Conflict of interest

The authors declare no conflict of interest.

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Sir,
Graft decentering in DSAEK: a risk factor for immune reactions?

Lamellar keratoplasties have extended the range of corneal transplantation since the late 1990s. Descemet's stripping (automated) endothelial keratoplasty (DSAEK/DSEK) as well as Descemet membrane endothelial keratoplasty (DMEK) are nowadays mostly preferred over penetrating keratoplasty (PK) because of lower refractive errors and a quicker visual rehabilitation,[1,2] and notably because of a lower incidence of graft-rejection episodes compared with standard penetrating keratoplasties.[3] Currently, there are only limited long-term data on rejection rates following DSAEK and DMEK. Price *et al*[2] confirmed immunologic graft rejections as the major cause for graft failure in DSAEK and PK. The risk of immune responses following DMEK is ~15 times lower than in PK.[4,5] For this reason, we hypothesize that the graft stroma is involved in triggering immune rejections. We herein examine whether graft diameter and in particular, the graft placement within the anterior eye chamber, represent risk factors for graft rejections following DSAEK.

Medical records of DSAEK patients with surgeries between 2008 and 2011 were reviewed for allograft rejections. Graft rejection was diagnosed in case of:

- presence of keratic leukocyte precipitates on the graft, but not on the recipient cornea and/or
- the presence of an endothelial rejection line on the graft and/or
- an increase of cells in the aqueous humour, and/or
- corneal edema not explained by rise of intraocular pressure.

Eyes with peripheral anterior synechiae or other anatomic anterior segment anomalies were excluded to reduce immunologic confounders as much as possible. For the same reason, we also excluded repeat keratoplasties and patients with a history of previous anterior chamber (AC) inflammation (eg, herpetic keratitis) from the start.

In 35 patients (18 females and 17 males) aged between 39 and 89 years (median 71 years), a postoperative anterior segment spectral OCT measurement (SS-1000 Casia, Tomey, Japan) had been recorded (average follow-up for 460 days, see Table 1).

The OCT images were used to define the central and peripheral thickness and position of the graft. Graft centering was determined as the averaged offset to the optical axis in 0°, 45°, and 90° sectional images. A single operator processed the images according to a planimetry protocol (Figure 1). We extracted two spatial features from each image: centration of the graft (absolute of the difference between A and B, 'de-center score') and the maximal thickness of the graft (distance between identification marks 3 *vs* 4 and 6 *vs* 7, respectively; Figure 1c). We averaged these parameters from the three OCT images of the 0°, 45°, and 90° degree meridians for each patient separately. Data were analyzed using the R platform (http://www.r-project.org/). A Cox proportional hazard model was fitted to predict the rejection risk. The investigator was masked for the rejection state to preclude any bias towards our hypothesis. Ethics approval was provided by the local Ethics Service Committee (Research Ethics Committee of Albert-Ludwigs-University Freiburg; Germany; reference: 71/11). Written informed consent was obtained from all patients involved in this study. This study adheres to the tenets of the Declaration of Helsinki.

We observed a total of six immune reactions (Figure 2). Cox regression revealed decentering of the corneal grafts as a highly statistically significant predictor of graft rejections (Table 2, $P = 0.007$, hazard ratio 1.067). The graft thickness seems also to be a predictor, albeit with contradictory correlation: the thicker the peripheral graft section—the higher the risk for a later graft rejection, whereas a thicker central graft diameter is associated with decreased risk for later immune rejections. The covariates 'graft diameter' and 'age at time of surgery' missed statistical significance.

Table 1 Study details

	Median	*Minimum*	*Maximum*	*1st quartile*	*3rd quartile*
Follow-up (days)	460	90	1565	350	550
Age (years)	71	39	89	66	77
Central graft thickness (pixels)	26.04	17.14	40.06	21.94	28.36
Decentering (pixels)	80.33	22.00	188.00	52.00	124.50
Operation techniques	● 1 femtosecondlaser-assisted operation and 34 microkeratome operations; thereof: ● 16 triple-operations and ● 19 standard DSAEK procedures				
Transplant diameters	Two 9.0 mm (one graft with a rejection episode) Two 8.5 mm (one graft with a rejection episode) 31 × 8.0 mm (four rejection episodes)				

