

# Endothelial cell loss and complication rates with combined Descemet's stripping endothelial keratoplasty and cataract surgery in a UK centre

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CLINICAL STUDY

## Abstract

**Purpose** To report 6-month, 1- and 2-year endothelial cell loss (ECL), intra- and postoperative complications in a large series of patients undergoing either Descemet's stripping endothelial keratoplasty (DSEK) or a combined phacoemulsification and DSEK in a UK centre.

**Patients and methods** Patients undergoing DSEK with or without concurrent cataract surgery were included in this retrospective study. Surgeries were performed between January 2006 and May 2013. Main outcomes included intra- and postoperative complications and percentage ECL.

**Results** DSEK was performed in 226 eyes (210 patients). Of these, 141 eyes (126 patients) underwent DSEK alone and 85 eyes (84 patients) underwent DSEK combined with cataract surgery. Excluding complex anterior segment pathology the mean percentage ECL at 6, 12 and 24 months was  $40.5 \pm 13.4$ ,  $45.1 \pm 14.6$  and  $53.1 \pm 13.0$  in the DSEK group and  $40.7 \pm 15.4$ ,  $42.6 \pm 15.3$  and  $49.6 \pm 16.5$  in patients undergoing the combined procedure, respectively. There was no significant difference in percentage ECL at 6 or 24 months between the two groups both in complex and routine cases. Intraoperative complications occurred in four patients undergoing DSEK and three undergoing combined procedure. Postoperative complication rates did not reach statistical significance between the groups.

**Conclusion** Mean ECL and complication rates were comparable at 6, 12 and 24 months in routine cases undergoing concurrent DSEK with cataract surgery and those undergoing

DSEK. These data support the combined procedure in patients requiring both cataract surgery and endothelial keratoplasty. Further collaboration to report endothelial cell counts from other UK centres should be encouraged.

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## Introduction

There are differences of opinion as to whether cataract surgery should be performed concurrently or sequentially in patients requiring both cataract surgery and Descemet's stripping endothelial keratoplasty (DSEK).<sup>1–3</sup> The combined procedure avoids the risks involved with a second surgical procedure and may offer more rapid visual rehabilitation; however, surgeons may be concerned regarding the use of viscoelastic during the cataract surgery influencing graft attachment.<sup>1</sup> Long-term outcomes, particularly endothelial cell counts, in the United Kingdom are infrequent in the literature.<sup>4</sup> The purpose of this study is to report and compare mean percentage endothelial cell loss (ECL) and complication rates in a large series of patients undergoing DSEK with and without concurrent cataract surgery.

## Materials and methods

Patients undergoing DSEK with or without concurrent cataract surgery were included in this retrospective study. An institutional audit review board gave prior approval of the study, which was conducted in accordance with good clinical practices and the Declaration of Helsinki.

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All patients were operated on at a single institution under the supervision of a single surgeon (EJH). There were no exclusion criteria relating to preoperative or intraoperative factors. Both eyes of the same patient were permissible, as were re-grafts. Data were collated between January 2006 and May 2013 and entered prospectively at each follow-up visit, utilising an electronic web-based database 'eyedata.org'. Donor tissue was provided by the UK Transplant service and accepted with endothelial cell density (ECD) >2000 cells/mm<sup>2</sup>.

Pupil dilation was performed in all patients preoperatively using G cyclopentolate 1% and G phenylephrine 2.5%. Phacoemulsification and posterior chamber intraocular lens (IOL) implantation was performed through a temporal clear corneal incision followed by DSEK. The phacoemulsification technique included primary chop, insertion of a three-piece hydrophobic acrylic IOL into the capsular bag and extensive viscoelastic aspiration prior to DSEK. IOL selection took into account the expected hyperopic shift often induced by endothelial keratoplasty.<sup>2,5</sup> The corneal epithelium was removed prior to biometry in those patients with significant preoperative corneal oedema, preventing accurate biometry measurement.

