the visual axis.
8. The donor cornea, when attached to the recipient cornea, behaves as one uniform refractive medium.
9. The refractive index of the donor cornea is the same as that of the recipient cornea.
10. The index of refraction of cornea and air does not change after surgery.
11. The angle q (the angle between the radius of curvature and the visual axis) in Figure A1 is much less than 1 so that $\sin \theta \sim 0$ and $\cos \theta \sim 1$.
12. The posterior corneal radius of curvature measured from post-surgical anterior segment optical coherence tomography (AS-OCT) readings approximates presurgical corneal posterior radius of curvatures.
13. Intraocular lens power calculations are precise and accurate.

Retrospective Review of DSEK Cases

We retrospectively reviewed the records of four pseudophakic patients who underwent DSEK at the Duke University Eye Center (Durham, NC). All patients in the series had endothelial dysfunction attributed to Fuchs' endothelial corneal dystrophy and had documented presurgical pachymetry and manifest refraction values. Refractive measurements were taken at least 3 months after surgery and within 2 weeks of AS-OCT imaging. Presurgical pachymetry

TABLE 1. Variables Used in the Gullstrand Eye Model

Variable	Description	Average Value/Figure	Standard Gullstrand Eye Model Variable
F_{cyc}	Power of the eye	58.6 D	Yes
F_{cornea}	Power of the cornea	43.0 D	Yes
F_{lens}	Power of the lens	19.1 D	Yes
d	Distance between second principal plane of the cornea and the first principal plane of the lens	0.0057 m	Yes
F_{ac}	Power of the anterior cornea	48.8 D	Yes
F_{pc}	Power of the posterior cornea	-5.88 D	Yes
t	Thickness of recipient cornea	0.0005 m	Yes
$t_{transplant}$	Thickness of corneal transplant graft	Figures 2, 3, 6-8	No
n_3	Index of refraction of aqueous humor	1.336	Yes
n_2	Index of refraction of cornea	1.376	Yes
n_1	Index of refraction of air	1.00	Yes
r_{ac}	Radius of curvature of anterior cornea	0.0077 m	Yes
r_{pc}	Radius of curvature of posterior cornea	0.0068 m	Yes
r_{pc}'	Radius of curvature of posterior cornea with transplant of even width throughout	Figures 2, 3, A1	No
r_{pc}''	Radius of curvature of posterior cornea with peripherally thicker donor cornea	Figures 3, 6, 7, A1	No
b'	Shortest distance between a point on the periphery of a uniform width corneal graft and the visual axis	0.0015 m was used in this paper, Figures 6, 7, A1	No
b''	Shortest distance between a point on the periphery of a nonuniform width corneal graft and the visual axis	0.0015 m used in this paper, Figures 3, 6, 7, A1	No

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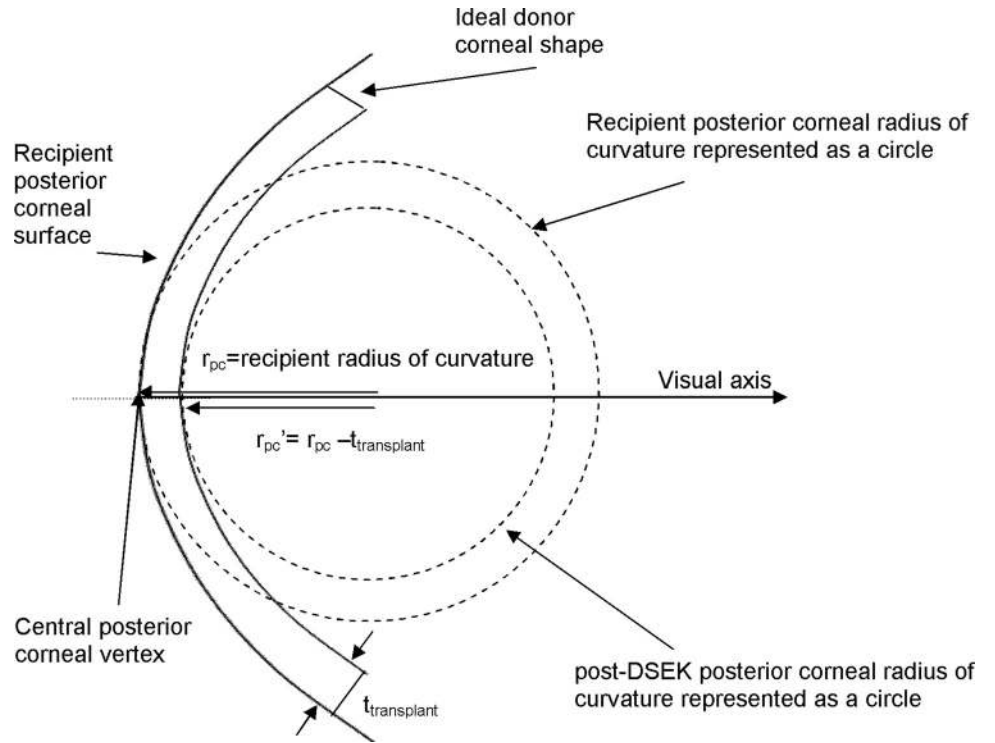


FIGURE 2. Calculation of post-DSEK posterior radius of curvature with a donor graft of even width throughout (ideal shape). The radius of curvature of the recipient posterior cornea, r_{pc} , and the post-DSEK posterior corneal radius of curvature, r_{pc}' , with an ideally shaped donor graft that parallels the recipient posterior curvature, are represented by *dashed circles* with different radii. The post-DSEK posterior corneal radius of curvature (with graft of even width throughout) is estimated to be the original radius of curvature minus the thickness of the donor cornea, $t_{transplant}$: $r_{pc}' = r_{pc} - t_{transplant}$.

measurements for corneal graft tissues were provided by Ocular Systems Inc. (Winston-Salem, NC). All DSEK grafts were cut with an 8-mm diameter. Exclusion criteria included non-corneal conditions that could affect visual acuity, such as retinal or optic nerve diseases and postoperative complications such as graft dislocation and rejection. This study was HIPAA (Health Insurance Portability and Accountability Act) compliant, was conducted according to the tenets of the Declaration of Helsinki, and was exempt from institutional review board approval.