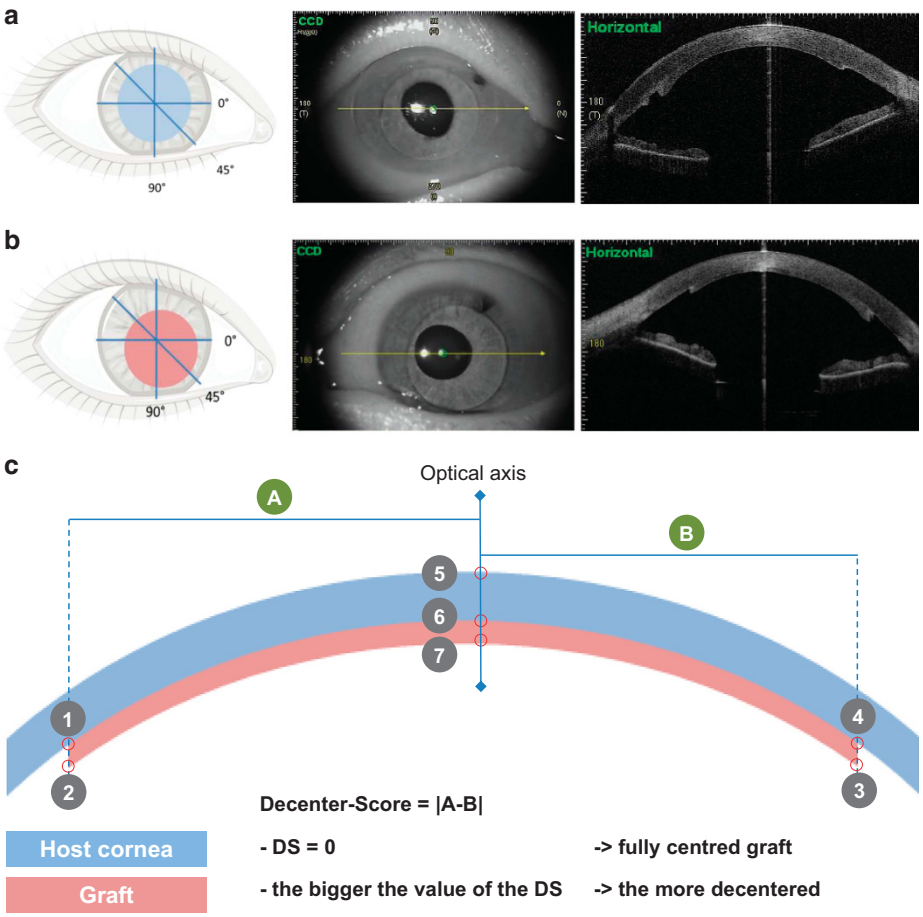

Figure 1 Decenter score. Centering was determined as the average offset to the optical axis in three sectional images (0°, 45°, and 90°. (a, b) Clinical examples of a slight (a) and a more decentered (b) DSAEK graft in two different patients; the second patient (b) developed a later corneal graft rejection. Besides the centering of the graft (average offset in three axes; defined in each axis as the value of the distances between a and b. (c) We also measured the central and peripheral transplant thickness (for the central graft thickness the distance between identification marks 6 *vs* 7 was measured; for the peripheral thickness the distances between marks 1 *vs* 2, respectively 3 *vs* 4 were measured). (c) All measurements were calculated in pixels by using the R platform.

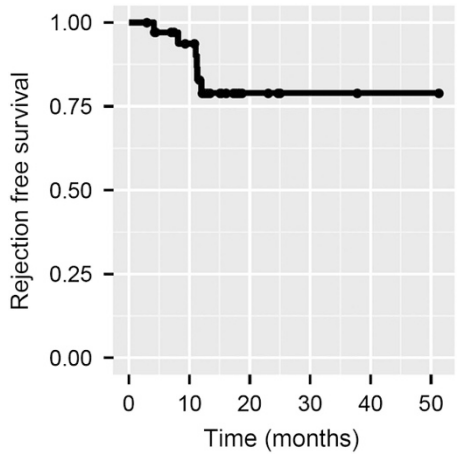

Figure 2 Kaplan–Meier plot. The plot shows the estimation of rejection-free survival after DSAEK determined with the Kaplan–Meier method ($n = 35$). All six rejections occurred within 1 year after transplantation.

Table 2 Cox regression model with the end point graft rejection

	Hazard ratio (HR)	*Standard error of the coefficient*	P
Decentering	1.067	0.0245	0.007
Peripheral graft thickness	1.216	0.1002	0.051
Central graft thickness	0.498	0.3143	0.027
Age	1.018	0.0553	0.75
Graft diameter	0.273	1.3986	0.35

Conclusions

Our data suggest that the DSAEK stroma may have a causative role in generating immune responses, that is, rejections seem to be favored by graft proximity to the AC angle. It may contribute to the migration of donor-derived antigen presenting cells (APCs) into the recipient's lymphatics (direct pathway). Alternatively, access to the graft of recipient APCs may be promoted by decentered graft positioning (indirect pathway).

Interestingly, cells infiltrating the anterior chamber (AC) belong to the innate immune system: the cellular infiltrate contains mainly monocytes and cells differentiating into APCs, that is, mainly macrophages.[6] These cells can also be found in the cornea—but as an intact Descemet membrane does not allow any cellular transmigration, it is widely believed, that cells in AC are recruited through iris vessels and ciliary body in the context of a breakdown of the immune privilege. Cells in the corneal stroma (eg, after DSAEK) or the exchange of allo-antigens through APCs coming from the AC and/or the AC angle (especially after DMEK, where there are no donor stromal APCs present) consequently must be crucial for the generation of an immune response.

In summary, the data may indicate an active role of donor-derived immune cells in the rejection process. Major limitation of our work is the size of the cohort; the importance of graft centration in DSAEK to minimize the risk for graft rejection therefore needs to be confirmed in a larger clinical setting.

Conflict of interest

The authors declare no conflict of interest.

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Sir,

Patient satisfaction in the Peterborough community specialist optometrist in glaucoma shared-care scheme

We note with interest the results published by Levy and Booth[1] on 'Patient satisfaction with Peninsula Optometry Community Glaucoma Scheme'. We have significant experience with our own community optometrist glaucoma scheme[2] and have recently collected satisfaction data.

Questionnaires were sent to 120 patients attending the community scheme and 120 patients in the hospital glaucoma service. Patients were questioned about the clinician they saw, and their satisfaction with the service overall (Table 1). Response rate was 57%.

Patients in the community scheme were asked whether they would like to continue with the scheme, whereas