RESONO OPHTHALMIC

THE **QMR®** EFFECT

It has been well-known for centuries that **electrical currents carry the signals that allow our body to work**. E.g., heart or leg muscles contract because they are stimulated by **a current**, we see or hear because eyes and ears generate and transmit electrical signals to our brain. More recently, electrical currents have been shown also to be able to stimulate the metabolism and increase **the natural regeneration of many cells and tissues**, at the basis of many repair and healing processes (see, e.g. [1,2]). These **electrical stimuli** are normally generated by the body itself, but they can also be **artificially generated** and applied by properly designed biomedical instruments. The main difficulty with this artificial stimulation is to create the correct signals, capable of interacting with the organism by **stimulating the natural regeneration processes**.
In this regard, some research activities carried out at the ***Telea Medical*** company have led to the discovery of a new physical effect, named **Quantum Molecular Resonance (QMR®)**, in which an alternating electrical signal containing a specific **range of frequencies, from 4 to 16 MHz**, appears to be in resonance, i.e., has the same frequency, with the molecular bonds in biological tissue. This particular situation allows to **maximize the transfer of power** from the electrical stimulus signal to the biological tissue, with a minimum heat dissipation.
This discovery was originally exploited by the company to develop a revolutionary cold electro-scalpel [3], which allows to obtain the effect of surgical cut without increasing the tissue temperature.
With subsequent experiments, it has been discovered that an electrical signal with an even wider range of **frequencies (from 4 to 64 MHz)** is able to obtain another important effect, namely the **stimulation of the metabolism and natural regeneration of biological tissue** and cells. It is possible **to explain this effect** based on various phenomena generated by the QMR stimulation and experimentally observed: mechanical deformation of the cell membrane and increase of calcium release [4], stimulation of adult stem cells. Using sophisticated micro-array techniques to evaluate gene expression, a recent in-vitro study on mesenchymal stromal cells has shown that QMR is able **to up-regulate genes** involved in the extracellular matrix (ECM) remodeling, embryogenesis, wound healing, and angiogenesis [5].
This new discovery has paved the way for **the application of QMR in various medical areas**, such as aesthetic medicine, antalgic medicine, and physiotherapy. It is of interest to note, for their possible application to the healing of corneal wounds, the remarkable results obtained by the QMR stimulation in the healing of deep wounds in the limbs [6].

(QMR® is a registered trademark of Telea Medical and patented worldwide).

REXON-EYE® BY RESONO OPHTHALMIC

In several **ophthalmic syndromes** and diseases, the pathological situation is created by the **malfunctioning of specific cells and tissues**, such as the lacrimal gland and the Meibomian glands for the dry eye disease (DED). By stimulating the metabolism and natural regeneration of these cells with **the QMR treatment**, we can reactivate their correct physiological behavior and restore a healthy situation in the treated patients.
Just with this goal, **the company Resono Ophthalmic**, created in 2014, developed the Rexon-Eye® device. It consists in a QMR generator equipped with **a special mask electrode**, to optimally apply the treatment to the ocular surface area. This device obtained the **CE mark** in 2016 as a 'Medical device for the treatment of ocular surface disorders' and, after additional clinical trials, it entered the ophthalmic market in 2018 as a therapeutic device. The Rexon-Eye device and treatment are currently **patented in Europe, USA, China, Republic of Korea, South Africa, Australia**, and are being patented in other countries as well.

THE REXON-EYE **TREATMENT**

The Rexon-Eye device is now **successfully applied in patients affected by DED**, aqueous deficient (**ADDE**) as well as evaporative (**EDE**) or **mixed** type [7, 8, 9, 10]. The QMR treatment promotes the regeneration **of the tear production system**, improving the activity of the glandular tissues involved (even the slight hyperthermia generated by the electric current on the ocular surface due to Joule effect can in some cases help to reactivate the physiological tear secretion). The induction of natural tears in larger volume and with better quality leads to a **physiological rebalancing of the tear film**, with significant results from the clinical and subjective point of view.
Unlike other devices on the market, which simply produce a heating of the treated area and therefore only alleviate the symptoms of the disease, Rexon-Eye applies a treatment capable **to stimulate the recovery of the normal function** of the involved organs.
The Rexon-Eye device can find a more general application in the treatment of various **disorders of the ocular surface**, i.e., in a series of pathological situations, determined or aggravated by a multiplicity of events (e.g., trauma, inflammation, deficiency, infections, etc. ...), that determine abnormalities of the ocular surface and of the composition of tear film, with an important impact on visual capability. In addition to dry eye disease (ADDE, EDE, or mixed), **Rexon-Eye has been shown to be effective** in significantly reducing cornea perforation in alkali burn animal models [11]. In ophthalmic practices, it is being applied also to successfully treat patients affected by **blepharitis, cornea wounds, or chalazions**.

