

1.3 Queratoprótesis y cultivo de células limbares

1.3.1 Resultados a largo plazo de osteo - osteodonto - queratoprótesis

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Purpose:

To analyse the functional and anatomical results of keratoprosthesis using tooth and tibial autograft.

Methods:

We reviewed 227 charts of patients that underwent osteo-keratoprosthesis (OKP) (n=82) or osteo-odonto-keratoprosthesis (OOKP) (n=145) at the Centro de Oftalmología Barraquer. Mean follow-up time was 8.4 years for OOKP and 3.5 years for OKP. Kaplan- Meier survival curves with 95% confidence interval (CI) were calculated for functional success, defined as BCVA >0.05. Anatomical success was defined as retention of the keratoprosthesis lamina. Visual Acuity by Time (VAT) Index with 95% CI was calculated for up to 2 years post- OKP and up to 6 years post-OOKP. Maximum visual acuity ever reached after the last step of the implantation of the keratoprosthesis was used as an indicator for the potential of the retina.

Results:

Based on Kaplan-Meier analyses, 10-year anatomical survival was 66% (CI 57–76) for OOKP and 47% (CI 27– 67) for OKP. Two-year functional survival was 63% (CI 55–71) for OOKP and 49% (CI 37–60) for OKP, and 10-year functional survival was 38% (CI 29–48) for OOKP and 17% (CI 5–28) for OKP. Multivariate analysis showed that neither surgical technique (OOKP or OKP), primary diagnosis nor age had a significant influence on the functional survival. However, a high maximum visual acuity ever reached post-op decreased the risk for functional failure. According to the VAT Index calculations, mean BCVA 2 years after OOKP was 0.33 (CI 0.28–0.41) and after OKP was 0.28 (CI 0.20–0.36).

Conclusion:

Although we found a tendency that OOKP had better anatomical results than OKP, this difference was not statistically significant up to 10 years post-op. Functional results for both techniques were not significantly different at the 2-year follow-up, but at 10 years they were. However, this difference was influenced by the retinal potential and not by the technique itself.

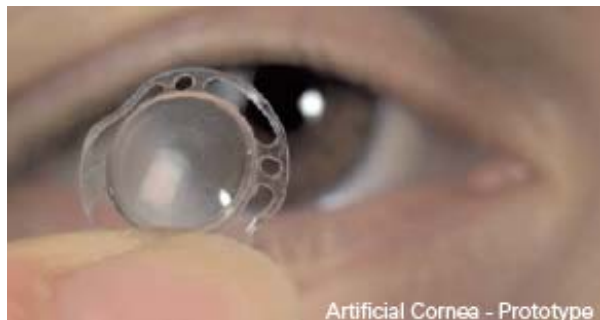
1.3.2 Proyecto Europeo: Córnea artificial

Development of an Artificial Cornea for the Human Eye



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Summary: SME-1 Co-operative Research (all areas of science and technology) Opacification of the cornea of the human eye results in the loss of vision and finally blindness unless corrected by a corneal transplant. In developed countries the standard surgical technology to restore vision is the replacement of the cornea by a human donor cornea in a penetrating keratoplasty.



More than 40.000 keratoplasties per year are performed in Europe and the United States each, with a continuous increase in recent years, and with success rates from more than 90 to less than 50 percent. Low success rates are associated with dry eyes, Herpes keratitis, corneal vascularization, recurring uveitis, acid burns, and traumatic anatomic structures of the anterior eye. The lack of donor corneas resulted in long waiting lists of patients in developed countries, and their non-availability in developing countries in millions of treatable blind people. There is a long history of attempts to replace the human cornea by alloplastic material with either disappointing results, or complicated multiple surgeries associated with severe drawbacks for the patient.

The CORNEA project will combine the invention of a novel corneal transplant by one SME partner with novel flexible ophthalmic polymers developed by a second, the manufacturing technology of a third, and the surgical instruments and technology of two more SME partners. This combined SME know-how will be merged with the surface modification technology to be developed by one RTD partner and the ophthalmic-surgical expertise, and preclinical and clinical research capacities of two more RTD partners. Thus the project CORNEA will combine several cutting-edge technologies in order to achieve a never before available implant design and precision of surgery, and open the chance to regain vision for otherwise blind people. It will give a long-term competitive advantage and profit to the members of the consortium, and secure existing and create new working places.

