Subretinal, Viscoelastic-Assisted, Endoscope-Guided Photothermal Ablation of Choroidal Neovascular Membranes by Erbium:YAG Laser

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BACKGROUND AND OBJECTIVE: The efficacy of endoscope-guided erbium:YAG laser, assisted by viscoelastic macular detachment, in subretinal ablation of choroidal neovascular membranes (CNVs) is evaluated.

PATIENTS AND METHODS: A high-repetition, midinfrared erbium:YAG laser was used subretinally to ablate CNVs in 2 patients. Ablation followed pars plana vitrectomy and macular retinal detachment using a viscoelastic substance, and was guided by a high resolution endoscope.

RESULTS: Visual acuity improved from 6/90 to 6/20, six months after treatment in 1 patient, and from finger counting from 1 meter to 6/30, three months after treatment in the other. The membranes showed no angiographic signs of activity postoperatively. However, a zone of stippled hyperfluorescence appeared in both patients, corresponding with the macular detachment area. This gradually diminished in size in both patients.

CONCLUSIONS: The surgical procedure was found effective in our preliminary research. The use of viscoelastic substance and endoscope is felt to contribute to the favorable outcome. The cause and significance of the retinal pigment epithelium damage are yet to be determined.

[Introduction]

Subfoveal choroidal neovascular membranes (CNVs) are sequelae of various ocular pathologies affecting the choroid-Bruch's membrane-RPE complex.1 Serous, and hemorrhagic exudation from these membranes, followed by the production of a local fibrous scar, lead to severe reduction in visual acuity (VA). Although laser photoagulation of such membranes associated with age-related macular degeneration (AMD) was found by the Macular Photocoagulation Study (MPS) group to result in a better visual outcome than observation only, VA almost invariably declined following treatment.2-7 This is attributed to transretinal photocoagulation being nonselective, and therefore destruction of the CNV is accompanied by thermal damage to the overlaying and underlying foveal photoreceptors, retinal pigment epithelium (RPE), and choriocapillaris.8-10

A previous attempt to prevent laser photoreceptor damage by using a subretinal delivery system resulted in better results, as reported by other authors.8-10 We report here our early experience in using an endoscope to guide the laser energy, in order to reduce photodamage to the pigment epithelium and choroid, and thereby improve visual acuity in patients with AMD...
in a disappointing visual outcome that was related to damage caused by laser energy to the underlying RPE and choriocapillaris.11

Recent experimental studies with erbium:YAG laser systems showed its suitability for high precision vitreoretinal surgery, including the ablation of epiretinal membranes (ERM).12-16 The 2940 nm wavelength emitted by the laser system corresponds to the maximal absorption peak of water. In a process known as photothermal tissue ablation, the water within the treated tissue, serving as a chromophore, strongly absorbs the laser energy. An expansion bubble forms and collapses within 600 μs. Collapse of the bubble (cavitation) is accompanied by sufficient mechanoacoustic energy to transect or ablate tissue. A sharp edged crater is formed surrounded by a 10-60 μm wide coagulated zone.12-13 The extent of this coagulative damage was shown to decrease further by using a high-repetition pulse rate.16 Considering these laser system's properties, it can theoretically be used in the subretinal space to directly ablate choroidal neovascular membranes while preserving the overlying photoreceptors and underlying choriocapillaris. Further more, the fibrous component of the membrane, which possibly contributes to the retinal damage by acting as a metabolic barrier between the photoreceptors and RPE and/or between the RPE and choriocapillaris, can be reduced in thickness, thereby diminishing its damaging effect.

We have used erbium:YAG laser subretinally to ablate subfoveal choroidal neovascular membranes in 2 patients. To further minimize unwanted damage to the surrounding healthy tissue, we have incorporated two additional factors to the surgical system. The first was the use of a viscoelastic agent (Healon GV®, Pharmacia & Upjohn, Peapack, NJ) to induce macular detachment. The substance, previously shown to be nontoxic when injected into the subretinal space of Yucatan pigs,17 provided a high and stable working space that enabled subretinal-instrument manipulation in a safe distance from the overlying photoreceptors and from RPE surrounding the treated membrane. The material's viscous nature also possibly protected tissue from damage caused by accidental instrumental touch.

The other innovative factor incorporated into the surgical system was the use of a high resolution endoscopic system that enabled controlled delivery of the laser energy directly to the visualized neovascular membrane. This obviated the need for safety margin treatment as practiced by the MPS.18 It also minimized unwanted laser damage that might have occurred by the less than optimal visualization of the subretinal tissues through the semitransparent detached retina in the process of subretinal laser ablation unaided by the endoscopic system.

We report our preliminary results of subretinal, viscoelastic-aided, endoscope-guided ablation of subfoveal choroidal neovascular membranes in 2 eyes of 2 patients, using a high repetition erbium:YAG laser system.