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PRACTICAL ASPECTS OF THE REXON-EYE TREATMENT

The use of the device **is intended for all the patients** who wish to undergo ocular surface therapies, with the exception of pregnant women, patients with active implantable medical devices (e.g., pacemakers or hearing aids), neonatal and paediatric patients, patients undergoing oncologic treatment.
The therapy is non-invasive, does not cause any pain, does not require analgesic products nor external cooling systems (e.g., gel) nor that the patient be laying down. Resono Ophthalmic is not aware of any kind of significant side effect that can be induced by the use of Rexon-Eye. During treatment, patients experience only a mild and **pleasant sensation of heat** in the area of skin under the mask.
In some patients, the pressure of the mask onto the eyelids may cause a temporary blurred vision at the end of treatment, which spontaneously disappears in a few minutes. According to our experience, this transient blurring may happen when the elastic band holding the mask in place is too tight. This is not due to any electrical event, but simply to the mechanical pressure of the mask onto the eyeball. Just make sure **to place the mask in good contact with the eye** but without exerting too much pressure on it. We advise the users to sit the patients in a reclining couch with the back pushed down, so that they are laying comfortably in an almost horizontal position, with no need to tighten the elastic band. At the end of the treatment, after the mask has been removed patients should be asked to stay a few minutes still with closed eyes, allowing the eyes to gradually readjust.
The **current treatment protocol** provides for 20 minutes sessions, with a 30 seconds alternation between eyes, one session per week over a 4 weeks total period. Power is initially set at 4 and can be individually adjusted, separately for each eye, so that the patient experiences a mild, comfortable and pleasant heat sensation.
As for any other type of therapeutic agent, the patient response to the Rexon-Eye therapy is characterized by **individual variability**: some patients exhibit an improvement in their conditions just after the first session, e.g., with an increased tear production; some others have to wait longer for the treatment to start the regeneration process. From the experience gathered so far with the QMR treatment in ophthalmology and other medical areas (aesthetic medicine, pain medicine, physiotherapy), improvements may require 1 or 2 months from the end of treatment to become stable.

ABOUT **THE CORRECT** REXON-EYE MASK **POSITIONING**

The electrical signal generated by Rexon-Eye, according to the therapeutic set-up parameters, is fairly reproducible and we do not expect any significant variation in time.
The mask, mainly its contact with patient's face, is probably the main source of possible variations in device functioning. We carefully test all masks, e.g., measuring the current generated in either eye electrode, to assure a correct and reproducible behavior. However, we cannot predict the anatomy of patient's eyes, the position of the mask upon them, and the strength of the elastic band onto it, which unfortunately are all crucial factors for the device functioning and effectiveness.
The QMR treatment delivers a signal that activates the therapeutic effect, i.e., the natural regeneration of cells. If the **power is too high**, it will only generate an unpleasant or even painful heat without adding any benefit. If it is **too low**, the electrical signal may not reach a level high enough to bypass the skin electrical resistance and stimulate the natural cell regeneration. As a guiding principle in setting-up the device power, the patient's sensation of heat is considered. In particular, in order to optimize the therapeutic effect, it is important that the patient declares that a mild and never unpleasant nor painful heat is felt during the treatment.
Heat is not by itself the therapeutic effect, but it is used only to assess that the QMR current enters the living tissues with **amplitude high enough** to stimulate the natural tissue regeneration. Since it is not possible to actually measure this current inside the eye, the perceived heat is used as an indirect measure. It is important to remark that **the sensitivity to heat can be different from patient to patient** and thus, even with the same therapeutic parameters, different patients may report different feelings. In addition, some patients may be more sensitive in one eye, e.g., because of specific anatomy, or unilateral lesions or disease. In general, a difference in power of 1 unit may considered acceptable.
More importantly, if the mask is not **symmetrically positioned** over the two eyes and thus the elastic band is tighter on one eye with respect to the other, on that eye the pressure will also be higher, the electrical resistance lower, the current higher, and the generated heat higher as well. Therefore, an excess in pressure may cause higher heat in one eye with respect to the other. Sometimes this feeling of higher heat is always on the same side; this may be because the operator who positions the mask on the patient always does it from the same side, thus reproducing a situation of possible asymmetry.
On this issue, we have carried out subjective tests on **the mask's wearability** and noticed that even by slightly moving the elastic band behind the head (or by placing the mask in a slightly different position), the pressure on one eye changes as compared to the other one and therefore the feeling of heat changes as well.
Therefore, we wish to make users aware of the importance of a **correct positioning of the mask and of the feeling of pressure it exerts on the eyelids**.

- We invite the operators to try the mask on themselves, to understand the effects of its different positioning on the heat sensation.
- In addition, we suggest them **to always ask for patients' feedback** about the correct "as symmetrical as possible" position of the mask and even encourage them, before the treatment is started, to personally adjust the mask to have the most comfortable and symmetrical fit.

By spending just 20 or 30 seconds before or during each treatment session, the operator and the patient **can find the best position of the mask** and thus reduce the incidence of a possible variability in heat sensation and **improve the overall effectiveness of the Rexon-Eye treatment**.

First tutorial to set up and use Rexon-Eye

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