RESULTS

DSEK Mathematical Model Derivation

Evidence suggests that the primary variable affected by DSEK surgery is the posterior radius of curvature, because the shape of the corneal transplant changes the shape of the posterior cornea.^{8,9} This theory is supported by the observation that the corneal posterior radius of curvature changes after DSEK sur-

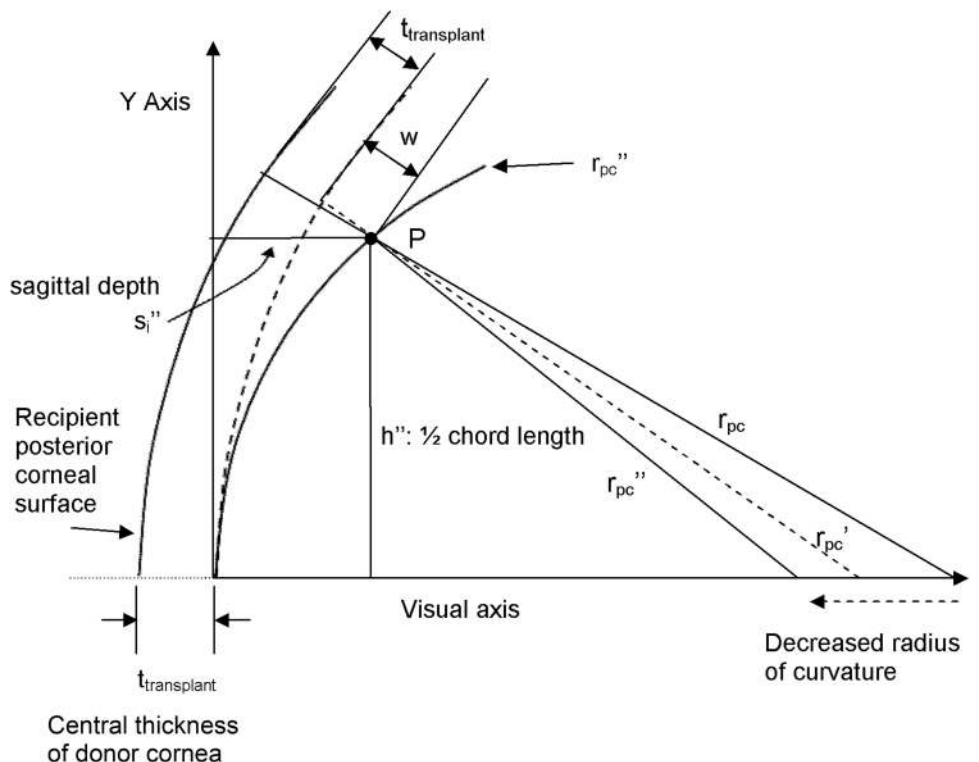


FIGURE 3. Thicker peripheral non-uniform grafts decrease the posterior radius of curvature, where r_{pc} (recipient radius of curvature) $>$ r_{pc}' (uniform DSEK radius of curvature) $>$ r_{pc}'' (nonuniform DSEK radius of curvature). The difference between peripheral and central graft thickness is represented by w . Point P represents a point along the DSEK graft that corresponds to a particular original recipient radius of curvature r_{pc} ; a uniform width post-DSEK radius of curvature, r_{pc}' ; and a nonuniform width graft post-DSEK radius of curvature r_{pc}'' . Here, $t_{transplant}$ is the central graft thickness, h'' denotes the shortest distance between point P and the central visual axis ($0.5 \cdot$ chord length), and s_i'' denotes the sagittal depth of point P, which is the shortest distance between the chord h'' and the Y axis.

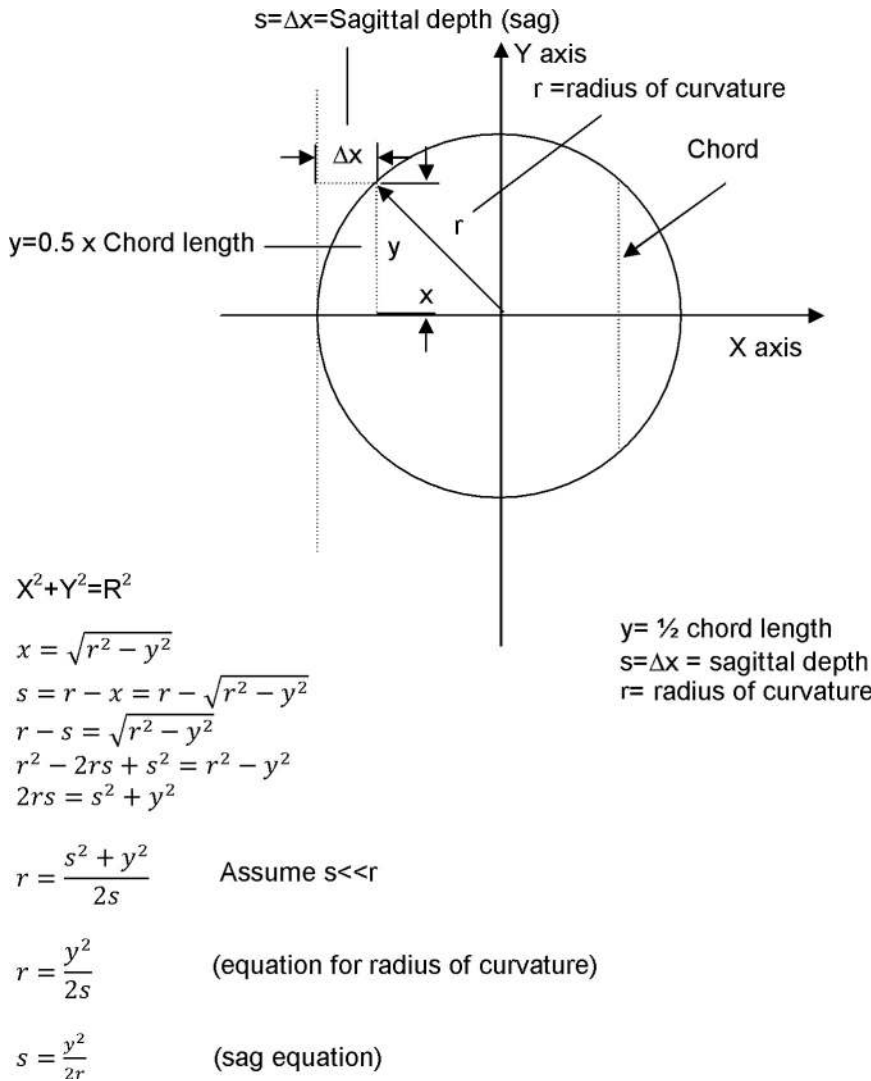


FIGURE 4. Radius of curvature estimation using the sagittal depth (sag) equation. The equation for sag contains three variables: sagittal depth, chord length, and radius (of curvature). The radius of curvature, r , is determined using the sag equation if the sagittal depth, s , and $\frac{1}{2}$ chord length, y , are known: $r = y^2 / (2 \cdot s)$.¹² This approximation assumes that the sag is very small compared with the radius of curvature. A large sag is shown for clarity.

gery¹⁰ and the CP ratio of transplanted corneal tissue correlates with refractive change after DSEK surgery.⁸

The change in the posterior radius of curvature affects the posterior corneal power (F_{pc} , in diopters), which is given by¹¹

$$F_{pc} = \frac{n_3 - n_2}{r_{pc}} \tag{1}$$

where n_3 is the index of refraction of the aqueous humor, n_2 is the index of refraction of the cornea, and r_{pc} is the radius of curvature of the posterior cornea (in meters). Reference values are listed in Table 1.¹¹

An ideally shaped corneal tissue would have a minimal effect on the radius of curvature and maintain a thin, uniform thickness throughout the graft, so that the posterior surface of the transplanted tissue would form a parallel curve with respect to the donor posterior surface (Fig. 2, r_{pc}'). Any deviation from parallelism will cause additional change, the value of which we wish to predict, in the power of the eye. By mathematically understanding how the donor CP ratio (Fig. 3) alters the geometry of the recipient cornea after surgery, the resulting change in the posterior radius of curvature can be determined.

