



Limbal stem cell transplantation



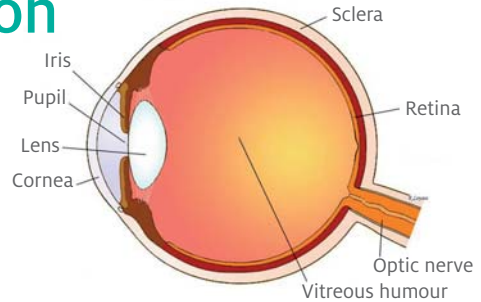
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Dear patient,

Welcome to the ophthalmology department of the Antwerp University Hospital. You will have a limbal stem cell transplantation in our centre.

This leaflet complements the explanation you received from your ophthalmologist and nursing staff during the consultation. As your follow-up appointments are also registered here, please make sure to bring the leaflet along to the hospital.

1. Eye construction and function



1.1 The eye

The eye is spherical and consists of the white of the eye or the 'sclera'. The retina is located on the inside. In front of the eye is the transparent cornea. Behind the cornea is the coloured iris, positioned in front of the lens and covering it, except for the pupil. This lens is normally clear and transparent.

The cornea and the lens disperse the incoming rays of light, so that the image ends up on the retina. This retina is located at the very back of the eyeball. The eyeball is on average 23,7 mm long. The optic nerve communicates the stimuli from the retina to the brain, where the image is finally perceived. If the image is directed precisely onto the retina you do not need to wear glasses. If the image falls just before or behind the retina, this deviation is corrected with glasses.

1.2 The limbus and LSCD

The limbus is the junction between the cornea (clear part of the eye) and the sclera (white part of the eye). The limbus is the site of stem cells for the cornea. These cells have the capacity to keep on dividing throughout a person's lifetime, replenishing cells that are being sloughed off. The limbal stem cells are few in number and can be damaged by a number of different disease processes, chemical injury, thermal burns, extended contact lens wear, etc: Limbal Stem Cell Deficiency or LSCD.

1.2 How can LSCD be treated?

If you have LSCD, conventional treatments like corneal transplants may not work as well, since you are not able to renew the outer layer (the epithelium) of your new cornea using your own limbal stem cells. This might lead to repeated corneal melting or perforation.

Current available treatment modalities include lubricating drops in cases of mild LSCD, or a surgical procedure in cases of severe LSCD where a piece of donor limbus is grafted onto the eye. Limbal grafts have a high rate of rejection. This is primarily because when limbal tissue is grafted onto the eye, unlike the cornea, it is highly vascularized (this means that it has a lot of blood vessels) and hence the tissue that is transplanted also contains a lot of other cells like white blood cells, that can cause an immune reaction (this means your body identifies them as 'foreign' and tries to get rid of them).

This new treatment strategy involves taking a small piece of the donor limbus and growing only the limbal stem cells from the biopsy onto an amniotic membrane. This membrane, along with the stem cells is transplanted onto the eye and covered with a bandage contact lens. The donor stem cells repopulate your cornea as well as secrete chemicals that attract stem cells from other parts of your body to help restore the outer layer of your cornea.

Once the epithelium of the cornea is restored, your vision may improve, but if you have had previous surgeries then it is possible that you might require further surgery to your eye before improvement of your vision is achieved. The stem cells act as a reserve and help repopulate the outer layer of a corneal graft that you might receive later on thereby improving the graft life.

2. Description of the research

2.1 Taking the biopsy

The proposed treatment is part of a clinical research protocol, the aim of which is to repopulate your cornea with limbal stem cells. In cases where one of your eyes is affected and the other has a normal population of stem cells, an “autologous cultivated limbal stem cell transplant” will be done. This means that a tiny biopsy is removed from the limbus of your good eye and sent to the laboratory. There are a few risks associated with taking the biopsy, namely: pain, bleeding, infection and a very low risk of possible induction of limbal stem cell deficiency in this eye.

