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Retinal Laser Therapy: Recent Unique Developments Behind the Brilliant Front Stage of Anti-VEGF Treatment

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Retinal Laser Therapy

"What does laser do on the retina?" "It is easy. It just destroys the RPE and surrounding tissues including photoreceptors." "For what?" "…to reduce oxygen consumptions mainly by photoreceptor outer segments in ischemic diseases, sometimes to coagulate retinal aneurisms, and to strengthen the retinal adhesion around the retinal holes or tears in order to avoid progression of retinal detachment". It was the almost perfect answer, even still not completely proven, at least it was the enough knowledge in daily clinical practice before. But today, we are facing to the necessity to know more in detail, for example, "What happens if the RPE cells are just warmed up to 45°C for 0.1s?", which we have almost never needed to consider before.

With the dramatic development of anti-VEGF treatment, it cannot be denied that necessity of retinal laser treatment has been reduced to some extent, although some retinal conditions still definitely require laser treatment. In particular, macular edema, through whatever the reason, is now treated mostly pharmacologically using anti-VEGF agents or corticosteroids, and the laser treatment, as grid photocoagulation, has been less and less performed in these days.

It is certainly understandable that photocoagulation on the macula is surely with high risk of eventual central or paracentral scotoma, which nobody wishes. But what if the damage extent is controllable below the significant damage threshold?

What has been used for a long time as a Merkmal of retinal photocoagulation was the mild whitening of the irradiated retina. It is now widely known that the apparent whitening may be a feature of the quite strong coagulation, which might involve the inner retina. The laser photocoagulation, which is not visible (=sub-visible) with funduscopy is so far called widely in clinical ophthalmology a "sub-threshold photocoagulation". Different new technologies have been introduced for the successful sub-visible photocoagulation; micropulse laser photocoagulation, which utilizes the microsecond-range pulse in order to avoid steep temperature increase at the irradiated site [1], and the endpoint management laser system, which utilizes 577 nm laser irradiation and its endpoint algorithms to automatically adjust the irradiated energy (power and time) according to the desired damage strength [2]. They have shown positive clinical effects in treatment of macular edema without leaving severe central scotoma [3]. These new technologies have surely changed clinicians' awareness in regard of the damage strength of retinal photocoagulation, and patients may obtain surely softer but effective treatment.

Desire to know is the motivation of science. The question has been always asked in the study field of retinal laser irradiation, "how much is the retinal temperature during irradiation on patients?" In retinal photocoagulation, the temperature and the time of the increased temperature are the major determinants of cell responses to the thermal stimulation. A working group in University of Luebeck has enabled the real-time temperature determination during photocoagulation using optoacoustic technique [4], and their online control system rather enables the automatic laser shut-off at the time point when the local temperature reaches the set temperature (AutoPhoN: Automatic Photocoagulation of the Retina) [5]. Intra-individual difference in pigmentation and other factors affecting laser absorption may alter the temperature increase among spots. This problem might be minimized by the installation of this system.

This AutoPhoN technique may also realize the controlled "sub-lethal" irradiation. In other words, non-invasive hyperthermia (photothermal) treatment on RPE cells is theoretically possible as one of the therapeutic options along with the lethal irradiation. Since sub-lethal laser-induced hyperthermia on the RPE under temperature control is a new concept, temperature-resolved RPE cell responses have been studied quite little to date [6]. We currently attempt to elucidate the temperature-dependent RPE cell responses in order to find optimal thermal dose for the beneficial hyperthermia treatment on the RPE [6]. Hyperthermia-induced cell functional manipulation is of our great interest. By the way, the term of "sub-threshold" is being gradually replaced recently by "sub-visible" or "sub-lethal" to avoid the confusion.

In retinal laser therapy, the time may come in the near future, when we ask by ourselves, "With which temperature do you want to treat this patient's retina?

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