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Review Article

Modern retinal laser therapy

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Abstract
Medicinal lasers are a standard source of light to produce retinal tissue photocoagulation to treat retinovascular disease. The Diabetic Retinopathy Study and the Early Treatment Diabetic Retinopathy Study were large randomized clinical trials that have shown beneficial effect of retinal laser photocoagulation in diabetic retinopathy and have dictated the standard of care for decades. However, current treatment protocols undergo modifications. Types of lasers used in treatment of retinal diseases include argon, diode, dye and multicolor lasers, micropulse lasers and lasers for photodynamic therapy. Delivery systems include contact lens slit-lamp laser delivery, indirect ophthalmocope based laser photocoagulation and camera based navigated retinal photocoagulation with retinal eye-tracking. Selective targeted photocoagulation could be a future alternative to panretinal photocoagulation.

Keywords: Retinal Laser, Photocoagulation, Therapy, Pattern laser, Micropulse laser, Navigated laser

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A brief history of retinal photocoagulation

Past laser photocoagulation concepts

Photocoagulation uses light to coagulate tissue. Medicinal lasers have become a source of light to produce tissue coagulation. The effect of laser interaction with retinal tissue had been studied earlier but it was not until Meyer-Schwickerath's report in 1954 that beneficial therapeutic effects of laser photic burns were recognized.[1] With Hans Littmann of Zeiss Laboratories they assembled the first xenon-arc photocoagulator in 1956.[2] The system was effective but it was difficult to focus beam to a small spot, treatments required long exposures and were often painful. Theodore Maiman, PhD, designed the first ophthalmic laser in 1960 at the Hughes Research Laboratories emitting monochromatic energy. Systems using ruby laser (694-nm wavelength) were among the first to be studied in ophthalmology.[3,4] They offered some variability in pulse durations and more precisely targeted treatments. They could be successfully applied therapeutically but intense chorioretinal destruction and frequent hemorrhaging soon showed to be an issue. The advent of argon laser marked a new milestone in retinal photocoagulation.[5,6]

Argon laser can use the blue (488-nm wavelength) and green (514-nm wavelength) light emission absorbed by both hemoglobin and melanin. The Diabetic Retinopathy Study[7] and the Early Treatment Diabetic Retinopathy Study[8] were large randomized clinical trials that have shown beneficial effect of retinal laser photocoagulation in diabetic retinopathy and have dictated the standard of care for decades. In DRS, argon laser had equal efficacy to xenon arc laser but in general produced less adverse effects. Later on water-cooled argon lasers have been replaced by air-cooled Nd:YAG frequency doubled lasers (532-nm wavelength). Other conditions, including age-related macular degeneration and retinal vein occlusion, were found to benefit from laser retinal photocoagulation, widening treatment indications.[9]

Introduction of dye lasers represented a further development. The design of a dye laser is similar to a pulsed solid-state

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laser with the laser crystal replaced by a dye cell.[10,11] Dye lasers can usually be used for a much wider range of wavelengths. The introduction of solid state lasers has offered an advantage of being less expensive and portable.

Past laser delivery systems

Mode of delivery is an important aspect of laser photocoagulation. While the ruby laser was attached to a monocular direct ophthalmoscope, subsequent generations of lasers could be attached to indirect ophthalmoscope, operating microscope or slit lamp. Endolaser photocoagulation (applied via a fiberoptic probe placed inside the eye) has shortened treatment times and improved results of vitreoretinal surgery. Coupling lasers with slit lamp improved laser delivery to the retina, especially for posterior pole application in the clinic.[12]

Modern laser technology developments and applications

Current laser photocoagulation concepts and techniques

The above-mentioned clinical trials and subsequent clinical experience by physicians established retinal photocoagulation as the standard treatment of choice for complications of diabetic retinopathy for over 40 years. Although clinically effective, retinal laser photocoagulation leads to collateral damage and side effects including reduced night vision, macular and peripheral scotomata with decrease in central and peripheral vision, exacerbation of macular edema and disruption of the retinal anatomy through scarring.[13–16]

In search for ways to spare retinal tissue yet achieving desired therapeutic benefit, the first attempts were aimed at titration of laser power to reduce tissue damage. Diode lasers (810-nm wavelength) were used to produce ''classically'' subthreshold (ophthalmoscopically less visible) burns in diabetic macular edema (DME)[17] and age-related macular degeneration (AMD).[18,19]

