OkuStim® therapy – Changing the course

Transcorneal electrical stimulation of the eyes can slow visual field progression in patients with retinitis pigmentosa .

Today, progression of degenerative diseases of the retina such as retinitis pigmentosa (RP) can already be slowed: the OkuStim® therapy was developed by Okuvision GmbH, the leading German provider in the field of ocular electrical stimulation, in close co-operation with ophthalmologists and scientists With gene and stem cell therapies not yet available for all forms of RP, OkuStim® therapy is currently the only clinically tested treatment approved for all forms of RP in Europe. OkuStim® is also the only CE-certified medical device for the treatment of RP, and can be used regardless of the respective gene defect.

The treatment – it all happens in the eye

OkuStim® therapy is based on transcorneal electrical stimulation of the eye, or TES for short. Transcorneal means that electrical impulses pass through the cornea and into the eye. The electricity spreads within the eye, also hitting the inner surface at the back of the eye called the retina. The weak electrical impulses have a neuroprotective effect here: they have a protective effect on the photoreceptors – the rods and cones in the retina. The body's own biochemical signalling pathways, which can be influenced using electricity, play a role here.[1,2,3] The consumption of oxygen in the cells in the central part of the retina demonstrably improves as a result of TES, indicating an increase in metabolism.[4] The precise mechanism of the cell-preserving effects has not yet been entirely clarified at the molecular level and is currently being researched in greater detail.[5] Nevertheless, the effect and safety of the therapy are clinically proven: TES can slow the progression of retinitis pigmentosa.[6,7,8]

The treatment – how the electricity gets into the eye

OkuStim® therapy does not involve any surgical procedures on the eye or the rest of the body at all. Its application is purely external: a thread electrode as fine as a hair is placed on the lower eyelid using an electrode holder that was specially developed for this purpose (OkuSpex®), where it comes into contact with the surface of the eye. The OkuStim® system is designed in such a way that the patient can quickly learn how to use it and perform the procedure at home themselves.

The OkuSpex® electrode holder is connected to a small, handheld device that delivers the electrical impulses. The strength of the stimulation depends on the patient's subjective tolerance level. This is determined by the ophthalmologist treating the patient and saved on the device. The therapy is used regularly once a week and the duration of stimulation is half an hour. The operation of the OkuStim® system is tailored to the needs of visually impaired patients: acoustic signals provide information about the progress of the stimulation and the operating modes of the OkuStim® to aid independent use.

What patients should know about OkuStim® therapy

The treatment is non-invasive

No medications are administered, and the therapy is purely physical with external application. There are therefore no side effects of OkuStim® therapy like there can be with the administration of medicinal products, surgery or genetic procedures.

Independent with medical supervision

OkuStim® therapy is only available on prescription. Patients can administer the OkuStim® therapy themselves at home for half an hour per week (Fig. 1). At least once a year, patients will need to see their eye care professional, who will provide specialist support for the treatment.

Fig. 1. | *Application of OkuStim therapy.*

Treatment is not linked to the genetic defect

OkuStim® therapy can be used in all RP patients regardless of which genetic defect has caused the disease in the individual case.[8] Moreover, the application does not exclude patients from possible future gene and cell-based therapies.

Playing it safe

The experience of more than 400 patients with their collective over one hundred years of application in clinical studies confirms that OkuStim® therapy is safe. There were no serious side effects related to the application. Symptoms of dry eye that often occur can be treated with eye drops.[8]

Establishing a routine

A retrospective study that was not conducted by Okuvision with around 100 patients showed that the positive impact of TES decreases after discontinuation of the therapy.[9] This means that treatment with the OkuStim® system should be applied as permanently as possible without long periods of interruption. If the patient's vision is so impaired that they are no longer able to perceive light or orientation is no longer possible, the therapy should be discontinued in consultation with the doctor providing treatment.

The earlier the better

In principle, the earlier in the disease progression the OkuStim® therapy is started, the more visual acuity can be preserved. The therapy can be started at any time regardless of the extent of the impairment of the visual field.[8]

Overview

The advantages of OkuStim® therapy

- The method works in a purely physical way with no administration of medicinal products.
- The application is non-invasive and no surgical procedures are performed on the body.
- OkuStim® therapy is safe and there are no known serious side effects.
- The therapy can be administered by patients themselves at home.
- The time commitment for patients is minimal at just half an hour per week.
- The therapy can be started in all stages of the disease. Therapy can be started at all stages of the disease. However, as only intact photoreceptors can be preserved, the earlier the therapy is started, the larger the area of the visual field that can be protected.

Restrictions and disadvantages

- Dry eyes are common. The symptoms can be treated with eye drops.
- OkuStim® therapy can only preserve what is still there. Photoreceptors that have already been destroyed cannot be restored with TES.
- OkuStim® therapy is not yet included in the catalogue of services covered by statutory health insurance. Costs may be covered in individual cases, but this needs to be requested and potentially negotiated.
- Statements about the efficacy can currently only be made in relation to patients with retinitis pigmentosa. Other degenerative diseases of the retina can be treated with OkuStim® therapy, but there are no data on efficacy supported by clinical evidence.