1.3.3 Cultivo de células limbares

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**Schepens Eye
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Introduction

Any process or disease that disturbs the integrity of the limbal stem cells which is located in the periphery of the cornea reduces the ability of the corneal epithelium to repopulate itself. Inadequate repopulation of the corneal surface may be secondary to a loss in the number of limbal stem cells and/or reduced function of these cells. Limbal stem cell deficiency may occur in a variety of hereditary and acquired corneal diseases. The acquired causes are the most frequent, and includes UV-radiation, acid burns, autoimmune disorders, and infections, including trachoma, which affects about 80 million people worldwide. The clinical symptoms of limbal stem cell deficiency include irritation, epiphora, blepharospasms, photophobia, pain and decreased vision.

Our research team works on various strategies for treating limbal stem cell deficiency. There are many ways to treat limbal stem cell deficiency. The most studied and promising recent technique is the method first described by Pellegrini et al in Lancet in 1997 called ex vivo expansion of limbal epithelial cells. The principle of the method is to transfer human limbal epithelial cells harvested from the patient itself, a living relative, or a cadaver cultured on various substrates in the laboratory onto the eyes of patients suffering from limbal stem cell deficiency.

Current technology

Several clinical studies have demonstrated very promising results of ex vivo expansion of limbal epithelial cells for treating limbal stem cell deficiency. However, there are many disadvantages of the current method: Firstly, the extensiveness of the method has been limited as it requires, in addition to adequate cell culture equipment, knowledge and experience of culturing limbal epithelial cells. Secondly, planning of the treatment has been a logistical nightmare as not all cultures succeed, i.e. no or little growth, alternatively get perceptibly infected (yellow medium/increased turbidity). Under these circumstances, the planned operations are cancelled. An obvious infection may also be noticed as late as on the operation day, which is especially regrettable for patients travelling long distances. Thirdly, lack of sterility control, i.e. the transplants may be infected without any noticeable colour/turbidity change of the medium, resulting in operation of infected tissue.

New technology

The Department of Ophthalmology at Ullevål University Hospital (Oslo, Norway) is the first to demonstrate the feasibility of storing cultured corneal epithelium. A patent application was filed on April 26, 2007 to protect the method of culture, storage, transportation, and microbiological assessment of human limbal epithelial cells (HLECs). The patent application also includes design of a kit for optimizing the process of culture and storage. The novel method has several benefits:

- 1) Storage of cultured corneal epithelium enables tissue to be transported from the laboratory to eye banks and eye departments worldwide. Compared to the surgical procedure, which is considered relatively simple, culture of corneal epithelium is resource-demanding accounting for the imbalance between kinds of treatment and treatment demands.
- 2) The tissue can be preserved at room temperature, which is an asset as the need for a heating cabinet is eliminated, simplifying logistics and reducing costs.
- 3) The production of cultured corneal epithelium at few centre of expertise is cost effective and may improve the quality of corneal tissues. European Union Directives* (on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage, and distribution of human tissues and cells) make strict demands on tissue engineering laboratories and will contribute to the centralisation of tissue production, hence increasing the demand for tissue storage and transportation. (*Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004, Commission Directive 2006/17/EC of 8 February 2006, and Commission Directive 2006/86/EC of 24 October 2006).
- 4) The transplants are eventually stored in a closed container, in contrast to the open culture setting where infection may occur at any time. As the tissue can be stored in at least one week, there is sufficient time to perform microbiological testing. Current insecure methods based on changes of the colour and turbidity of the medium are replaced by more polite and exact diagnostics.
- 5) Tissue storage maintains the original characteristics of the tissue for at least one week, hence offering flexibility in scheduling the transplantation.
- 6) Possibly reduced need for immunosuppression (reduced nuclear factor kB activity). However, further studies are warranted.

Future perspectives

The advantages of storing limbal epithelial cells, apply equally to other cultured cell types. Hence, we are currently working on storage and transportation of conjunctival epithelial cells based on our experiences from limbal epithelial cells. In the near future we plan to expand to new cell types. Simultaneously, we will work on improving the culture and storage protocols for treating limbal stem cell deficiency.

Merits for the research group

Since 2007 the original project, led by Torstein Lyberg, has resulted in 20 publications, two patent applications, extensive funds, publicity (EuroNews, which is the largest news channel in Europe, among others), extensive international collaboration, and three research awards last year.