The procedure for DSEK surgery was standard and has been described in detail elsewhere.<sup>6</sup> The DSEK technique included manual dissection of the donor material using an artificial anterior chamber and a Morlet lamellar dissector. An anterior chamber maintainer was utilised during donor insertion. Graft insertion was performed by one of three techniques: the Utrata forceps, the Busin glide (Moria USA, Doylestown, PA, USA) or the Tan Endoglide (Angiotech, Reading PA, USA/Network Medical Products, North Yorkshire, UK). The choice of insertion technique was dependent entirely on surgeon preference at the time of the procedure and not on patient-related factors.

Main outcomes measured included intra- and postoperative complications and percentage ECL at 6 months, 12 months and 2 years. The former included graft interface fluid, re-bubble, graft rejection and graft failure. The presence of any degree of interface fluid was included in the analysis for postoperative complications. A re-bubble procedure was performed in patients' with diffuse interface fluid, progression of interface fluid, interface fluid involving the central 6mm of the graft or graft dislocation into the anterior chamber. All patients were managed using the same follow-up and drop regime. At each visit, a slit-lamp examination was performed and standard parameters (visual acuity, intraocular pressure, pachymetry) were recorded. Percentage ECL was obtained by measuring the donor central ECD using a corneal confocal microscope (Confoscan4; Nidek Technologies, Inc., Padova, Italy) at 6,

12 and 24 months and comparing this to the baseline preoperative Corneal Tissue Service (CTS) measurements.

Sub-group analyses were performed for complex versus routine grafts, based on preoperative and intraoperative characteristics. Complex grafts were defined as grafts with complicated anterior segments (Iridocorneal Endothelial syndrome, surgically managed glaucoma) and grafts with intraoperative complications.

Statistical analysis was performed using SPSS software version 20.0 (IBM Corp., Armonk, NY, USA).  $\chi^2$ -tests were utilised to compare categorical data for example complication rates, and independent sample *t*-test utilised for continuous data with significant differences reported at the  $P < 0.05$  level.

Multivariate analysis was performed to identify variables, which may influence the percentage ECL. Variables included patient age, gender, initial endothelial cell count (ECC), donor age, procedure performed (DSEK or phacoDSEK), previous glaucoma or glaucoma surgery, re-do procedures and complications peri/postoperatively (interface fluid, re-bubble, rejection, raised intraocular pressure).

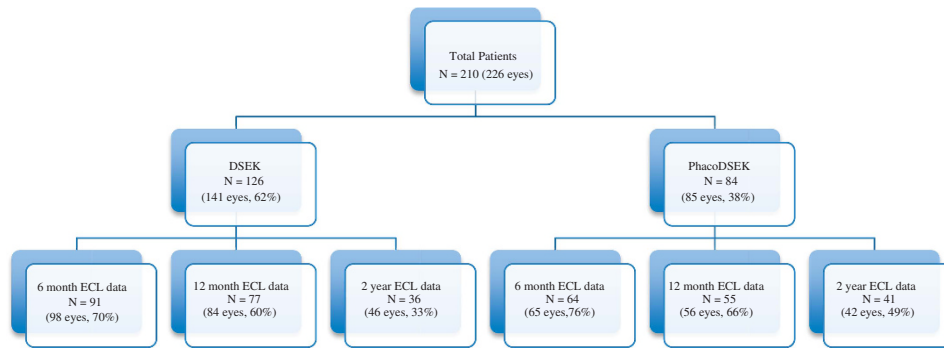
## Results

### *Patient recruitment*

DSEK was performed in a total of 226 eyes (210 sequential patients). Of these eyes, 141 eyes (126 patients) underwent DSEK alone and 85 eyes (84 patients) underwent DSEK combined with cataract surgery. In the DSEK group, 49 eyes (39 patients) were complex grafts and 92 eyes (87 patients) were routine. In the DSEK combined with cataract surgery group, 9 eyes (9 patients) were complex grafts and 76 eyes (75 patients) were routine. Patient recruitment, demographics and operative details are provided in Figure 1 and Table 1, respectively. Of the 141 eyes undergoing DSEK alone, 134 were pseudophakic, 6 were aphakic and 1 patient remained phakic. In the latter patient, DSEK was performed in a blind eye (previous childhood trauma) for painful bullous keratopathy.

