Recurrence of Keratoconus Following Keratoplasty

Nigel H Brookes*, Rachael L Niederer, Doron Hickey, Charles NJ McGhee, Trevor Sherwin

*New Zealand National Eye Bank and Department of Ophthalmology, University of Auckland, Auckland, New Zealand

Over the last 35 years there have been 13 case reports published claiming recurrence of original keratoconus post-keratoplasty...

Ferjo. 1972; Jaffe. 1974; Abelsohn et al., 1980; Offenkand et al., 1983; Rubinfeld et al. 1960; Ecksteins et al., 1995; Vermeyen et al., 1994; Kreuter et al., 1995; Stobbe, 2006; Krevoy et al., 2001; Thalassinis and Ekberg, 2004; Mougeot et al., 2003; Orai et al., 2007

...there have also been 5 retrospective studies published unsuccessfully examining keratoconic regrafts for signs of keratoconus recurrence...

Tuff and Gregory, 1995; Lin et al., 2000; Clonon et al., 2000; Zadok et al., 2005; Toujeau et al., 2006

Our study aimed to examine corneal buttons removed following repeat penetrating keratoplasty for signs of recurrence of keratoconus.

The first study to compare keratoconic grafts clinically and histologically with grafts for other conditions.

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Questions
Does keratoconus recur in the graft?
Is this true keratoconus?
Was there undiagnosed keratoconus in the donor tissue?
Has the keratoconus returned from the recipient tissue?
Can we decipher which cells are responsible?

Corneal buttons and patient history was collected from 27 patients with failed grafts undergoing repeat keratoplasty.

Results - Original Donor
Donor Age: 68.4 ± 14.9 years
Death-Preservation: 17.1 ± 4.0 hours
Cell Density: 2998.1 ± 283.4 cells/mm²

* Pseudophakic bulbar keratopathy, trauma, Fuch's endothelial dystrophy, Congenital glaucoma, herpes simplex, fungal arte
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Results - Recipient

Age at regraft: 56.6 ± 16.3 years

Time since original graft: 14.8 ± 13.2 years

BCVA at regraft: 6/79 (LogMar 1.12 ± 0.43)

Results - Recipient

Ethnicity

Results - Recipient

Regraft Indication

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Experimental Method

- Fixation (2.5% paraformaldehyde)
- Cryosectioning (40μm anteroposterior)
- Immunohistochemical labelling

Experimental Method

- Cathepsin B/G
  Proteolytic enzymes known to be active in the keratocytes/stroma in keratoconus
- Integrin α3β1/Laminin
  Labels epithelial basement membrane (and nerves, scar tissue) to assist interpretation of anterior cornea architecture

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**Experimental Method**
- Microscopy: 215 mounted sections

**Experimental Method**
- Image Analysis: custom software ‘Xsection’
  - deformable grid

**Experiment Method**
- Thickness and labelling intensity profile
  - 174,000 measurements

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Results - Failed Graft

Epithelial Incursions

- 52% Host
- 48% Graft

Results - Failed Graft

% Corneas
Stromal thinning wrt Host

Results - Failed Graft

% Corneas
Epithelial thickening wrt Host

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Results - Failed Graft

% Corneas
Cathepsin B/G Labelling
Stroma > Epithelium

Results - KC v Other

• No significant differences (p>0.05):
  subject age, gender, ethnicity, history of decompensation, number of previous grafts, epithelial incursions, thinning at the GHJ, thinning in the graft itself, epithelial thickening in the graft, or increased stromal labelling of Cathepsin B/G

Results - KC v Other

• Significant differences (p>0.05):
  epithelial thickening at the graft-host junction,
  high astigmatism
  less likely to have a history of high IOP
  less likely to have a history or rejection

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Conclusions

- No recurrence of keratoconus found
- Confirms retrospective studies
- ‘Keratoconus signs’ also found in regrafts of other conditions

Conclusions

- Keratoconus signs masked by graft failure pathology
- Difficult to detect ‘early’ keratoconus even in isolation
- Deinnervated post-keratoplasty cornea is abnormal anyway causing abnormal pathology

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