In cases where either, both your eyes are affected, or you have only one eye, an allogenic transplant will be performed. This means the limbal biopsy will be taken from either the limbus of a close relative or a donor eye from the cornea bank. The same procedure will be performed and you will receive an “allogenic cultivated limbal stem cell transplant”.

2.2 Growing the Stem Cells

In the laboratory, your stem cells from the biopsy will be stimulated to grow, under optimal growth conditions, onto an amniotic membrane (the innermost membrane of the placenta which is obtained at the time of C-section, screened and processed by the eye bank UZA, for ophthalmological purposes). It will take approximately 2 to 3 weeks before your stem cells have expanded and formed a thin layer on the amniotic membrane, ready for transplantation.

2.3 The surgery

A surgery will be scheduled depending on your case you will receive either general or local anesthesia. When used properly, local anesthetics are safe and have few major side effects. However, in high doses local anesthetics can have toxic effects caused by their being absorbed through the bloodstream into the rest of the body (systemic toxicity). This may significantly affect your breathing, heartbeat, blood pressure, and other body functions. Because of these potential toxic effects, equipment for emergency care will be immediately available when local anesthetics are used. In case general anesthesia (GA) is used; you will be assessed by an anesthesiologist a day before to ensure that you are fit to receive GA.

There are a few side effects of GA, most of them are minor and include sore throat or irritation of the throat and voice box. There are a few potentially serious side effects of GA which include aspiration pneumonia, changes in blood pressure or heart rate or rhythm, heart attack, stroke, malignant hyperthermia. Death or serious illness or injury due solely to anesthesia is very rare.

During the surgery, the cultivated stem cells along with the amniotic membrane will be transplanted onto your eye. You will be asked to wear a bandage contact lens in order to protect the transplanted cells for a few days. There are some risks that may be associated with the surgery, including bleeding, infection, corneal scarring and perforation. There is a small possibility that glaucoma may develop after the surgery. Other potential risks involve infection transmitted from donor cells.

2.4 After the surgery

You will be observed closely by your doctor following the surgery and will receive some drops and will be given directions on how to instill them into your eye. If you are experiencing pain, light sensitivity and decreasing vision in the days following surgery, please inform your doctor.

Follow-up examinations after completion of the treatment will be performed on a weekly basis for the first month. You will be given a schedule for further follow-up visits by your doctor.

If you are a patient that receives an “allogenic cultivated limbal stem cell transplant”, your doctor may decide to prescribe you with immunosuppressant drugs. These medicines are prescribed either topically (as drops to put in your eye) or systemically (oral tablets), in order to reduce the risk of your immune system rejecting the transplanted cells.

3. Special Tests

3.1 Impression Cytology

There are a number of special tests that will have to be performed in order to monitor your eye before and after the surgery. One of these tests is called “Impression Cytology”. This test will be performed under topical anesthesia (eye drops that will numb the surface of your eye). You will be asked to keep your eyes open while a special sterile membrane is gently pressed onto your cornea and will lift off a superficial layer of cells. These cells can then be analyzed using special staining techniques in the laboratory. This gives us important information regarding the ongoing disease process and helps us monitor your treatment accordingly.

It is a relatively safe test, but there is a low risk of infection or damage to the surface of the eye. In case you have received an allogenic cultivated stem cell transplant, one of these samples will be sent for DNA analysis. Once donor DNA is no longer detected on the surface of your eye, and your eye has managed to grow its own cells, the treatment to suppress your immune system, can be stopped.

3.2 Ocular Confocal Scanning

Another test that will be performed is “Ocular Confocal Scanning”. This is a non contact test (which means that the machine will not be in contact with the surface of your eye at any point) that is performed with a special machine called a “Confoscan”. You will be asked to rest your chin on a special stand in the machine and to look straight ahead without blinking, while the machine takes a series of photographs of the different layers of your cornea.

This test also gives us important information regarding the surface of your eye. Since it is a non contact test, it is very safe, but since you are asked to keep your eyes open it is possible that you may have mild irritation, but this should be temporary.