### *Donor ECL*

Mean percentage ECL and mean exact cell counts at 6, 12 and 24 months for both groups for all cases and routine cases (in which complex anterior segment pathology was excluded) are shown in Table 2. Mean percentage ECL at 12 months was significantly lower in patients undergoing the combined procedure; however, this difference was not significant when adjusting for complex cases. There was no significant difference in percentage ECL at 6 or 24 months between patients undergoing DSEK and those



**Figure 1** Patient recruitment. DSEK was performed in a total of 226 eyes (210 patients). Of these eyes, 141 eyes (126 patients) underwent DSEK alone and 85 eyes (84 patients) underwent DSEK combined with cataract surgery. Patient numbers (and number of eyes) with available ECL data at 6 months, 1 year and 2 years are shown in the above figure.

**Table 1** Patient demographics

	DSEK N = 141 eyes	PhacoDSEK N = 85 eyes	P-value
Mean patient age (years ± SD)	73.63 ± 12.29	68.49 ± 8.20	P = 0.001
Mean donor age (years ± SD)	70.35 ± 20.87	71.29 ± 14.46	P = 0.713
Gender, male	61 (43.3%)	31 (36.5%)	P = 0.314
<i>Primary indication</i>			
FED	74 (52.5%)	79 (92.9%)	P ≤ 0.001
PBK	39 (27.7%)	0	
ICE	5 (3.5%)	2 (2.4%)	
Multiple surgery	11 (7.8%)	0	
ABK	6 (4.3%)	0	
Failed PK	4 (2.8%)	0	
Other	2 (1.4%)	4 (4.7%)	
Mean donor CTS preoperative ECC	2562.94 ± 276.62	2546.19 ± 167.76	P = 0.614
Grade of surgeon consultant	109 (77.3%) cases	68 (80%) cases	P = 0.687
<i>Insertion technique</i>			
Tan endoglide	80 (56.7%)	55 (64.7%)	P = 0.662
Busin glide	39 (27.7%)	18 (21.2%)	
Forceps	10 (7.1%)	6 (7.1%)	
Not recorded	12 (8.5%)	6 (7.1%)	

Abbreviations: ABK, Aphakic bullous keratopathy; CTS, Corneal Transplant Service; DSEK, Descemets stripping endothelial keratoplasty; ECC, endothelial cell count; FED, Fuchs Endothelial Dystrophy; ICE, Iridocorneal Endothelial; IOL, intraocular lens; PBK, Pseudophakic bullous keratopathy; PK, Penetrating keratoplasty.

undergoing the combined procedure both in complex and routine cases.

### Complications

No complication occurred in any patient during phacoemulsification and lens implant. Intraoperative complications during the endothelial keratoplasty stage occurred in four patients undergoing DSEK and three patients undergoing the combined procedure. In the former, these included graft prolapse with reinsertion ( $n = 2$ ), incarceration of the graft edge into the paracentesis requiring repositioning ( $n = 1$ ) and dehiscence of the graft-host interface requiring resuturing in a patient who had previously undergone a full

thickness penetrating keratoplasty ( $n = 1$ ). In the latter group, intraoperative complications included graft prolapse with reinsertion ( $n = 1$ ), extrusion of the AC maintainer during graft insertion ( $n = 1$ ) and incorrect orientation of the graft requiring repositioning ( $n = 1$ ).