The radius of curvature is a quantity that approximates the curvature of a surface and is the radius of the approximating

circle (Fig. 2). For the cornea, this model makes several assumptions: the cornea is symmetric around the center of the visual axis (assumption 6), the curvature at the central corneal vertex lies along the visual axis, and the posterior radius of curvature r_{pc} can be visualized by drawing a circle with radius r_{pc} (Fig. 2). Because a uniformly wide donor corneal surface would lie parallel to the recipient posterior surface, the post-DSEK radius of curvature with a uniform width graft is given by $r_{pc}' = r_{pc} - t_{\text{transplant}}$, where $t_{\text{transplant}}$ is the thickness of the donor graft (Fig. 2).

However, in practice, donor corneal tissues are often cut unevenly and are often thicker at the periphery than at the central vertex^{6,8} (Fig. 3). As the thickness along the periphery of the posterior cornea increases with the graft's peripheral thickness, the posterior radius of curvature decreases (Fig. 3). To help understand this change in radius of curvature, two other quantities can be determined: the chord length and the sagittal depth. One half of the chord length (b'' in Fig. 3) represents the shortest vertical distance between a peripheral point on the posterior post-DSEK corneal surface and the visual axis. The sagittal depth (s_1'' in Fig. 3) represents the shortest horizontal distance along the visual axis between the chord length and the central region of the posterior post-DSEK cornea.

To estimate the post-DSEK radius of curvature with a donor cornea that reflects this nonuniform width, the sag of the

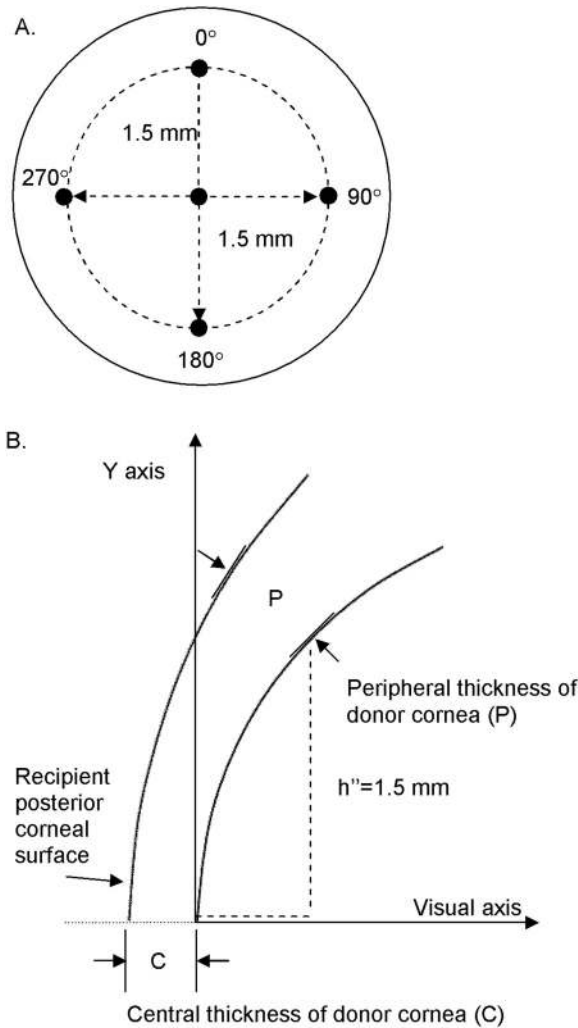


FIGURE 5. Diagram of central to peripheral (CP ratio) measurements taken from corneal graft. (A) Position of pachymetry measurements taken on donor graft at the vertex and 1.5 mm away from the vertex at 0°, 90°, 180°, and 270°. (B) Representation of the ratio of central to peripheral thickness (CP ratio = C/P). P is the average of the peripheral graft thicknesses measured in (A).

CP : central to peripheral donor graft ratio = C / P
 h'' = distance from central vertex to graft periphery where graft thickness is measured = 1.5 mm

circles formed by different radii of curvatures, representing a relationship between the sagittal depth, chord length, and radius of curvature, can be determined and used to estimate the post-DSEK posterior corneal radius of curvature. The sag (or sagittal depth) equation can be rewritten to find the radius of curvature (derived in Fig. 4¹²): $r_{pc} = (0.5 \cdot \text{chord length})^2 / (2 \cdot \text{sagittal depth})$. Because presurgical AS-OCT and anterior eye segment measurements (Pentacam; Oculus, Wetzlar, Germany) were not available for these patients, their presurgical posterior radii of curvatures were estimated using the sag equation and post-DSEK AS-OCT measurements of sagittal depth and chord length, excluding donor graft thickness. The recipient's posterior radius of curvature was assumed to be unchanged before and after surgery and to be unaffected by endothelial stripping (assumptions 2 and 3).

Using the estimated presurgical posterior radius of curvature and the CP ratio of the corneal transplant, we developed a mathematical model to estimate the change in refractive power of the cornea and eye after DSEK surgery. Presurgical CP ratios of each pre-cut corneal transplant were taken by using pachymetry measurements at the vertex and 1.5 mm from the vertex of the cornea at 0°, 90°, 180°, and 270° around the vertex and were provided by Ocular Systems Inc. (Fig. 5). Presurgical CP ratio measurements were calculated by dividing the central graft thickness by the average of the peripheral

graft thicknesses (central graft thickness/average of peripheral graft thicknesses; Fig. 6B). As illustrated in Figure 3, a donor cornea with a thicker periphery compared to its central thickness has a steeper curvature and will result in a smaller radius of curvature r_{pc}'' when compared with the curvature of an ideal donor cornea with even thickness throughout r_{pc}' . After the difference in the sag between a donor cornea of even thickness (CP ratio = 1) and a nonuniform width donor cornea (with a CP ratio not equal to 1) is calculated, the nonuniform post-DSEK radius of curvature, r_{pc}'' , can be estimated by the equation (derivation shown in the Appendix)

$$r_{pc}'' = \frac{1}{\frac{1}{r_{pc} - t_{\text{transplant}}} + \frac{2t_{\text{transplant}} \left(\frac{1}{CP} - 1 \right)}{b'^2}} \quad (2)$$

Because the peripheral thicknesses of each graft used in the graft CP ratio calculations were taken using pachymetry 1.5 mm from the vertex, we used $b' = 1.5$ mm throughout this study. The calculated post-DSEK radius of curvature can then be used to calculate the power of the post-DSEK posterior cornea (equation 1).

