Bowman layer transplantation for treatment of corneal contour deformations

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To determine whether corneal stabilization can be achieved using a BL onlay and minimize the risk of complications which occur during more invasive techniques. This would also be a technically less demanding surgical procedure.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Anterior eye structural change, deposit and degeneration
Study type	Interventional

Summary

ID

NL-OMON55641

Source
ToetsingOnline

Brief title
BL transplantation

Condition

- Anterior eye structural change, deposit and degeneration
- Eye therapeutic procedures

Synonym
Corneal contour deformation / corneal disease

Research involving
Human

Sponsors and support

Primary sponsor: Melles Hoornvlieskliniek Rotterdam
Source(s) of monetary or material Support: Melles Hoornvlieskliniek Rotterdam (MHR).

Intervention

Keyword: Bowman layer, Cornal contour deformations, Keratoconus

Outcome measures

Primary outcome

- Corneal curvature and pachymetry (thickness of the cornea) measured using a Pentacam apparatus and an Anterior Segment Optical Coherence Tomography apparatus (AS-OCT) (standard procedures).

Secondary outcome

- Endothelial cell density, as assessed by specular microscopy and confocal microscopy;

- visual acuity, measured by the optometrist using a Snellen chart (standard procedure);

- number of complications.

Study description

Background summary

Full-thickness keratoplasty is often complicated by high astigmatism, suture-related problems, ineffective wound healing, and allograft rejection. Fewer complications may be expected when only the diseased anterior or posterior corneal layers are replaced by donor tissue, or when the cornea is reinforced by addition of healthy tissue.

Recently, a new approach has been used for treating advanced progressive keratoconus by implanting only an isolated Bowman layer (BL) graft in the recipient*s mid-stromal pocket to remodel the corneal curvature. The obtained reduction of ectasia was stable for at least up to 2 years after the intervention. Advantage of transplanting only BL is that this is an acellular corneal structure and the risk of allograft rejection is negligible. Even though this technique proved to have a low risks of intraoperative complications, inserting the BL transplant into a very thin corneal (advanced

keratoconus) is a challenging manoeuvre. In this study we want to investigate a possibility to use a less invasive technique for implanting the BL, with the aim to stabilize corneal contour deformations by fixating the graft onto the cornea. The advantage of this technique is that the ocular integrity is largely preserved with onlay BL graft positioning and, therefore, posterior scarring related to inflammation is avoided.

Study objective

To determine whether corneal stabilization can be achieved using a BL onlay and minimize the risk of complications which occur during more invasive techniques. This would also be a technically less demanding surgical procedure.

Study design

Cohort study.

44 consenting adult patients with corneal contour deformations will be included.

All patients will undergo one experimental procedure in one eye.

Before the procedure, and at 1 day, 1 week, 1 month, 3 months, 6 months, 9 months, and 12 months, all eyes will be evaluated using slit-lamp biomicroscopy, Pentacam imaging, specular microscopy, optical coherence tomography (OCT), and confocal microscopy. Best corrected visual acuity and complications will be documented at all examinations.

If necessary, patients will undergo an additional photorefractive keratectomy (PRK) to correct corneal surface irregularities.

In the event of procedure failure, standard BL transplantation will serve as a back-up procedure for given eye.

Intervention

With the patient under local anesthesia, the corneal epithelium is removed. The Bowman graft is immersed in 70% ethanol for 30 seconds to remove remnant cellular material, thoroughly rinsed with balanced salt solution, and stained with trypan blue (VisionBlue; DORC International BV). The Bowman graft is then carefully positioned onto the host cornea, unfolded, and centered, using a rigid contact lens to transfer the tissue. Tissue is fixated spontaneously by dehydration and, if needed, extra donor tissue layers could be applied to further stabilize the cornea. A soft contact lens is positioned onto the eye at termination of the surgery. Postoperative medication includes topical chloramphenicol 0.5% (6 drops daily for one week, then reduce to 2 drops daily

for an extra week and then stop) and dexamethasone 0.1% (4 drops daily for 1 month and then stop) and switch to fluorometholone 0.1% (4 drops daily up to 3 months and then taper by 1 drop every 3 months). Stop after 1 year.
The corneal epithelial wound healing process (a natural response of regenerating tissue) will re-establish the integrity of the eye surface.

PRK is an established procedure and will be performed (if indicated) according to standard protocol (Vestergaard 2014).

Study burden and risks

Benefits are that corneal contour deformations could be treated and stabilised using minimally invasive procedure thereby avoiding the need of an intraocular intervention, avoiding problems related to cell-containing grafts (rejection, failure, detachments). The greatest advantage of this novel technique is the fact that it only involves topical or local anaesthesia and can be performed rather fast (compared to conventional transplants). Compared to the mid-stromal BL transplantation, this novel experimental technique may cause less of a burden for the patient, because the ocular integrity is largely preserved. The restoration of the scraped epithelial cell layer is fast, leading to a possible faster post-treatment recovery. Also, the recovery of the visual acuity is expected to be quicker than with all currently available keratoplasty techniques, since it is basically an 'extra-ocular' procedure with limited effect on the eye's function. The risk of damaging the structure of the cornea during procedure is very low because this is an extraocular procedure; therefore there is no manipulation inside the eye.

Also, there is potential risk that epithelial cells may incompletely cover the transplant. In case that this experimental *onlay* Bowman layer transplant procedure does not give the desired results, the patient would need to undergo a second operation, namely having a second Bowman Layer transplant inserted inside a mid-stromal corneal pocket. We do not expect any negative effects of having both transplants in-situ. However, re-operation poses a burden on patients.

With PRK there may be low risk of damaging the cornea, although probably smaller than normally, as in this case the laser treatment will probably not reach the cornea of the patient because it is sheltered by the transplant(s).

Understanding the limitations and uncertainties of this new transplantation procedure, we believe that benefits will outweigh the risks. Compared to more invasive mid-stromal Bowman Layer transplantation, the novel experimental technique may cause less of a burden for the patient, because the ocular integrity is largely preserved. Also, the restoration of the scraped epithelial cell layer is fast, leading to a possible faster post-treatment recovery.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Progressive keratoconus, or corneal contour deformation
- Indication for a corneal transplant or surgery
- 18 years and older
- Agree to return for 1 day, 1 week , 1 month, 3 months, 6 months, 9 months, and 12 months post-procedure follow-up visits

Exclusion criteria

- Concomitant ocular disease and/or a contraindication for this type of treatment (e.g. inflammation of the eye, uveitis etc), or any type of circumstances that may be expected to adversely affect the efficacy of the surgery.

- Excluded from the study are patients with a severe corneal scarring, e.g. hydrops or contact lens induced opacifications
- Severe diabetes
- Unable to clearly understand the language used in the clinic (Dutch or English)
- Inability to give informed consent for any reason
- Pregnant or nursing

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-08-2017
Enrollment:	44
Type:	Actual

Ethics review

Approved WMO

Date:	17-07-2017
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	16-06-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	21-01-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	19-05-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	13-05-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL60780.098.17