Graft interface fluid, re-bubble and graft rejection occurred in 21 (14.9%), 15 (10.6%) and 19 (13.5%) patients, respectively, undergoing DSEK and 11 (12.9%), 11 (12.9%) and 7 (8.2%) patients undergoing combined procedure. These complication rates did not reach statistical significance between the two groups. Graft rejection was more frequent in the DSEK group; however, this did not reach statistical significance ( $P = 0.232$ ) (Table 3). There were no primary graft failures in the entire cohort.

**Table 2** Mean percentage endothelial cell loss and mean endothelial cell count

	DSEK N = 141 eyes		PhacoDSEK N = 85 eyes		P-value
	% ECL	ECC cells/mm <sup>2</sup>	% ECL	ECC cells/mm <sup>2</sup>	
<i>All cases</i>					
06 months	44.51 ± 14.85	1438 ± 412	41.91 ± 16.20	1492 ± 446	P = 0.292
12 months	49.79 ± 17.33	1331 ± 485	43.71 ± 16.21	1451 ± 447	P = 0.040
24 months	54.46 ± 14.41	1201 ± 389	49.93 ± 16.36	1311 ± 464	P = 0.171
<i>Routine cases</i>					
	DSEK N = 92 eyes		PhacoDSEK N = 76 eyes		
06 months	40.46 ± 13.40	1500 ± 354	40.72 ± 15.39	1503 ± 458	P = 0.921
12 months	45.13 ± 14.59	1425 ± 451	42.62 ± 15.30	1487 ± 434	P = 0.385
24 months	53.09 ± 13.01	1244 ± 351	49.63 ± 16.45	1320 ± 473	P = 0.328

Abbreviations: % ECL, percentage endothelial cell loss; ECC, endothelial cell count.

**Table 3** Complication rates

Complication	DSEK N = 141	PhacoDSEK N = 85	P-value
Interface fluid	21 (14.89%)	11 (12.94%)	P = 0.683
Re-bubble procedure	15 (10.64%)	11 (12.94%)	P = 0.599
Graft rejection episode	19 (13.48%)	7 (8.24%)	P = 0.232

**Multivariate analysis**

Variables significantly associated with increased percentage ECL at 6, 12 and 24 months are shown in Table 4 (a–c). The effect of DSEK *vs* combined PhacoDSEK on percentage ECL was insignificant when adjusting for other variables at all three time points (*P* = 0.608, 0.786 and 0.251 at 6, 12 and 24 months).

**Discussion**

Our findings of comparable ECL and complication rates when performing DSEK with and without concurrent cataract surgery support recent literature advocating combined DSEK with Cataract surgery.<sup>1,2</sup> Our intraoperative complication rate (7/226 eyes, 3.1%) is comparable to recent literature.<sup>7</sup> Mean ECL at 12 months was significantly lower in the combined procedure group when including all cases; however, this difference was not significant when adjusting for complex cases. Price *et al* reported that ECL was significantly less when DSEK was performed as a combined procedure. However, unlike our cohort, the graft insertion incision differed between the two groups.<sup>3</sup>

When comparing patient demographics, a significant difference between the two groups was found for patient age (significantly lower in the combined procedure group) and primary indication. The former could in part be explained by the number of patients with PBK in the

DSEK group being of an increased age having already undergone cataract surgery with subsequent decompensation. Primary indication for endothelial keratoplasty significantly differed between the two cohorts with the majority of cases performed for FED in the combined procedures group. There was no significant difference between the two cohorts for other patient demographics including insertion technique (*P* = 0.662).