3.3 Schirmer's test

One of the other tests to be performed is called the "Schirmer's test". This test is done to test whether or not your eye is able to produce enough tears to keep the surface of your eye moist and in optimal condition for the transplanted stem cells to grow and survive. Again this test will be performed after using drops to numb the surface of your eye. A strip of special sterile paper will be put inside your lower eyelid and the length of paper wetted by your tears is recorded.

This test is commonly performed and is very safe, although there may be a very low risk of infection or damage to the surface of your eye. If the value is less than 5mm, you might need insertion of "punctal plugs" at the time of surgery. These are tiny silicone stoppers that are inserted into the small ducts that drain the tears from your eyes into your nose. These plugs are not permanent and can easily be removed if required. If they have been inserted properly there is generally no problems associated with them, but improperly positioned punctal plugs may cause irritation. There is also a low risk of infection.

4. Medication

4.1 Autologous serum drops

One of the drops that you will be asked to regularly instill in your eye/s, is called “autologous serum drops”. These drops are prepared from the clear part of your blood. Briefly, about 100mls of blood will be drawn from your arm and sent to the pharmacy where the serum (clear part of your blood) will be separated and stored in 2.5ml bottles in the freezer. After the surgery, you will be instructed on how often you will require instilling these drops into your eye/s.

This autologous serum provides nourishment for the transplanted cells and promotes good cell growth. Since these drops are preservative free, you will be required to thaw a new bottle each day and throw away any unused serum after 24hours. This is done to prevent contamination; there is a risk of infection if proper instructions are not followed. Since handling blood products carry an increased risk of transmitting infections to the people handling your blood, your blood will be screened for HIV, Hepatitis B and C before blood is taken to prepare autologous serum drops as greater precautions need to be taken in such cases.

4.2 Immunosuppression

In case you are scheduled to receive an allogenic transplant from a living related donor, both you and the donor will be required to give blood samples which can be tested for compatibility. If there is a high degree of compatibility, it is possible that you may not be required to take drugs to suppress your immunity (body’s natural defense system).

In cases where there is good matching of donor tissue your body will not perceive it as “foreign” or mount an “immune response” against this transplanted tissue. If the donor is not well matched, in order to prevent an “immune response” and eventual rejection of the transplant, drugs will be given to suppress your immune system. These drugs are called immunosuppressants.

Pretreatment assessment

Since immunosuppression means that your body’s normal defense mechanisms will be reduced, before you can receive this treatment, you will have to undergo a series of tests including a chest X ray, blood and urine tests for signs of infection and a complete physical examination to insure that you are in good health. A blood test for HIV must be performed or else immunosuppression may lead to disastrous consequences in the unlikely event that you have contracted this disease and your doctor is unaware of your condition. If you are receiving a transplant from a cadaveric donor you will have to undergo treatment with immunosuppressants.

The department of nephrology, UZA, routinely performs kidney transplants and has great experience in dealing with transplant patients receiving immunosuppressive treatment; hence they will be monitoring you closely while you are receiving this treatment.

Side effects

These drugs have the potential to cause side effects including, in the case of Cyclosporin A (a drug often prescribed for immunosuppression in transplant patients), gum hyperplasia, convulsions, peptic ulcers, pancreatitis, fever, vomiting, diarrhea, confusion, breathing difficulties,

numbness and tingling, pruritus, high blood pressure, potassium retention and possibly hyperkalemia, kidney and liver dysfunction (nephrotoxicity & hepatotoxicity), and an increased vulnerability to opportunistic fungal and viral infections. Since you will be carefully and closely monitored it is unlikely that any of these adverse effects will be long lasting or permanent.

Prednisolone (a drug also often prescribed in transplant patients), if prescribed to you will only be for a short while in order to keep the possible side effects to a minimum. The major side effects include high blood glucose levels, especially in patients who already have diabetes mellitus or are on other medications that increase blood glucose levels, depression, mania, unusual fatigue or tiredness, blurred vision, abdominal pain, peptic ulcer, infections, painful hip or shoulder, osteoporosis, acne breakouts, insomnia, reduced libido, weight gain, stretch marks, facial swelling, nervousness, rash, increased appetite and hyperactivity.