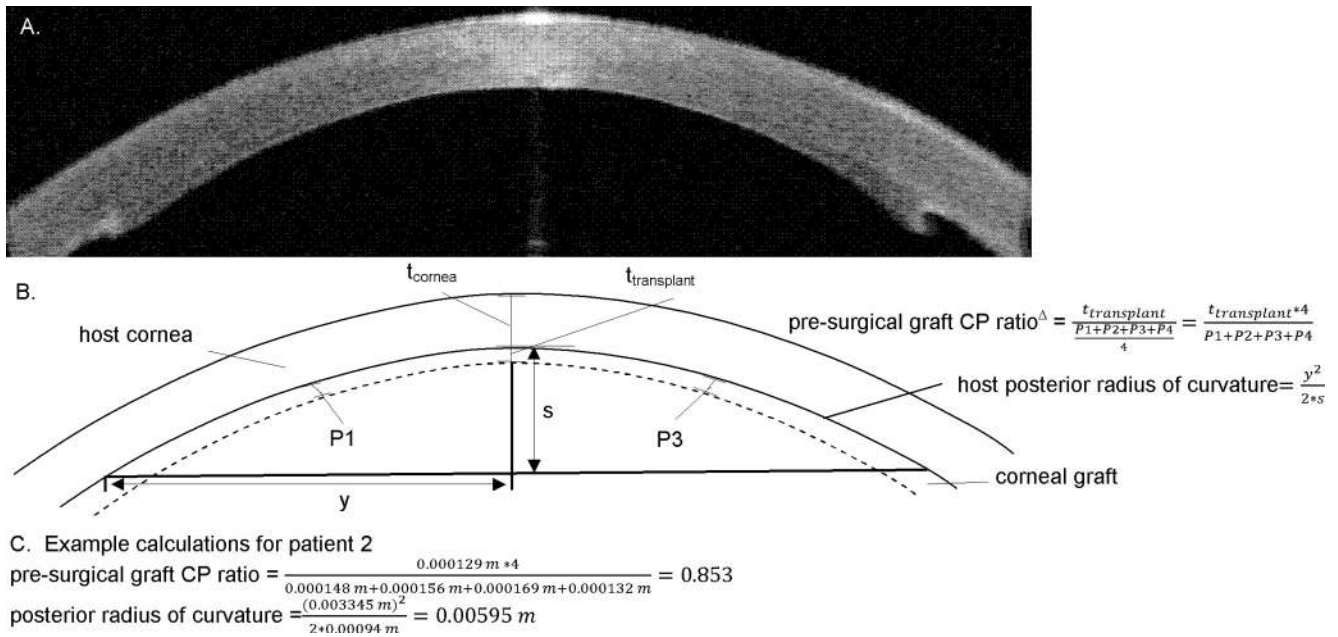


FIGURE 6. Example AS-OCT and calculations for patient 2. (A) Post-DSEK AS-OCT image. (B) AS-OCT with labels for peripheral graft thicknesses (P1, P3), t_{cornea} (host corneal thickness), $t_{\text{transplant}}$ (graft central thickness), s (sagittal depth to host cornea = 0.94 mm), and corresponding y ($0.5 \times$ chord length to host cornea = 3.345 mm). (C) Example calculations using the data from patient 2 (Table 2) to determine the presurgical graft CP ratio and posterior radius of curvature (values obtained from post-DSEK AS-OCT image, excluding the corneal graft). ^ΔThis cross section of the graft identifies two peripheral thicknesses of the graft (0° and 180°). P2 and P4, at 90° and 270°, are above and below this plane of view. Presurgical CP ratios were calculated with presurgical pachymetry values provided by Ocular Systems Inc. (Winston-Salem, NC).

While the majority of refractive changes are predicted to arise from the posterior corneal surface, the graft slightly changes the thickness of the cornea and thus changes the distance between the second principal plane of the cornea and the first principal plane of the lens. Because these effects typically contribute less than 8% of the refractive change of the eye, they will not be discussed in detail here, but the equations are given later (equations 5 and 6) and will be included in calculations of the power of the eye.

In summary, the presurgical measurements and calculations necessary for predicting refractive change after DSEK include the following steps:

1. Measure corneal thickness (e.g., pachymetry).
2. Calculate the presurgical corneal posterior radius of curvature using the equation $(0.5 \cdot \text{chord length})^2 / (2 \cdot \text{sagittal depth})$, which is derived from the sagittal depth (sag) equation (Figs. 4, 6). The chord length and sagittal depth in the sag equation are measured from a presurgical AS-OCT image. Alternatively, the posterior radius of curvature can be directly measured by using an anterior segment evaluation (Pentacam; Oculus).
3. Obtain presurgical graft thickness and CP ratios using pachymetry and data provided by the eye bank that provides the corneal transplants.
4. Use the equations given below to estimate the refractive changes in the power of the eye after DSEK surgery.

To estimate the refractive changes in the power of the eye after DSEK, first determine the corneal power, which depends on the central graft thickness and is given by

$$F_{\text{cornea+DSEK}} = F_{\text{ac}} + F_{\text{pc+DSEK}} - \left(\frac{t + t_{\text{transplant}}}{n_2} \right) (F_{\text{ac}}) (F_{\text{pc+DSEK}}) \tag{3}$$

where $F_{\text{cornea+DSEK}}$ is the power of the cornea after DSEK, F_{ac} is the power of the anterior cornea, $F_{\text{pc+DSEK}}$ is the power of

the posterior cornea after DSEK, and t is the distance between the anterior and posterior surfaces of the recipient cornea (corneal thickness). The transplant thickness is added to the host corneal thickness to obtain the new combined corneal thickness ($t + t_{\text{transplant}}$). In equation 3,

$$F_{\text{ac}} = \frac{n_2 - n_1}{r_{\text{ac}}} = \frac{1.376 - 1.00}{0.0077} = +48.8 \tag{4}$$

where n_1 is the index of refraction of air and r_{ac} is the radius of curvature of the anterior cornea (average r_{ac} is 0.0077 m^{11}),

$$F_{\text{pc+DSEK}} = \frac{n_3 - n_2}{r_{\text{pc}}''} \tag{1}$$

where

$$r_{\text{pc}}'' = \frac{1}{\frac{1}{r_{\text{pc}} - t_{\text{transplant}}} + \frac{2t_{\text{transplant}} \left(\frac{1}{\text{CP}} - 1 \right)}{b'^2}} \tag{2}$$

Finally, the overall power of the eye with the graft is given by

$$F_{\text{eye+DSEK}} = F_{\text{cornea+DSEK}} + F_{\text{lens}} - \frac{d}{n_3} (F_{\text{cornea+DSEK}})(F_{\text{lens}}) \tag{5}$$

where $F_{\text{eye+DSEK}}$ equals the power of the eye after DSEK, $F_{\text{cornea+DSEK}}$ equals the power of the cornea after DSEK, F_{lens} equals the power of the lens (the average lens is estimated to be 19 D¹¹ or it can be replaced with the pseudophakic IOL power), and

A.

$$F_{ac} = \frac{n_2 - n_1}{r_{ac}} = \frac{1.376 - 1.00}{0.0077} = +48.8$$

$$F_{pc+DSEK} = \frac{n_3 - n_2}{r_{pc}''} = \frac{n_3 - n_2}{\frac{1}{\frac{1}{r_{pc}} - t_{transplant}} + \frac{2 * t_{transplant} * (\frac{1}{CP} - 1)}{h'^2}}$$

$$F_{cornea+DSEK} = F_{ac} + F_{pc+DSEK} - \left(\frac{t + t_{transplant}}{n_2} \right) (F_{ac})(F_{pc+DSEK})$$

$$d = 0.005678 - \left(-1 * \frac{n_3 * (t + t_{transplant}) * F_{ac}}{n_2 * F_{cornea+DSEK}} + (t + t_{transplant}) \right)$$

$$F_{eye+DSEK} = F_{cornea+DSEK} + F_{lens} - \frac{d}{n_3} (F_{cornea+DSEK})(F_{lens}) \longrightarrow \text{Refractive change} = F_{eye+DSEK} - F_{eye \text{ without DSEK}}$$