In 1990 Pankratov developed the micropulsed diode laser. Producing a train of millisecond laser pulses separated by variable quiet intervals, micropulsing allowed selective treatment of the retinal pigment epithelium (RPE) and sparing of the neurosensory retina.[20,21] Early use of micropulsed lasers reduced but did not eliminate thermal retinal damage due to use of high treatment powers and / or micropulse duty cycles, as well as the continuing belief in the need to produce at least some laser-induced thermal retinal injury to achieve a therapeutic effect. This long-held maxim was called into question by the later finding that use of particular micropulsed laser parameters (high-density/low-intensity ''true'' Subthreshold Diode Micropulse laser, or ''SDM'') is clinically effective without any laser-induced retina injury detectable by any currently available retinal imaging modality, or known adverse treatment effects. Non-destructive and thus non-inflammatory, SDM has been reported effective for a number of disorders and uniquely allows safe transfoveal treatment in eyes with good visual acuity.[19,22,23] SDM has also been uniquely shown to increase, rather than decrease, retinal sensitivity by microperimetry at the locus of laser application.[24]

In 1992 Reginald Birngruber and colleagues introduced application of even shorter microsecond continuous-wave laser pulses. These microsecond laser pulses also selectively target the retinal pigment epithelium (RPE) sparing the photoreceptors and other intraretinal cells.[25,26] Such short-pulse continuous wave laser cause explosive vaporization of melanosomes and formation of cavitation bubbles resulting in cell death and subsequent proliferation and migration of RPE cells to restore the integrity of the defective RPE layer.[25] The clinical term adopted for this approach has been ''Selective Retina Therapy'' or SRT.[26]

Another concept to use laser therapy with minimal collateral damage is transpupillary thermotherapy (TTT) using near-infrared (810-nm wavelength) laser, low irradiance and long exposure (1 min), and large retinal treatment spots. TTT continues to be used in the treatment of small choroidal melanomas, nowadays in combination with other modalities such as brachytherapy.[27,28] However, former use for neovascular AMD and other macular disorders has been abandoned due to higher efficacy of intravitreal anti-angiogenic therapy and the risk of inadvertent macular photocoagulation and visual loss.[29]

Also in the 1990s, a new concept of targeting choroidal vessels in the neovascular membrane emerged using a photosensitizer activated by red/near-infrared laser and became known as photodynamic therapy (PDT). The original photosensitizer phthalocyanine was replaced by the liposomal benzoporphyrin derivative complex with affinity to endothelium of newly formed blood vessels.[30–32] The latter is commercially known as verteporfin which was the first pharmacologic treatment for AMD.[33] The PDT treatment causes intraluminal vascular occlusion with subsequent regression of choroidal neovascular membrane.[34] With time, its use in AMD has been replaced by more effective and less destructive intravitreal anti-angiogenic therapy. It still remains a treatment option or supplemental therapy in some pathologic choroidal conditions.

Current laser delivery systems

Developments in laser technology lagged behind developments in other areas of retinal field such as imaging, pharmacology and genetics. Most innovations in laser therapy in previous decades have focused on laser adjustments such as spot size and pulse duration. However, two major developments took place in recent years.

In 2006, OptiMedica Corp. (Santa Clara, CA) introduced PASCAL pattern scan laser photocoagulator with a 532-nm laser used for standard photocoagulation procedures that can apply a uniform pattern of many laser spots at one time.[35] Due to short pulse duration, the heat is decreased resulting in less thermal damage. The pattern laser technology allows equidistant spacing of individual spots and fairly consistent retina burns. The PASCAL laser allows ophthalmologists to perform macular grid treatments effectively and panretinal photocoagulation more rapidly with less pain than conventional lasers.[36,37] At present, it is one of the most common laser delivery systems.

The second major development was introduction of new laser platform called NAVILAS (OD-OS, Inc. Germany) which uses retinal navigation and fundus camera based delivery. This 532-nm pattern-type eye-tracking laser integrates live color fundus imaging, red-free and infra-red imaging, fluorescein angiography with photocoagulator system.[38–40] After image acquisition and making customized treatment plans by physicians including marking areas which will be coagulated the