4.3 Pregnancy and lactation

In the case of pregnant women, these drugs can cross the placenta and harm your developing fetus. Hence if you are of childbearing age, it is necessary to use contraception during the course of this immunosuppressive treatment. A pregnancy test will be performed just prior to starting treatment. If you are a lactating mother, you must stop breastfeeding as whilst you are taking these medicines, they are also being secreted into your breast milk and could adversely affect your child.

5. Goal of a limbal stem cell transplantation

The main goal is to investigate whether limbal stem cells that have been expanded on the amniotic membrane and then transplanted into eyes with LSCD, are able to effectively repopulate the cornea and prevent repeated corneal graft rejection.

5.1 Expected benefits

For the patients eligible to receive cultivated limbal stem cell transplants, a positive effect can lead to improved visual acuity and help prevent corneal graft rejection following future corneal transplants. In the event that your corneal surface is compromised you will be scheduled to receive a corneal graft. We hope research can teach us more about treating LSCD. This might enable us to improve the treatment and hence help other patients with LSCD in the future. However, nobody can predict whether you will directly experience the benefit of a limbal stem cell transplantation.

5.2 Contact

In case of problems or questions, please contact your physician for more information.

Antwerp University Hospital

- Dr. Carina Koppen, Telephone: +32 (0)3 821 48 06
- Dr. Inge Leysen, Telephone: +32 (0)3 821 48 10

6. For your doctor

All possible information about your health can help us to operate on you under the very best circumstances. For that reason, please have your doctor fill out this section.

Doctor Information

.....

.....

.....

List of present medication

	Medicine	x/day
1/
2/
3/
4/
5/
6/

7. Outpatient treatment

We want to make your stay at the UZA as pleasant and smooth as possible. However a waiting time may be caused by serious or difficult and lengthy interventions specific to a university hospital. We thank you in advance for your understanding.

7.1 Date of the biopsy

Biopsy on your right eye on: / /

Biopsy on your left eye on: / /

7.2 Hospital admission planning

To find out the precise date and time that you will be admitted to the hospital, you can telephone on..... / / and / / **between 2 p.m. and 4 p.m., tel. 03 821 48 41.**

7.3 Registration and check-in at reception office

Follow **route 163** to the **day treatment hospital** on the **3rd floor**. You report and sign in there. After surgery we will bring you to the day hospital (route 78).

7.4 Anaesthetic

Local anaesthesia

- › Food and drink permitted (a light meal is permissible).
- › Take your medicine as you usually do. You are allowed to continue using blood thinners. Your ophthalmologist will provide you more information.

General anaesthesia

› **Preoperative anaesthesia consultation**

Before you undergo surgery, please visit the anaesthesiologist on / / to hours. You may eat and drink before this consultation. The consultation is located on route

- › Do not eat or drink from midnight onwards on the day before your operation, or follow the advice of the anaesthetist. Diabetes patients must not use their anti-diabetic medication.

7.5 General tips

a) What to bring when admitted to hospital?

- Sufficient medication for the whole day
- SIS and UZA-cards (SIS-Social Information System)
- This information brochure

b) Points to note

- Do not bring money or jewels.
- Do not use make-up.
- Report to the nursing staff if you have been seriously ill since your last visit.
- You do not need to change your clothing before the operation. A catheter will be inserted into your arm. For this reason, please dress in comfortable clothing.
- The visiting hours are ongoing.

c) Can I drive after surgery?

You are **not** permitted to drive a vehicle after surgery. Make sure that someone will be there to pick you up or take public transportation.

8. Short stay hospitalisation

We want to make your stay at the UZA as pleasant and smooth as possible. However a waiting time may be caused by serious or difficult and lengthy interventions specific to a university hospital. We thank you in advance for your understanding.

8.1 Surgery date

Biopsy on your right eye on: /..... /.....

Biopsy on your left eye on: /..... /.....

8.2 Hospital admission planning

To find out the precise date and time that you will be admitted to the hospital, you can telephone on /..... /..... and /..... /..... **between 2 p.m. and 4 p.m., tel. 03 821 48 41.**

8.3 Registration and check-in at reception office

Report to the reception desk in the entrance hall.