B. Example calculations for patient 2

$$r_{pc}'' = \frac{1}{\frac{1}{0.00595 - 0.00129} + \frac{2 * 0.00129 * (\frac{1}{0.853} - 1)}{0.0015^2}} = 0.00522 \text{ m}$$

$$F_{ac} = 48.8$$

$$F_{pc} = \frac{-0.04}{0.00522} = -7.66D$$

$$F_{cornea+DSEK} = 48.8 - 7.66 - \frac{0.000816 + 0.000129}{1.376} (48.8)(-7.66) = 41.4D$$

$$d = 0.005678 - \left(-1 * \frac{1.336 * (0.000816 + 0.000129) * 48.8}{1.376 * 41.4} + (0.000816 + 0.000129) \right) = 0.00581m$$

$$F_{eye+DSEK} = 41.4 + 19 - \frac{0.00581}{1.376} (41.4)(19) = 57.1D$$

$$F_{eye \text{ without DSEK}} = 57.9 D (t_{transplant} = 0, CP = 1)$$

$$F_{eye+DSEK} - F_{eye \text{ without DSEK}} \approx -0.8D \approx 0.8D \text{ hyperopic shift}$$

CP ratio = the central to peripheral ratio of the corneal graft
 d = the distance between the second principal plane of the cornea and the first principal plane of the lens
 F_{ac} = the power of the anterior cornea F_{cornea+DSEK} = power of the cornea post DSEK F_{eye+DSEK} = power of the eye post DSEK
 F_{eye without DSEK} = power of eye before DSEK F_{lens} = power of the lens F_{pc+DSEK} = the power of the posterior cornea post DSEK
 h' = the chord length at which the CP ratio is measured n₁ = air index of refraction
 n₂ = corneal index of refraction n₃ = aqueous humor index of refraction r_{pc} = recipient corneal posterior radius of curvature
 r_{pc}'' = the post DSEK posterior radius of curvature with non-uniform width corneal graft
 t = recipient corneal thickness t_{transplant} = corneal graft thickness

FIGURE 7. DSEK mathematical model equations. (A) Calculating the refractive change after DSEK using the DSEK mathematical model equations. To estimate the refractive change after DSEK surgery, the difference in the power of the eye before and after graft placement should be calculated: postsurgical power (F_{eye+DSEK}) – presurgical power (F_{eye without DSEK}, with t_{transplant} = 0, CP = 1) = refractive change in eye power. The hyperopic shift is -1 × refractive change. (B) Example calculations using standard values (Table 1) and measurements from P2 (Table 2). Presurgical graft CP ratio = 0.853 and estimated presurgical posterior radius of curvature = 0.00595 m for P2 (calculated in Fig. 6); 19 D was used for the power of a natural lens (F_{lens}).¹¹

$$d = 0.005678 - \left[-1 \cdot \frac{n_3 \cdot (t + t_{transplant}) \cdot F_{ac}}{n_2 \cdot F_{cornea}} + (t + t_{transplant}) \right]. \quad (6)$$

The derivation will be shown below in step A1. A summary of the above equations and sample calculations are shown in Figures 6 and 7.

5. Next, the power of the eye *without* the graft is calculated by using the same equations, where t_{transplant} equals 0, the CP ratio is 1, and r_{pc}'' equals the measured presurgical corneal posterior radius of curvature.

6. The difference between the two powers is calculated F_{eye+DSEK} – F_{eye without DSEK}. This difference is the predicted refractive change after DSEK surgery.

A1. According to the Gullstrand eye model, in equation 5, d equals the distance between the second principal plane of the cornea and the first principal plane of the lens (1st principal plane of lens – 2nd principal plane of cornea). The first principal plane of a normal lens is approximately 0.005678 m posterior to the cornea.¹¹ The location of the second principal plane of the cornea is given by

$$-1 \cdot \frac{n_3 \cdot (t + t_{transplant}) \cdot F_{ac}}{n_2 \cdot F_{cornea}} + (t + t_{transplant}). \quad (7)$$

The point of reference is from the vertex of the anterior cornea. Negative values represent positions in front of the

anterior cornea (outside the eye), and positive values represent positions behind the anterior cornea (inside the eye).

The DSEK Mathematical Model Approximates Refractive Changes after DSEK Surgery

We analyzed four patients, each of whom underwent a DSEK procedure and satisfied the inclusion criteria: two women and two men, with an average age of 72 years (range, 56 – 85 years). Fuchs' dystrophy was the indication for DSEK surgery in all four cases. Of the four procedures, three were pseudophakic DSEK procedures, and one was a triple procedure with DSEK, phacoemulsification, and intralocular lens implantation. Post-operative refractive and AS-OCT measurements were taken an average of 13 months after surgery (range, 3.6–23 months; Tables 2, 3).

The average corneal thickness was 700 μm (range, 570–820 μm, SEM 27 μm) before surgery and 580 μm (range, 490–630 μm, SEM 30 μm) after surgery, with an average decrease of 120 μm (range, –330–7 μm, SEM 73 μm), excluding the graft. Measurements were taken approximately 13 months after surgery (range, 3–23 months SEM 5 months). The average presurgical and postsurgical central graft thicknesses were 128 μm (range, 95–147 μm, SEM 12 μm) and 152 μm (range, 100–200 μm, SEM 18 μm), respectively, with an average increase per graft of 24 μm (range, 8–53 μm, SEM 10 μm). Surprisingly, the average presurgical and postsurgical CP ratios were 0.85 and 0.87, respectively, with an average change of 0.02 (range, –0.02 to +0.09). Although these data were taken at various time intervals at least 3 months after surgery, the variation in CP ratio changes were less than the variations in

