CORNEAL TRANSPLANTATION

New approaches suggest bright future

by Sean Henahan in Milan

Although traditional penetrating keratoplasty (PK) is still very useful for full-thickness pathology, selective lamellar keratoplasty is now proving increasingly useful for treating specific diseases, reported Donald Tan MD at the 3rd EUCORNEA Congress.

“Particularly exciting are the new technologies for endothelial reconstruction now on the horizon,” said Dr Tan who chaired a session entitled “Endothelial Cell-Based Therapies for Corneal Reconstruction,” organised by the Asia Cornea Society.

He highlighted the three major advances that have been made recently. First, better donor tissue inserters have been developed for Descemet’s stripping automated endothelial keratoplasty (DSEK).

“These tissue inserters may be similar to IOL shooters in terms of how they are used, or use the glide or pull-through principle, which affords better surgical control of the donor during donor insertion and tissue manipulation in the AC, as compared to standard taco folding techniques. The ultimate goal is to decrease endothelial cell loss, which is currently around 30 per cent and the studies on the most recent inserters such as the EndoGlide, are beginning to show even lower cell loss rates in the region of around 15 per cent cell loss at one year. This represents a major improvement when compared to PK, in which endothelial cell loss is around 40 per cent at one year.”

Second, ultrathin DSAEK donor tissue preparation has been becoming more precise.

“I think we’re reaching the limits of microkeratome technology. The goal is to equal the results of DMEK, which is the most anatomically pure form of endothelial cell replacement. But the greatest challenge in DMEK is transplanting a monolayer of cells without significant endothelial cell damage. Scrolling of the donor tissue remains a problem, as it remains highly challenging to unscroll the donor in the eye without damaging endothelial cells,” he noted.

With that in mind, Dr Tan and his team developed a disposable mat (D-Mat) which, when used with the EndoGlide Ultrathin donor insertion device, offers surgeons enhanced control within the anterior chamber. The D-mat is a flexible, circular, disposable 15-micron-thick polymer mat designed to prevent scrolling of donor Descemet’s membrane, and essentially mimics the stromal layer in a DSAEK donor, thus allowing the newer DSAEK techniques to be utilised in DMEK surgery.

“The D-Mat for DMEK allows us to avoid touching the tissue between stripping and insertion into the anterior chamber,” said Dr Tan.

Instead, the D-Mat is grasped as it is inserted into the EndoGlide donor insertion device. Once inserted into the anterior chamber, the surgeon pulls in just the donor DM tissue, leaving the D-Mat inside the EndoGlide chamber, and this prevents inadvertent donor inversion and also makes it easier to manipulate the donor into position in the AC.

“The next step might involve femtosecond laser technology coupled with real-time, high-resolution corneal imaging, to perform ultrathin DSAEK donor preparation, which may further enhance lamellar corneal surgery, but this is still some way off.”

On the less distant horizon, human endothelial cell culture might soon make endothelial cell reconstruction a reality, reported Dr Choun-Ki Joo of the Catholic University of Korea in Seoul, during the same session.

“A major problem for the surgical treatment of posterior corneal pathology is the current shortage of donor tissue. We are working on a solution for this problem via tissue engineering,” said Dr Joo.

Dr Joo discussed the advances he and his team made in developing a “real artificial cornea.” This was a combination of a scaffold constructed from recombinant human collagen and cultured corneal endothelial cells.

“We need to develop a tissue-engineered layer so that we can move beyond conventionally processed human donor corneas,” Dr Joo concluded.

Dr Jodhibir Mehta, a colleague of Dr Tan’s at the Singapore National Eye Centre, continued on a similar topic with his talk on the effect of nano-printing on human endothelial cell culture. Getting corneal endothelial cells to grow is tricky. Their environment is crucial, he noted.

“Cultured cells are like children. They will observe their environment to see how they should behave, so we have to provide them with the ideal environment in which to proliferate,” said Dr Mehta.

This involves creating a functional reconstruction of corneal endothelium using nano-topography.

“We are able to use soft lithography to create patterns on a nanoscale. This is necessary because endothelial cells are very sensitive to surface morphological cues. They are able to detect the difference between micro- and nano-sized features.” The work has led to endothelial cell cultures with good intercellular interdigitation and tight junctions as well as significant adhesion of the cells to the surface structure.

Dr Ray Tsai, of Taipei Eye Center in Taiwan, raised the question of whether human corneal endothelial cells could be harvested, allowed to undergo ex vivo expansion and then be transplanted back into the human eye. The goal would be to set up a system for human corneal endothelial cell (HCEC) banking, similar to that now in place for whole human corneas.

“Our work has shown that HCECs could be viable transplanted onto a denuded human cornea,” said Dr Tsai, taking us a big step closer to this goal.

In a related presentation Dr Shigeru Kinoshita, of the Kyoto Prefectural University in Japan took this one step further.

“The ultimate goal of surgeries like DSAEK and DMEK is to obtain a high endothelial cell density with good physiological function using donor corneal endothelial cells. But what if we could simply inject cultured endothelial cells into the anterior chamber?”

This is precisely what he and his team have done, albeit in animal models.

“We have injected cultured human corneal endothelium, in combination with ROCK inhibitor, into monkey eyes, with good results,” said Dr Kinoshita.

After injection, a face-down position is maintained for three hours, after which they observed good adhesion of the cells to Descemet’s membrane. Some delegates wondered whether the cells might simply disappear into the trabecular meshwork, but Dr Kinoshita responded that this was not the case. Indeed, human trials are tentatively planned for 2013.