8.4 General Anaesthetic

> Preoperative anaesthesia consultation

Before you undergo surgery, please visit the anaesthesiologist on /..... /..... to hours. You may eat and drink before this consultation. The consultation is located on route

- > Do not eat or drink from midnight onwards or otherwise follow the advice given to you by the anaesthetist. Diabetes patients must not use their anti-diabetic medication.

8.5 General tips

a) What to bring when admitted to hospital?

- Sufficient medication for at least two days
- SIS and UZA-card
- This info brochure
- Nightwear and toiletries

b) Points to note

- Do not bring money or jewels.
- Do not use make-up and remove nail varnish from fingernails and toenails.
- Report to the nursing staff if you have been seriously ill since your last visit.

c) Visiting hours

Monday to Friday from 4 p.m. to 8 p.m.

Saturday and Sunday from 2 p.m. to 8 p.m.

8.6 Check-up appointments

After the operation you will visit for check-ups at the ophthalmic consultation department (route 122).

1. / / at hours

2. / / at hours

3. / / at hours

4. / / at hours

5. / / at hours

6. / / at hours

9. Surgical preparations

9.1 Consultation

During the consultation we perform a number of eye tests. These are necessary to calculate the focal power (strength) of the artificial lens that will replace your own lens.

9.2 Preoperative anaesthesia consultation

If you undergo surgery under general anaesthesia, the ophthalmology consultation nurse makes an appointment for you with for anaesthesia consultation.

The anaesthetist will examine you and if necessary, request additional tests such as:

- Radiography of the lungs
- Visit to the heart specialist
- Taking blood

9.3 Preoperative preparations in the (day treatment) hospital

In preparation for the surgery we will administer eye drops into the eye to be operated upon to temporarily enlarge your pupil.

Just before you go to the operating theatre, it is best for you to go to the toilet again, even if you feel that it is unnecessary.

9.4 Anaesthetic

Depending on the surgery, your general health and your age, either a local or a short general anaesthetic will be administered.

a) Local anaesthesia

With local anaesthetic only your eye will be anaesthetised. That usually takes place through means of eye drops.

- Use of medication (discuss this too with your ophthalmologist/doctor).
 - You are allowed to take your general medication according to your usual schedule.
 - Diabetes patients take their usual anti-diabetes medication.
 - Blood thinning medication can also be used.
- You do not need to have an empty stomach, you can eat and drink. A light meal before the operation is permitted.
- You are set-up with a catheter before leaving for the operating theatre.
- Patients who use a hearing aid must keep this in the ear opposite the eye to be operated upon to allow communication.
- If you have dental prostheses you can keep it in place.

b) General anaesthesia

You are completely anaesthetised.

- You must have an empty stomach commencing from midnight onwards (do not eat or drink anything and do not smoke) unless the anaesthetist gives you different advice.
- Remove your dental prostheses before leaving for the operating theatre.
- Do not wear glasses, a hearing aid, wig, hairpins or bra.
- Do not wear make-up
- At home, remove nail varnish from fingernails and toenails.

In the operating theatre you will be set-up with an infusion in your arm through means of which the anaesthetist will administer medication. After the operation you will wake up in the recovery. As soon as your general condition allows, you will be taken back to the ward.

10. The biopsy

During the surgery, a small biopsy of the eye limbus will be collected for culture purposes in the laboratory.

Duration

The surgery, preparation and after care take approximately 30 minutes.

11. The surgery

During the surgery, the damaged tissue at the surface of the cornea is removed before placing the stem cells and the amniotic membrane on the eye.

Duration

The surgery, preparation and after care take approximately 2 hours.

Video recording

If your eye shows interesting aspects in the fields of science or education, the operation will be recorded on video. In this video, your face is not recognisable. Your anonymity is totally assured on this video.

12. After care

How do you take care of your eye after surgery?

12.1 Eye cap

You will be given an eye cap, a hard plastic cover to prevent you rubbing your eye. Wear this at night or while resting the first week after surgery.