Grafts of suitable thickness were achieved with manual dissection of the donor material utilising an artificial anterior chamber and a Morlet lamellar dissector. Published literature reports comparable ECL in donor tissue cut either manually or with a microkeratome.<sup>3,4,8</sup>

The postoperative ECC was obtained using confocal microscopy (Confoscan4). Both confocal and specular microscopy are validated objective methods to evaluate corneal endothelial morphology. As specular microscopy measures a smaller area of endothelial cells, one could perceive that this technique may over-count, particularly at lower cell counts. However, Farhan *et al* recently found no statistically significant difference between the SP-2000P specular microscopy and Confoscan4 confocal microscopy, reporting both methods can be used interchangeably to measure ECD.<sup>9</sup> The mean ECL was obtained by comparing the postoperative Confocal ECC with the preoperative ECC data measured by the CTS. The preoperative ECC were taken before these culture-medium preserved corneas were put into Dextran to deswell, which has been shown to lead to a loss of endothelial cells in excess of 8%.<sup>10</sup> Consequently, the actual preoperative ECC is likely to be lower than that provided by the eye bank. Despite this, our mean ECL are comparable with recent literature.<sup>2,5</sup> Long-term outcomes, particularly ECCs in the UK, are infrequent in the literature.<sup>4,11</sup>

Following multivariate analysis, endothelial keratoplasty performed for indications other than Fuchs Endothelial dystrophy was associated with a higher

**Table 4** Multivariate analysis to determine factors influencing the percentage ECL at (a) 6 months, (b) 12 months and (c) 24 months

Model	Unstandardised coefficients		Standardised coefficients	t	Sig.
	B	Std. error	Beta		
<i>(a)</i>					
Interface fluid	16.771	3.560	0.334	4.711	0.000
Indication	9.085	2.389	0.270	3.803	0.000
Initial ECC	-0.017	0.006	-0.192	-2.708	0.008
<i>(b)</i>					
Rejection	13.738	3.708	0.289	3.705	0.000
Indication	11.051	3.006	0.287	3.676	0.000
Interface fluid	8.171	3.836	0.161	2.130	0.035
<i>(c)</i>					
Indication	9.928	3.798	0.261	2.614	0.011
Re-bubble	11.156	4.828	0.230	2.311	0.023
Initial ECC	-0.017	0.008	-0.200	-2.007	0.048

percentage ECL at all times points. Other variables associated with higher percentage ECL included initial ECC at 6 and 24 months, graft dislocation at 6 and 12 months, graft rejection at 12 months and re-bubble at 24 months. Whether DSEK was performed with or without concurrent cataract surgery did not significantly increase percentage ECL when adjusting for other variables at each time point.

Our findings support combined endothelial keratoplasty with cataract surgery in appropriate patients. Our current practice is to offer the combined procedure to patients with cataract and evidence of corneal epithelial or stromal oedema. In those with FED without epithelial or stromal oedema, we recommend simple cataract extraction with lens implantation using a soft shell technique having explained the risk of postoperative decompensation and deliberately choosing a low myopia postoperative refractive target. Given the accommodative advantage of a crystalline lens in the younger population, patients younger than 50 years of age with visually insignificant cataract and a relatively deep anterior chamber should be offered DSEK alone.<sup>12-14</sup> With endothelial keratoplasty continually evolving, it will be pertinent to establish the role of combined cataract surgery in these newer techniques.<sup>14,15</sup>

In conclusion, mean ECL and complication rates were comparable at 6, 12 and 24 months in routine cases undergoing concurrent DSEK with cataract surgery and those undergoing DSEK. To our knowledge, this is the largest UK data series reporting ECCs. It supports the combined procedure in patients requiring both cataract surgery and endothelial keratoplasty and enables comparison with existing published data from the global ophthalmic community. Further collaboration with other corneal units to report ECCs from UK centres should be encouraged.

## Summary

### What was known before

- There are differences of opinion as to whether cataract surgery should be performed concurrently or sequentially in patients requiring both cataract surgery and Descemet's stripping endothelial keratoplasty.
- Long-term outcomes, particularly endothelial cell counts in the United Kingdom, are infrequent in the literature.

### What this study adds

- To the best of our knowledge, this is the largest prospective data series reporting endothelial cell counts in the United Kingdom.
- Our findings support combined endothelial keratoplasty with cataract surgery in appropriate patients.

## Conflict of interest

The authors declare no conflict of interest.

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