Sir,
The incidence of diabetic retinopathy requiring treatment is also low in the under 90 age group

The paper by Tye *et al*[1] looking at the incidence of diabetic retinopathy that needs treatment in the over-90s appears to imply that the detection rate of diabetic retinopathy, which might need treatment and actually goes on to treatment, in this group is unacceptably low; however, the figures are similarly low in the whole annual photographic diabetic screening program. The sample size of only 179 might give a misleading picture. In the reported study, the incidence was 2/179 (1.12%); one of these had laser, thus bringing the incidence rate down to 0.56%. In the Newcastle and North of Tyne screening program, 43 571 diabetics were screened between April 2014 and March 2015 leading to 120 R3A (active proliferative diabetic retinopathy) and 814 R2/M1 (severe non-proliferative and maculopathy) referrals, which is at a rate of 2.14%. Incidentally, the number sent for a slit lamp clinic, as they were un-gradable on photography, was 1134 (2.60%) and an additional 13% of diabetics on the single-collated register did not attend for screening. Of those who were un-gradable, if the incidence of referable diabetic retinopathy was the same as in the other screened patients at 2.14%, then only 24 patients would be expected to have referable retinopathy. Of the 934 who were referred to hospital, <200 were treated although on follow-up some more may eventually be treated; 200/43 571 gives an incidence rate of 0.46%, which was actually less than in the over-90 cohort reported.

The screening service is effective at detecting retinopathy that might need treatment and preventing blindness,[2] however at increasing cost. A systematic review in 2014 looked at the evidence for extending the screening interval beyond 1 year in the UK and did not find robust evidence to support this due to the lack of randomized trials of such an approach.[3] What it did not seem to address is what annual incidence rate justifies screening annually and based on that if any group could have less frequent screening or no screening at all. This is a cost–benefit argument where decisions need to be made on what level of risk of missing sight-threatening retinopathy is acceptable.

Conflict of interest

The authors declare no conflict of interest.

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Sir,
The translaminar pressure difference as an index for neurotoxic burden in the anterior part of the optic nerve

We read with great interest the review recently published in *Eye* by Siaudvytyte *et al*[1] and would like to comment while presenting an additional viewpoint.

Siaudvytyte *et al*[1] mentioned a study by Killer *et al*[2] on normal-tension glaucoma (NTG) patients who showed a decreased cerebrospinal fluid (CSF) flow between the basal cisterns and the subarachnoid space surrounding the optic nerve (ON), and proposed that this could explain why patients with NTG have lower intracranial pressure (ICP). Killer *et al*[2] concluded that the disturbance of CSF dynamics in this specific CSF pathway can be explained by ON compartmentation. It is not fully clear to us how this could explain why NTG patients have lower ICP.

Siaudvytyte *et al*[1] further noted that a higher translaminar pressure difference (TPD), that is, the difference of intraocular pressure (IOP) minus ICP, may lead to abnormal function and ON damage due to deformation of the lamina cribrosa, changes in axonal transport, altered blood flow, or a combination of them all. In view of many arguments against the hypothesis that the translaminar imbalance between the IOP and ICP caused by low ICP could have a role in the pathogenesis of glaucoma through a higher TPD acting across the optic nerve head,[3] we present an alternative viewpoint according to which the imbalance between IOP and ICP may reflect the imbalance between production and clearance of neurotoxins in the anterior part of the ON. Indeed, previous findings at least suggest that high IOP may generate inflammatory proteins and neurotoxins, such as amyloid-β (Aβ) that is a hallmark protein in Alzheimer's disease, that could then be cleared via the CSF.[4] Our hypothesis postulates that a higher concentration of neurotoxins may be the physio-pathological mechanism causing axonal damage in NTG as well as in high-tension glaucoma. In NTG, diminished clearance of Aβ from the ON may predominate as a result of a general decline in CSF turnover caused by decreased CSF production (and thus lower ICP).[5] In high-tension glaucoma, IOP-induced Aβ generation may predominate and even a mild decline in general CSF flow may result in glaucomatous ON damage. From this point of view, the TPD, calculated as the difference of IOP minus ICP, may be considered as an index for neurotoxic burden in the anterior part of the ON.

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.