12.2 Eye drops

You will receive eye drops to allow the eye to heal optimally. Even at home you must continue to use the drops for four weeks after surgery. You take the eye drops home along with an additional prescription in case you need a spare bottle. Instructions on how to use the eye drops follow in this brochure

12.3 Points to note

Get in touch with your cataract surgeon or the ophthalmic consultant if:

- You experience pain in the eye that was operated on
- Your operated eye becomes redder
- Your sight becomes noticeably poorer than when you first left the hospital

12.4 What are you allowed to do after the operation?

- You are allowed to use the eye that has been operated on for reading or watching TV.
- Your glasses will be modified five weeks after the operation. Up until that time you will need to decide for yourself whether you feel more comfortable with or without wearing glasses. You might possibly wish to have the lens removed from your glasses on the side you were operated on.
- You are allowed to shower and wash your hair while keeping your eyes closed. **Be very careful not to allow any soap to get into the recently operated eye.**
- All daily activities are permitted (shopping, cooking, reading, watching TV, etc).

12.5 What are you not allowed to do for a week after the operation?

- Rubbing in the recently operated eye.
- Carrying out heavy physical labour.
- Picking up/carrying heavy objects.
- If you wish to cycle or drive during the first week after the operation consult your ophthalmologist beforehand.

13. Eye drop instructions



Instructions for using the eye drops

- Tilt your head slightly backwards.
- Using your index finger, pull your lower eyelid downwards.
- Let a drop fall into the middle of the red conjunctiva sac.
- Release your eyelid and close carefully.
- Keep your eyes close for 30 seconds and do not blink.
- Never touch your eye with the eye drop bottle or your finger(s)!
- If you are using two different types of eye drops use each type with a five minute break between each session.
- Ask family members or friends for assistance if you cannot manage.

Any questions?

- You can call us by telephone from Monday to Friday between
8.30 a.m. and 5 p.m.: consultation ophthalmology: 03 821 35 56
Nursing staff day treatment hospital: 03 821 54 00
After 5 p.m. and during weekends you can contact the
emergency services: 03 821 38 06
- You can also contact us by e-mail:
E-mail consultation ophthalmology: oftalmologie.poli@uza.be
E-mail nursing staff at the day treatment hospital:
verpleging.oogheekunde@uza.be

Ophthalmology department

- **Diensthoofd**
Prof. dr. M.J. Tassignon
- **Achtersegment chirurgie**
Dr. R.M.E. Smets - Prof. dr. M.J. Tassignon
Dr. J. Van Looveren
- **Botuline**
Dr. L. Smet- Dr I. Leysen
- **Chirurgie orbita - Traanwegen**
Prof. dr. V. De Groot
- **Cornea - Contactlenzen**
Dr. C. Koppen - Dr. I. Leysen
- **Elektrofysiologie - Microperimetrie**
Prof. dr. sc. T. Coeckelbergh
- **Endocrinopathie**
Dr. I. Leysen
- **Glaucoom**
Prof. dr. V. De Groot - Dr. S. Kiekens
- **Kinder oogheekunde**
Dr. I. De Veuster
- **Visuele revalidatie**
Prof. dr. M.J. Tassignon - Dr. I. De Veuster
Mevr. D. Godts - Dhr. J. Claeys - Prof. dr. sc. T. Coeckelbergh
- **Subjectieve functionele onderzoeken**
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- **Optische functionele onderzoeken**
Prof. dr. sc. J. Rozema
- **Medische retina**
Dr. R.M.E. Smets - Dr. J. Van Looveren
- **Neuro-Oogheekunde**
Dr M. Van Lint
- **Oculaire weefselbank**
Dr. C. Koppen - Dr. N. Zakaria - N. Bostan
- **Oftalmogenetica**
Dr. R.M.E. Smets – Dr. I. De Veuster
- **Oftalmologische oncologie**
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- **Beeldvorming achterste oogsegment**
Dr. R.M.E. Smets - Dhr. R. Leysen
- **Biometrische beeldvorming**
Prof. dr. sc. J. Rozema

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