Introduction:
Corneal transplantation has been in routine practice to treat corneal endothelial diseases like Bullous Keratopathy, in which either the whole cornea or the partial cornea (the endothelium alone) is transplanted from the cadaver donor to the recipient with the endothelial disease [1]. In whole corneal or partial corneal transplant one cadaver donor’s cornea can be used to treat one recipient cornea only, which leads to a huge global shortage of donor corneas [2]. At this juncture Yokoo et al isolated and expanded corneal endothelial precursors using the sphere forming assay in vitro [3] and demonstrated the in vivo transplantation of these corneal endothelial precursors in a rabbit model of bullous keratopathy [4]. Following this, we studied the transportation of cadaver donor derived corneal endothelial tissue (CET) from human cadaver donors in a thermoreversible gelation polymer (TGP) (4) based transportation cocktail without cool preservation and demonstrated the viability of human corneal endothelial precursor (HCEP) cells isolated from these CETs even after 72 hours of transportation without cool preservation [5]. This was done to suit the conditions existing in developing nations like India where hospitals might be located far from eye banks and maintaining cold chain preservation is relatively difficult. Further, these HCEPs were expanded in vitro using a polymer based expansion protocol [5]. This was the first step in the realisation of the dream of ‘Eye for eyes’ in a manner suitable for Indian conditions.

Hurdle faced in Clinical Translation and its solution:
After HCEP transplantation, the eye balls need to be fixed 24-36 hours facing down, to facilitate the gravity-assisted settling of the cells injected into the anterior chamber on to the endothelium which is possible in animals but difficult in humans. To overcome this hurdle, we used the nanocomposite gel sheet (D25-NC gel sheet) developed by Haraguchi [6] as a supporting material to support the HCEP cells during transplantation and the HCEP transplantation using this NC gel sheet was successfully demonstrated in a cadaver bovine’s eye cornea [7]. Thus the second step in the ‘Eye for eyes’ mission was accomplished.

The Pilot Clinical study:
The study was undertaken in three patients, two suffering from bullous keratopathy and one patient with congenital corneal dystrophy after proper informed consent. The right eye was affected in each patient and the transplantation of HCEP cells were done in these right eyes. 6 x 10^4 HCEP cells were done in these right eyes. 6 x 10^4 HCEP cells isolated from one human cadaver donor cornea were expanded using the polymer based protocol [5] for 26 days. After expansion, the 5x10^5 HCEP cells obtained were divided into three portions. Using the NC gel sheet as supporting material approximately 1.6 x 10^5 HCEP cells suspended in saline were infused into the anterior chamber between the recipient endothelium and the NC gel sheets in each patient. The extension arms of the NC gel sheets were buried under the conjunctiva and sutured. All the three patients were kept under observation and examined using slit lamp at regular intervals. After three days the NC gel sheets were removed done under topical anaesthesia and sent for microscopic examination. There were no HCEP cells attached to the NC gel sheet, removed three days after transplantation. In all the three patients, on post-operative Day 11, the cornea became clear with no evidence of bullae. The patients are under long term follow-up.

Conclusion:
The eye for eyes concept has become a reality by combining the strengths of clinical expertise with cell culture and synthetic material technology in a manner which is easy to reproduce both in the laboratory and clinically.
References:


