

# Chapter 4.3

## Long-term survival of 136 and 141 year old geriatric corneal grafts in a single patient, a case report.

submitted

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## **Abstract**

### **Purpose**

We describe the first well documented case of a patient whose donor grafts reached the age of 136 respectively 141 year. The histology of the endothelium of these very old grafts is described.

### **Case Report**

In 1948 and 1955, a young woman received corneal grafts because of keratitis tuberculosa (scrophulosis) from elderly (80 and 92 years old) donors. She had re-grafts done at the age of 82 year. The cumulatively 136 and 141 year old buttons were examined for histology. The 136 year old button had an endothelial cell density of  $964 \pm 212$  cells/mm<sup>2</sup>, severe pleomorphism and polymegathism, a large zone of cornea guttata and pigment deposits in the periphery. The 141 year old button had an endothelial cell density of  $792 \pm 14$  cells/mm<sup>2</sup>. Large cells were observed with moderate signs of pleomorphism and polymegathism. Blood vessel ingrowth was evident in the stroma of both grafts.

### **Discussion**

This case report demonstrates that corneal grafts can become more than 130 years old, nearly two times a normal life span.

Good quality elderly donor corneas may improve the vision of the recipients for 50 years or longer, which questions the validity of setting an upper age limit for cornea donors.

One might debate whether corneas of geriatric donors displaying not any morphologic sign of degeneration are not superior to those of young donors, who do not yet reveal their vulnerability for degeneration. Finally, corneas less elastic and soft, such as geriatric corneas might be preferred for the preparation of corneal lamellae and mushroom shape grafts, an area which is increasingly popular.

The use of good quality geriatric donor corneas could help reduce that deficit in the numbers of acceptable potential donors and thus justify their higher cost. Consequently, the argument of higher discard rates in elderly donors may be reversed. Selecting donor corneas from elderly donors might then be considered as cost effective. Failure to do so would inevitably lead to an increase in the already long lists of patients who are awaiting a corneal transplantation.

### **Key words**

Corneal grafting, graft survival, endothelial cell density, organ culture, donor age, pleomorphism, polymegathism

## Introduction

We describe the first well documented case of a patient, whose donor grafts reached the age of 136 respectively 141 year. The histology of the endothelium of these very old grafts is described.

## Case report

An 82 year old woman was seen in 2004 because of severe visual complaints.

In 1948 and in 1955 penetrating corneal transplants were performed in her right and left eye, respectively, because of corneal opacities caused by keratitis tuberculosa (scrophulosis). The diameters of the donor grafts were 5 mm and 5.5 mm, respectively. Whole globe retrieval with a moist chamber storage at 4 degrees C was the method of preservation. An 80 year old donor was used for her right eye and a 92 year old donor for the left.

Directly after surgery, visual acuity for both eyes was finger counting (0.05). In 1979, visual acuity for her right and left eyes was 0.5 and 1.0. The corneal grafts and visual acuity remained stable for many years. In 1985, a reversible rejection of the graft in the right eye was registered but visual acuity returned to 0.5 after treatment.

In 1989 developing nuclear cataracts were observed. In 1992, visual acuity was 0.1 and 0.5 and grafts were still clear. In 1997, visual acuity had decreased to 0.1 and 0.25 because of dense cataracts and drusen in the maculae.

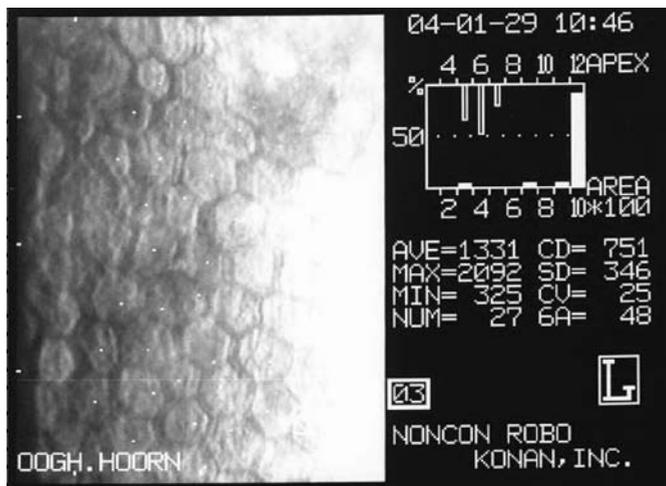
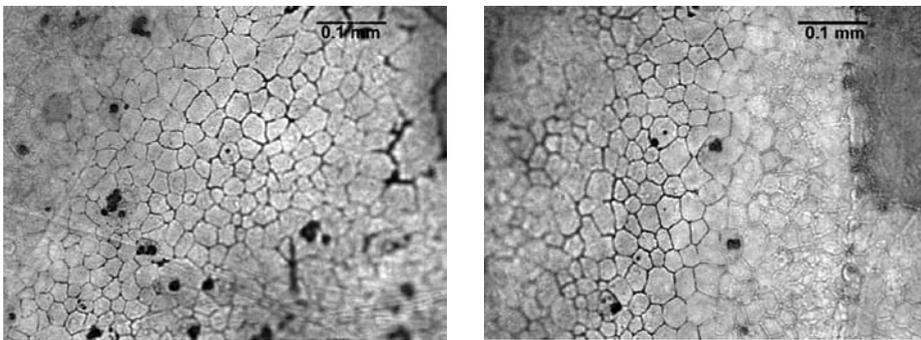


Figure 1: Non contact endothelial microscopy of the left cornea.

In 2004 she was referred to our department. Best corrected visual acuity then was finger counting (FC) for the right eye and 0.1 for the left eye. The corneas showed small diameter, reasonably clear grafts, through which very dense cataracts could be seen.

Within an interval of 5 months, two triple procedures (a penetrating keratoplasty, cataract extraction and lens implantation) were performed for her right and left eye, respectively. A 7.5 mm trephine was used for both corneal grafts.

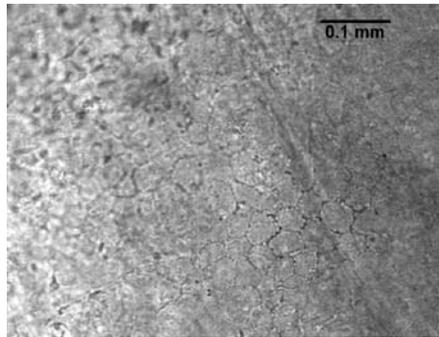
The removed donor buttons were histologically examined after coloring with Alizarin red. At the time of investigation the donor tissue age was 136 year in the right eye and 141 year in the left. Endothelial photographs were taken with a Konan non-contact endothelial microscope. It was not possible to obtain a photograph of the 136 year old graft suitable for counting. The 141 year old corneal graft had a cell count of 700/mm<sup>2</sup> (figure 1).



*Figure 2: The 136 year old cornea button: Histology of the endothelium is shown with the cell density of  $964 \pm 212$  cells/mm<sup>2</sup>. Severe pleomorphism and polymegathism and in the periphery a large zone of cornea guttata with pigment deposits are shown.*

Histology is shown in figures 2 and 3. The 136 year old button had an endothelial cell density of  $964 \pm 212$  cells/mm<sup>2</sup>, measured with the Gunderson method, severe pleomorphism and polymegathism and a large zone of cornea guttata with pigment deposits in the periphery. The 141 year old button had an endothelial cell density  $792 \pm 14$  cells/mm<sup>2</sup>, large diameter cells and moderate signs of pleomorphism and polymegathism.

Since the newer grafts were 2 mm larger in diameter than the first, vascular ingrowth was visible both in the ring of recipient stroma and in de first grafts.



*Figure 3:  
The 141 year old cornea button: Histology of the endothelium  
is shown with a cell density of  $792 \pm 14$  cells/mm<sup>2</sup>*

## Discussion

This case report demonstrates that corneal grafts can become more than 130 year old, nearly two times a normal life span. Good quality elderly donor corneas may improve the vision of the recipients of those grafts for 50 years or longer, which questions the validity of setting an upper age limit for cornea donors.

Beck summarised the published studies between 1979 and 1998, which addressed the effect of donor age on the survival of corneal grafts (Beck et al. 1999). None of those studies reported any significant effect of donor age on the clinical outcome of the transplanted grafts. However, the reviewed studies were mostly uncontrolled and retrospective and no sound conclusions could be made because of confounders, such as recipient age, initial diagnoses for grafting and/or short follow-up periods. Pels confirmed these observations in a group of 1394 patients, receiving corneas from three different age groups with a follow-up of five years (Pels et al. 1999).