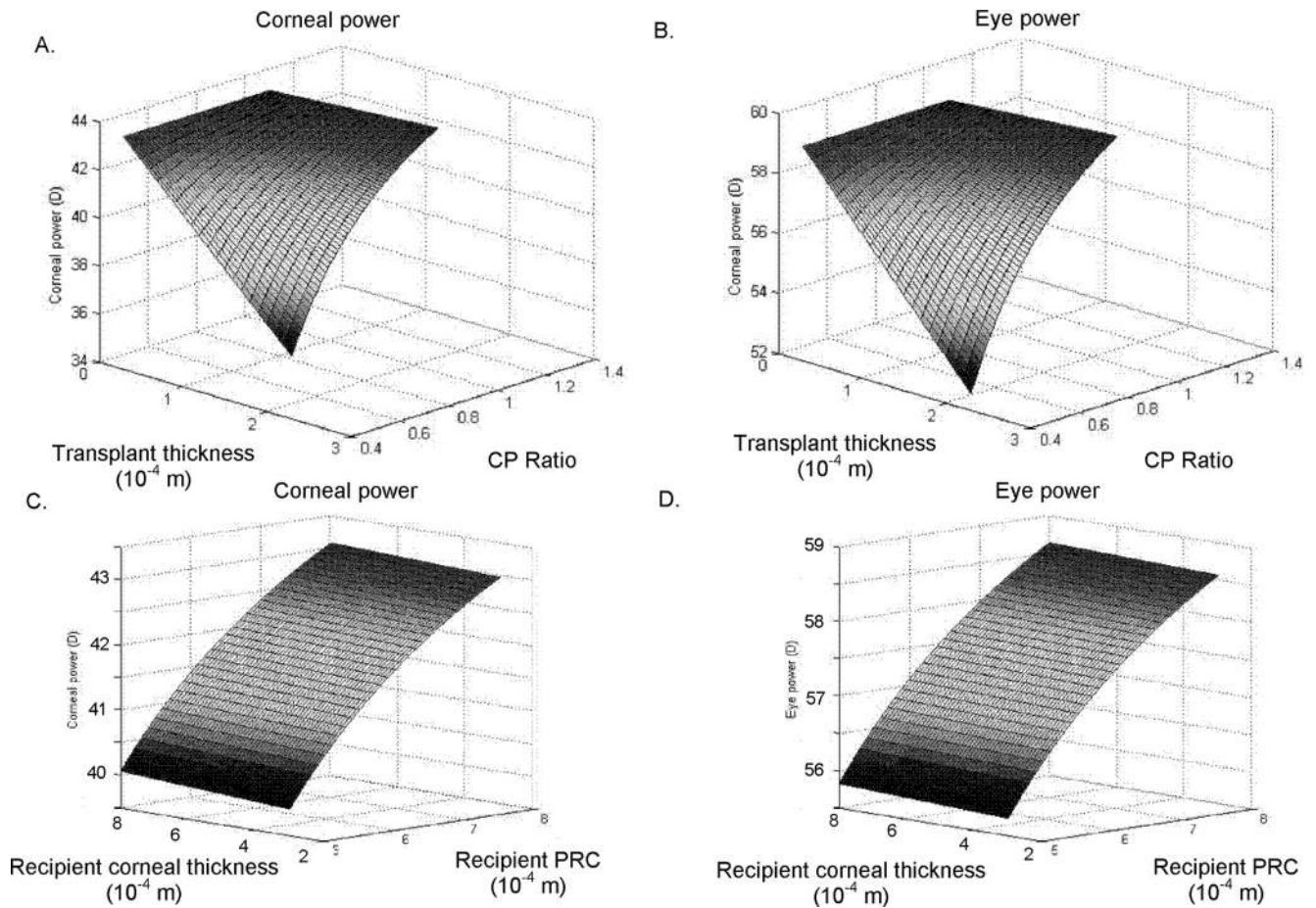


FIGURE 8. The relation between DSEK model variables and eye or corneal power. Corneal (A) and eye (B) refractive power versus transplant thickness and donor CP ratio. Corneal (C) and eye (D) refractive power versus recipient corneal thickness and recipient posterior radius of curvature (PRC). Chord length (*b*) = 1.5 mm for (A–D), posterior radius of curvature = 6.8 mm for (A) and (B), and transplant thickness = 100 μ m and CP ratio = 0.8 for (C) and (D). (Images generated in MatLab; The MathWorks, Natick, MA).

central graft thickness (3.5% vs. 19%), suggesting that there is less change in the CP ratio of the corneal grafts when compared with the change in central thickness over time. The average pre-DSEK corneal posterior radius of curvature, estimated from postsurgical AS-OCT images using the posterior radius of curvature derived in Figure 4 and excluding graft thickness (example shown in Fig. 6) was 5.8 mm (range, 5.3–6.2 mm), and the average measured post-DSEK radius of curvature, including graft thickness, was 5.4 mm (range, 5.0–

5.7 mm), indicating an average decrease of 0.45 mm (range, 0.1–0.8 mm) from pre- to post-DSEK surgery. The average predicted radius of curvature after graft placement was 5.1 mm (range, 4.8–5.4 mm) with an average predicted decrease in curvature of 0.7 mm per graft (0.5–0.8 mm; Tables 2, 3).

The mean preoperative and postoperative refractive errors in spherical equivalents were -0.75 D (range, -1.5 – 0.5 D) and 0.14 D (range, -0.69 – 1.25 D), respectively, with an average hyperopic shift per patient of 0.89 D (range,

TABLE 2. Measured and Predicted Refractive Changes after DSEK Surgery, Based on Presurgical Measurements

Pt	Procedure	Pre-op Central Corneal Thickness (μ m)	Pre-op Central Graft Thickness (μ m)	Pre-op Graft Peripheral Thickness (μ m)	Pre-op Graft C:P Ratio	Posterior Radius of Curvature without Graft (mm)	Predicted Posterior Radius of Curvature with Graft (mm)	Measured Refractive Change (D)	Predicted Hyperopic Corneal Refractive Change (D)	Predicted Hyperopic Shift of Eye (D)
1	DSEK	650	142	159, 167, 163, 151	0.89	5.27	4.74	1.0	0.79	0.75
2	DSEK	816	129	148, 156, 169, 132	0.85	5.95	5.22	0.75	0.88	0.83
3	DSEK	573	147	129, 163, 199, 186	0.87	5.80	5.09	1.0	0.91	0.86
4	Triple	764	95	112, 86, 141, 140	0.79	6.19	5.37	0.82	0.93	0.88

Corneal thickness was measured with pachymetry; radius of curvature was calculated from postsurgical AS-OCT images; graft thickness and graft ratios were measured and calculated using pachymetry measurements. Peripheral thicknesses were measured 1.5 mm from the vertex of the graft. The pre-op graft CP ratio was calculated by dividing the pre-op central graft thickness by the average of the peripheral graft thicknesses. Predicted hyperopic corneal refractive shift and predicted hyperopic shift of the eye are the predicted changes in the cornea and eye, respectively, based on the DSEK mathematical model calculations.

TABLE 3. Post-DSEK Corneal Measurements

Pt	Procedure	Post-op Corneal Thickness without Graft (μm)	Measured Post-op Radius of Curvature with Graft (mm)	Post-op Graft Thickness (μm)	Post-op Graft C:P Ratio	Measured Refractive Change (D)	Age	Time Post-op
1	DSEK	600	5.35	150	0.88	1.0	85	2 years (23 months)
2	DSEK	490	5.71	150	0.83	0.75	56	2 years (22 months)
3	DSEK	580	5.00	200	0.89	1.0	73	5 months
4	Triple	630	5.34	110	0.88	0.82	72	3 months

Corneal thickness, post-DSEK radius of curvature, graft thickness, and CP ratios were based on post-DSEK AS-OCT images.

0.75–1.0 D). The average predicted refractive corneal power (hyperopic) shift by our mathematical model was 0.88 D (range, 0.78–0.93 D), which was, on average, 98% (range, 78%–117%) of the measured refractive change. When the corneal power change and the total change in corneal thickness are used to calculate the overall change in the power of the eye, the average predicted refractive change in the eye is 0.83 D (range, 0.75–0.88 D), which is a mean of 93% (range, 75%–110%) of the measured refractive change (Tables 2, 3).

DISCUSSION

Several studies have found that DSEK surgery can result in hyperopic refractive shifts up to 3.0 D,^{5–8,13,14} with averages close to 1.0 D. In particular, the posterior radius of curvature has been suggested to be the main refractive component that changes after surgery.^{7,10} This change can be modeled by calculating the change in sag of the presurgical posterior corneal surface to estimate the change in posterior corneal power after DSEK surgery. We developed a mathematical model to estimate the hyperopic shift after DSEK surgery. The variables for the model include preoperative corneal thickness, graft

thickness, graft CP ratio, and recipient posterior corneal curvature.