What third parties say

The **German Society of Ophthalmology** (Deutsche Ophthalmologische Gesellschaft, DOG) is the medical and scientific expert association for ophthalmology in Germany. It references electrostimulation as a treatment option for RP in its current guideline.[10]

In its assessment, the **German Institute for Quality and Efficiency in Health Care** (Deutsche Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, IQWiG) sees potential for TES to provide a patient-relevant benefit in patients with RP.[11]

PRO RETINA Deutschland e.V. is a self-help organisation for people with degenerative diseases of the retina. The Working Group on Clinical Questions (Arbeitskreis Klinische Fragen, AKF) of its Scientific and Medical Advisory Board rates OkuStim® application as safe in patients with retinal dystrophy and has no objections to its controlled use in patients with RP and other hereditary retinal dystrophies such as cone-rod dystrophies, choroideremia and Usher syndrome.[12]

Clinical studies

An initial clinical study (EST1) with RP patients in 2011 showed that electrostimulation of the retina is both effective and safe.[7] A follow-up study (EST2) and an observational study (TESOLA) conducted in 2014 and 2016 confirmed the safety of regular use.[6,13] In a study conducted at the University Hospital of Basel (2019), increased consumption of oxygen in the centre of the retina could be demonstrated after six months of OkuStim® therapy with the vascular diameters remaining the same, indicating increased metabolism.[4]

New evidence

An exploratory assessment of data from the previous study, EST2, was published in 2023. It showed that the deterioration of the visual field in patients with RP after a year of regular TES treatment was lower by up to 64 percent compared to untreated eyes and by up to 72 percent compared to placebo treatment.[8] The data also show that the efficacy was highest with the stimulation strength between 0.8 and 1.0 mA.[8] As a result, working with the maximum possible stimulation strength is recommended, depending on the individual tolerance level.

Looking to the future

In summer 2021, another observational study began in patients using the OkuStim® system. The goal was to take stock of the objective and subjective long-term benefits of TES. The data are currently being evaluated.

Further data on the long-term efficacy are needed for electrostimulation of the retina to be added to the catalogue of services covered by statutory health insurance in Germany. These data are currently being collected in a trial at 17 German eye clinics commissioned by the Federal Joint Committee (Gemeinsamen Bundesausschuss, G-BA).[14] It will continue until 2026 and is being organised and managed by the University Eye Hospital Tübingen.[15]

About retinitis pigmentosa

Retinitis pigmentosa, or RP for short, is a hereditary, degenerative disease of the retina caused by genetic changes. These changes lead to the gradual death of the visual sensory cells (rods and cones) in the retina. In Germany, the disease occurs in around one in every 4,000 inhabitants.[16] The initial impairments in vision often only occur during childhood. Night blindness is an early symptom. In patients with mild progression, the disease often only appears in later life. An increasing loss of visual field is typical, with the visual field narrowing from the periphery and into the centre of vision.[17] Tunnel vision can be preserved for a relatively long time, with the patient only able to see with a small, central part of their normal visual field, but this section is often very clear. Over time, RP can lead to total blindness. Around half of those affected are legally blind by the age of 55.[17]

Application of the OkuStim® therapy

Medical prescription

OkuStim products are only available on medical prescription following the diagnosis and determination of suitability for treatment and tolerance in order to ensure that patients receive regular check-ups – at least once a year.

Determination of the individual stimulation strength

The doctor determines the individual current amplitude for electrical stimulation. The maximum tolerable level should be chosen.

Therapy process

The patients use the stimulation once a week for 30 minutes at home and regularly attend the clinic for check-ups (every 6-8 months but at least once per year).

Stimulation parameters

Biphasic electrical impulses, duration of impulse 10 ms, frequency 20 Hz.

Handling the OkuStim® system

The operation of the OkuStim® system is easy and tailored to the needs of the patients. It offers the acoustic output of system notifications that can even be used by patients in the advanced stage of the disease.

Availability

The OkuStim® system is an active medical device with CE labelling. It is available in Europe. You can find clinical centres and sales partners on **www.okuvision.de/en/where-to-get-it/**

NOT FOR SALE IN THE USA

Indications for OkuStim® therapy

TES therapy with OkuStim® is suitable for the treatment of

- patients with retinitis pigmentosa (including that caused by syndromes such as Usher syndrome)
- patients with similar diseases of the retina such as cone-rod dystrophy or choroideremia.

Contraindications

OkuStim® therapy should not be used by patients with acute inflammation of the eyes and in blood vessels that are undergoing growth processes that could be accelerated by the electrical stimulation (ocular neovascularisation of any origin, macular oedema, arterial or venous occlusion, diabetic retinopathy, age-related macular degeneration).

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