Various donor selection procedures are used by eye banks. Data of the Minnesota eye bank (Probst et al. 1997) showed that 50% of the donors, older than 75 years, were suitable for grafting. Unfortunately, the conclusions of this study were based on the analysis of a small number of cases (n=50).

The Amsterdam Cornea Bank recently performed a multivariate logistic regression analysis to identify the factors which significantly affect the suitability of donor corneas for grafting in a total of 14027 cases. Donor age (variation 0-102 years, mean 66 years) was identified as one of the most important factors. There was an inverse correlation between increasing donor age and the proportions which were judged suitable for transplantation

(Pels et al 1999). The probability of accepting donors aged 75 years or older was only 50%. That result is in concordance with the results of an analysis of 9250 donor corneas published earlier (Armitage and Easty 1997) and with the results published by Probst. Others (Gain et al. 2002) found a greater discard rate because of reduced endothelial cell quantity and quality for donors older than 85 years of age (38 %) than for younger donors (20.2%). However, during organ culture, the cell loss in the older group was lower, 4.2%, compared to 9.2% in the younger age group.

Consequently, the four previous reports support the hypothesis that it is possible to have good clinical outcomes with corneas from old donors. However, since there was pre selection on the basis of endothelial cell density and morphology in the recent studies, it was not possible to show a direct relationship between donor age and corneal transplantation outcome.

Analyses of 3173 results in our National Cornea Follow-up Registry revealed no significant differences in graft survival in patients receiving older donor corneas (>85yrs) versus grafts from younger donor age groups. Stratification on indications for grafting also did not reveal any significant differences (unpublished data). Those corneas were all organ cultured, selected and preserved in one cornea bank and transplanted by more than 20 different corneal surgeons in the Netherlands.

Gain reported comparable graft survivals and visual outcome results at 24 months for patients who received grafts from donors who were older than 85 years versus those who received grafts from younger donors when the corneas were allocated without age matching.

There are very few publications on the survival of very old donor tissue. Meyer (Meyer 2000) (Meyer et al. 2001) reported the results of 69 donors whose ages were 95 years or older. This group was compared to 21 young donors, ages younger than 55 years of age at the time of transplantation. All of those grafts were used for young keratoconus recipients. After a follow-up of 8-20 years he reported no significant differences in endothelial cell density and visual acuity after surgery.

Armitage (Armitage et al. 2003) described a bi-exponential decay model for the endothelial cell loss in the postkeratoplasty period and after cataract surgery. According to that model, if the critical cell density is 500 cells/mm<sup>2</sup>, it could be concluded that, with an initial cell density of 2500 cells/mm<sup>2</sup>, the graft could be functioning for at least 30 years.

For the patient cited in this case study, in which two random, non HLA-selected donor corneas in one recipient both survived for more than 4 decades, the graft in the right eye reached an age of 136 years and the graft in the left eye 141 years, surviving 56 and 49 years post keratoplasty. Some possible explanations for their extremely long survival times may have been that:

- Both donor corneas had a high endothelial cell density of excellent quality. However, we may assume that the chance for a good endothelial cell quality as well as a high cell count would be unlikely since both donors had a high age.
- Both eyes had undergone no further surgery in the fifth decade interval between their keratoplasties in 1948 and 1956 and their re-transplantation in 2004.
- The indication for keratoplasty was a stromal keratitis, therefore the recipient's endothelium may have been of rather good quality.
- Both grafts had small diameters (5 and 5.5 mm), which entails that the spreading of endothelial cells from the recipient cornea to the donor site has been proportionally large.

Unfortunately, the selection of suitable older donor corneas is inevitably expensive because of their high discard rates. The rationale and/or evidence for age selection other than working expenses in the donor chain may be revealed by the results of the ongoing Cornea Donor Study in the USA (Cornea Donor Study Group 2005).

The size of the pool of potentially suitable young donors is reducing. On the one hand by the long term wear of contact lenses that may affect the corneal quality (Setela et al. 1998), on the other hand by the increasing popularity of refractive surgery. Thus, the proportion of discarded potential donor corneas in the younger age groups would rise, together with the economic cost of screening for good corneas.

In addition one might debate whether corneas of geriatric donors displaying no morphologic sign of degeneration are not superior to those of young donors, who do not yet reveal their vulnerability for degeneration. Finally, corneas less elastic and soft, such as the geriatric corneas might be preferred for the preparation of corneal lamellae and mushroom shape grafts, an area which is increasingly popular.

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