Our mathematical model suggests that, in theory, an ideal corneal graft would be one cell layer thick without any variation in thickness, because such a graft would have negligible effects on refraction (Fig. 8). Conversely, thicker tissue grafts with smaller CP ratios result in larger hyperopic shifts. With regard to preoperative recipient corneal measurements, a larger recipient corneal thickness and recipient presurgical posterior radius of curvature result in relatively smaller hyperopic shifts.

Of the four variables of our mathematical model, the two variables that can be controlled with graft cutting (graft tissue thickness and CP ratios) can have a significant effect on refractive changes, where the smaller the CP ratio and the larger the graft thickness, the larger the refractive changes (Tables 4, 5; Fig. 8). Variations in the recipient posterior radius of curvature can also affect the refractive change, but variations in the recipient corneal thickness have the least effect on the overall refractive changes. For example, with a recipient corneal thickness of 0.5 mm, graft corneal thickness of 0.16 mm, posterior radius of curvature 6.8 mm, and CP ratio of 0.90, the predicted refractive change is 0.70 D. Increasing the recipient corneal

TABLE 4. Predicted Refractive Change in Recipient Cornea and Eye Based on Variable Transplant Thickness and Fixed Corneal Thickness CP Ratio and Preoperative Posterior Curvature of 6.8 mm¹¹

Corneal Thickness (μm)	C:P Ratio	Transplant Thickness (μm)	Predicted Posterior Radius of Curvature (mm)	Predicted Change in Corneal Power (D)	Predicted Change in Eye Power (D)	Predicted Hyperopic Refractive Shift (D)
500	—	0	6.80	0.00	0.00	0.00
500	0.7	100	5.34	-1.56	-1.45	+1.45
500	0.7	105	5.28	-1.63	-1.52	+1.52
500	0.7	110	5.23	-1.71	-1.59	+1.59
500	0.7	115	5.17	-1.79	-1.67	+1.67
500	0.7	120	5.12	-1.87	-1.74	+1.74
500	0.7	125	5.07	-1.94	-1.81	+1.81
500	0.7	130	5.01	-2.02	-1.88	+1.88
500	0.7	135	4.96	-2.10	-1.96	+1.96
500	0.7	140	4.91	-2.18	-2.03	+2.03
500	0.7	145	4.87	-2.25	-2.10	+2.10
500	0.7	150	4.82	-2.33	-2.17	+2.17
500	0.7	155	4.77	-2.41	-2.25	+2.25
500	0.7	160	4.73	-2.49	-2.32	+2.32
500	0.7	165	4.68	-2.56	-2.39	+2.39
500	0.7	170	4.64	-2.64	-2.46	+2.46
500	0.7	175	4.60	-2.72	-2.53	+2.53
500	0.7	180	4.55	-2.80	-2.61	+2.61
500	0.7	185	4.51	-2.87	-2.68	+2.68
500	0.7	190	4.47	-2.95	-2.75	+2.75
500	0.7	195	4.43	-3.03	-2.82	+2.82
500	0.7	200	4.39	-3.10	-2.90	+2.90

Estimates are based on the DSEK mathematical model. A negative change in corneal or eye power corresponds with a positive refractive (hyperopic) shift in manifest refraction.

TABLE 5. Predicted Refractive Change in Recipient Cornea and Eye Based on Variable CP Ratio and Fixed Corneal Thickness, Transplant Ratio, and Preoperative Posterior Curvature of 6.8 mm¹¹

Corneal Thickness (μm)	C:P Ratio	Transplant Thickness (μm)	Predicted Posterior Radius of Curvature (mm)	Predicted Change in Corneal Power (D)	Predicted Change in Eye Power (D)	Predicted Hyperopic Refractive Shift (D)
500	—	0	6.8	0.00	0.00	0.00
500	1.0	100	6.70	-0.07	-0.07	+0.07
500	0.985	100	6.64	-0.12	-0.12	+0.12
500	0.97	100	6.58	-0.17	-0.17	+0.17
500	0.955	100	6.52	-0.23	-0.22	+0.22
500	0.94	100	6.45	-0.29	-0.27	+0.27
500	0.925	100	6.39	-0.35	-0.33	+0.33
500	0.91	100	6.33	-0.41	-0.39	+0.39
500	0.895	100	6.26	-0.47	-0.45	+0.45
500	0.88	100	6.20	-0.54	-0.51	+0.51
500	0.865	100	6.13	-0.61	-0.57	+0.57
500	0.85	100	6.06	-0.68	-0.64	+0.64
500	0.835	100	5.99	-0.75	-0.70	+0.70
500	0.82	100	5.93	-0.83	-0.77	+0.77
500	0.805	100	5.86	-0.91	-0.85	+0.85
500	0.79	100	5.78	-0.99	-0.92	+0.92
500	0.775	100	5.71	-1.08	-1.00	+1.00
500	0.76	100	5.64	-1.16	-1.09	+1.09
500	0.745	100	5.57	-1.26	-1.17	+1.17
500	0.73	100	5.49	-1.35	-1.26	+1.26
500	0.715	100	5.41	-1.45	-1.35	+1.35
500	0.7	100	5.34	-1.56	-1.45	+1.45
500	0.685	100	5.26	-1.67	-1.55	+1.55
500	0.67	100	5.18	-1.78	-1.66	+1.66

Estimates are based on the DSEK mathematical model. A negative change in corneal or eye power corresponds with a positive refractive (hyperopic) shift in manifest refraction.

thickness to 0.7 mm and the recipient posterior radius of curvature to 8.0 mm only reduces the refractive change to 0.65 D. In contrast, decreasing the CP ratio to 0.8 and increasing the corneal graft thickness to 0.2 mm increases the refractive change to 1.87 D. It is important to note that this positive manifest refractive change (hyperopic shift) corresponds with a negative change in eye power. This change is demonstrated by the fact that after DSEK surgery, as the overall power of the eye decreases (a decrease or negative power change), a stronger eyeglass prescription (an increase or positive eye glass refractive change) is needed to compensate.

Interestingly, the model also suggests that not all refractive changes result in hyperopic shifts. Grafts with CP ratios greater than ~ 1 can result in greater refractive power (myopic shift) of the cornea and eye (although other variables can also affect the ratio at which the shift becomes myopic). Perhaps with improved dissection of donor tissue and more precise control of the corneal graft CP ratio and thickness, a specific donor corneal shape can be cut to target a refractive goal for the patient.

While this mathematical model predicted more than 90% of the measured hyperopic shifts in the four cases studied, there are several caveats that should be considered. The difference between the measured and predicted refractive changes may be due in part to error in refractive and corneal measurements and the assumptions listed in the Methods section. It is also unclear how much the recipient corneal posterior radius of curvature changes after Descemet stripping, because presurgical posterior radius of curvature measurements (e.g., presurgical AS-OCT or anterior segment measures [Pentacam; Oculus]) were not available for these patients. In addition, other factors may account for the remaining hyperopic shift. Our mathematical model assumes that there is no change in recipient or graft corneal thicknesses over time, but previous studies have shown that corneal deturgescence occurs at the central and peripheral regions of the corneal graft after DSEK surgery⁶ and

that graft thinning stabilizes after ~ 6 months.⁹ Furthermore, a prospective study showed that the central pachymetry was significantly decreased from 0.70 to 0.66 mm¹⁵ 6 months after DSEK surgery. Additional studies are needed to determine how much graft CP ratios and recipient corneal thicknesses change 6 months after surgery, when compared to their preoperative thicknesses, and whether they stabilize or continue to change beyond 6 months. The four cases studied, with a range of postoperative measurements ranging from 3 months to 2 years, suggest that the CP ratio does not change dramatically over time. Finally, a larger prospective study would be helpful in determining the true predictive accuracy of the mathematical model.

Nevertheless, we present an effective initial model for estimating refractive changes after DSEK surgery. The average predicted hyperopic shift of 0.83 D and change in radius of curvature of 0.7 mm are similar to previously reported changes after DSEK surgery.^{4-6,10} The model demonstrates that the hyperopic shift depends on at least four variables, and that can explain why correlations between two variables (e.g., graft thickness with hyperopic shift) may not appear significant if other variables are not held constant. Furthermore, this is also the first model to predict refractive changes based on an individual's presurgical measurements.

In conclusion, this simplified DSEK model offers a detailed mathematical understanding of the hyperopic shift that occurs after DSEK surgery. Although further studies will be helpful in refining and determining its precision, the model offers a potential first step in developing a tool for determining the power of intraocular lenses to be used in combined DSEK and cataract procedures.

Acknowledgments

The authors thank Ocular Systems, Inc., for graft measurements and Frank Merritt Gammage for help with AS-OCT imaging.

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APPENDIX

Derivation of the Post-DSEK Posterior Corneal Radius of Curvature

Based on the diagram in Figure A1, it can be seen that

$$b' = b'' + w \sin \theta \tag{8}$$

$$s_i'' = s_i' + w \cos \theta. \tag{9}$$

These expressions can be simplified by assuming that θ is small, so that $\sin \theta \sim 0$ and $\cos \theta \sim 1$ (assumption 11). Using these approximations,

$$b' = b'' \tag{10}$$

$$s_i'' = s_i' + w \tag{11}$$

Using the sag equation (Fig. 4) to calculate the radii of curvature of r_{pc}' and r_{pc}'' , we find

$$s_i' = \frac{(b'')^2}{2r_{pc}'} \tag{12}$$

$$s_i'' = \frac{(b'')^2}{2r_{pc}''} \approx \frac{(b'')^2}{2r_{pc}'} \tag{13}$$

where the approximation in equation 13 uses equation 10. Taking the difference of the two sags ($s_i'' - s_i'$) results in

$$\frac{1}{r_{pc}''} = \frac{1}{r_{pc}'} + \frac{2(s_i'' - s_i')}{b'^2} \tag{14}$$

Equation 11 can be rewritten as

$$s_i'' - s_i' = w. \tag{15}$$

Note that the difference at the periphery of the donor graft (between the graft of nonuniform thickness and the idealized graft with even thickness throughout) can be defined as

$$w = t_{transplant} \left(\frac{1}{CP} - 1 \right) \tag{16}$$

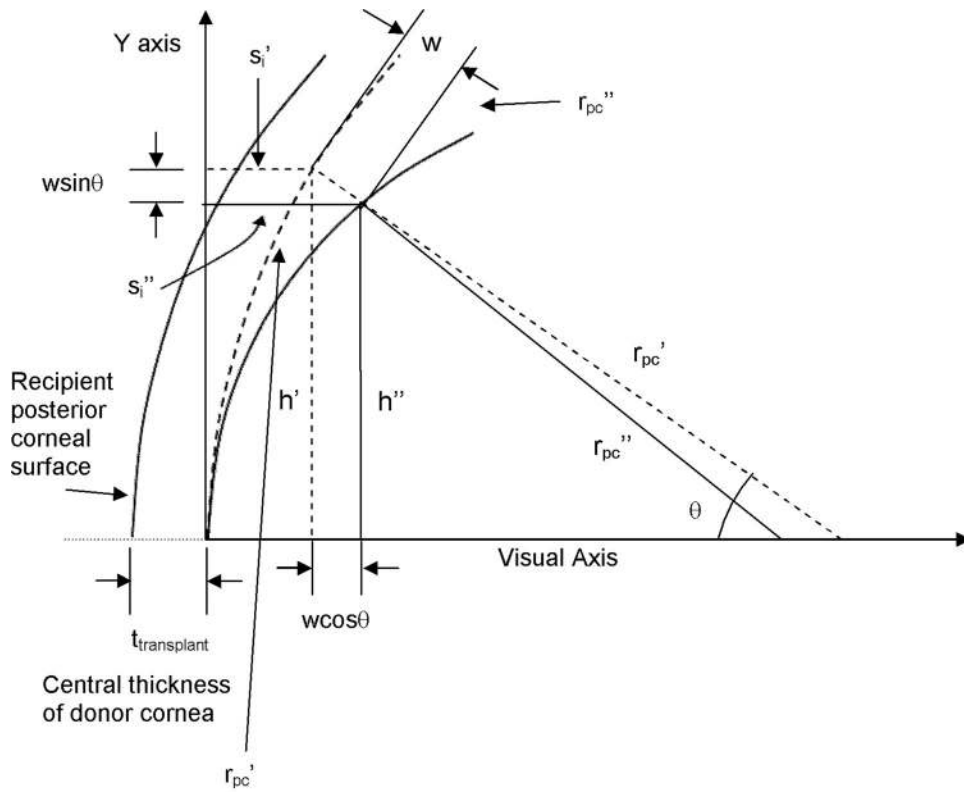
where CP is the central to peripheral ratio of the donor cornea at height b'' away from the central axis of the donor cornea and $t_{transplant}$ is the transplant thickness at the vertex or central region. A value of $w = 0$ means that the graft is of uniform width.

Equation 14 can have ($s_i'' - s_i'$) replaced with $t_{transplant}[(1/CP) - 1]$, because both are equal to w , and the equation can be rewritten to determine the new radius of curvature which is given by

$$r_{pc}'' = \frac{1}{\frac{1}{r_{pc}'} + \frac{2t_{transplant} \left(\frac{1}{CP} - 1 \right)}{b'^2}} \tag{2}$$

Since $r_{pc}' = r_{pc} - t_{transplant}$,

$$r_{pc}'' = \frac{1}{\frac{1}{r_{pc} - t_{transplant}} + \frac{2t_{transplant} \left(\frac{1}{CP} - 1 \right)}{b'^2}}$$



- r_{pc}^1 : radius of curvature of an ideally shaped donor cornea with even thickness
- r_{pc}^2 : radius of curvature of a donor cornea with non-uniform peripheral thickness (post-DSEK posterior corneal radius of curvature)
- h^1 : distance from central visual axis to point on posterior cornea corresponding to r_{pc}^1
- h^2 : distance from central visual axis to point on posterior cornea corresponding to r_{pc}^2
- θ : angle between central visual axis and r_{pc}^1
- s_i^1 : sag of posterior corneal curvature corresponding to h^1 and r_{pc}^1
- s_i^2 : sag of posterior corneal curvature corresponding to h^2 and r_{pc}^2
- $t_{transplant}$: central thickness of donor cornea
- w : peripheral donor transplant thickness – central thickness of donor cornea
- $w \cos \theta$: vertical distance between s_i^1 and s_i^2
- CP : central to peripheral donor graft ratio at point $h^2 = t_{transplant} / (w + t_{transplant})$
- $w = t_{transplant} (1/CP - 1)$

FIGURE A1. The posterior surface of the cornea with graft after DSEK surgery.