PATIENTS AND METHODS

Laser System
We used a solid-state, 300 μs erbium:YAG laser system (VersaPulse Select Erbium: Coherent, Palo Alto, CA) that emits 2940 nm of light. The energy levels ranged from 0.2 to 2.5 mJ per pulse, and the repetition rate is adjustable in the range of 2 to 200 Hz. The laser output is coupled to a high transmission (80%) midinfrared fiber, 2m long (Coherent), and coupled to its distal end with a 20-gauge intraocular quartz fiberoptic endprobe. The probe we used was straight and tapered with a tip diameter of 100 μm. The laser system has a red diode aiming beam, and is activated by a foot switch.

Endoscope System
We used a high resolution, solid-rod, gradient index technology-based endoscope (Insight-4000 MicroEndoscope: Insight Instruments Inc. Sanford, FL) with a 20-gauge, 50 degree subretinal probe. The endoscope incorporates an internal 300 watt Xenon light source coupled to a bundle of 30-μm fibers embedded perpendicularly around the Grin lens. The system was prefocused for a working distance of less than 2-mm. The image received by the system was delivered to a 21-inch monitor, and recorded along with images from the operating microscope video camera for further evaluation and documentation.

Surgical Procedure
A conventional three-port pars plana vitrectomy was performed in 2 eyes of 2 patients, 1 with AMD-related sub-RPE choroidal neovascular membrane, and the other with presumed ocular histoplasmosis syndrome (POHS)-related subretinal CNV. In both cases, a temporal approach was used. The vitrectomy was completed with the removal of the posterior vitreous face. A small retinotomy was performed along
the horizontal raphe, approximately 3-mm from the border of the neovascular membrane using the tip of a V-Lance blade (Alcon Laboratories Inc. Fort Worth, TX). Commercial viscoelastic hyaluronic acid preparation (Healon GV®, Pharmacia & Upjohn, Peapack, NJ) was then slowly injected through the retinotomy site, using a 27G canula, which produced a high and stable detachment of the macular neurosensory retina. Because of the relative difficulty of the viscoelastic material to dissect under the attached retina, a high tension was built inside the detachment bubble during injection that caused the retinotomy to stretch and acquire a final diameter of approximately 1 mm in both patients. The endoscope probe was inserted through the stretched retinotomy and the neovascular complexes were visualized. The erbium:YAG laser endoprobe was then introduced through the same retinotomy site, its tip held in contact or near contact with the membrane surface, at an angle nearly tangential to it. The laser was activated by the surgeon while moving the probe tip in scanning motion over the identified membrane. Laser bursts of 200 pulses per second, each pulse 300 μsec long were used in both cases. Pulse energy was gradually increased, starting with 0.2 mJ, until moderate uniform tissue whitening, denoting accumulation of debrided material on the membrane surface, was achieved.

After laser ablation was completed, subretinal hyaluronic acid was passively aspirated using a silicone-tipped canula. This was followed by fluid-air and air-gas exchange using a nonexpanding concentration of sulfur-hexafluoride (SF6) gas. The patients were postoperatively instructed to lie face down. Argon laser burns were applied around the retinotomy as soon as visibility allowed.

Case 1

A 38-year-old male was diagnosed as suffering from POHS-related subfoveal membrane in his right eye (Figure 1) with VA reduced to 6/90. A pars plana vitrectomy and a retinotomy along the temporal raphe were performed as described earlier. Using the subretinal endoscope, a round subfoveal fibrovascular membrane was visualized lying under the retina, its borders clearly identified. Erbium:YAG laser treatment was then applied to the membrane surface. The desired tissue effect was obtained with pulse energy levels that ranged from 2 to 2.5 mJ. The surgical procedure was carried out without intraoperative complications. One week later, a retinal detachment was detected and treated with intraocular injection of an expandable volume of SF6 and face down positioning. This failed to reattach the retina and a fluid air exchange, followed by air-SF6 exchange, and laser treatment around the retinotomy were performed two days later. The procedure had to be repeated twice more in the next two months because of the recurrence of the detachment. During the last procedure, approximately eight weeks after membrane laser ablation, a 360° peripheral laser treatment and phacoemulsification followed the fluid-gas exchange. The retina remained attached thereafter.

Examining the retina nine weeks after membrane ablation, a fibrous scar measuring approximately 1.3×0.8 mm was seen at the original location of the neovascular membrane. This was accompanied by a corresponding blocked fluorescence with late staining on fluorescein angiogram (FA) (Figure 2). Surrounding the fibrous scar was a zone of speckled window defect hyperfluorescence measuring approximately 3×2 disc diameters that corresponded roughly with the area of
surgical macular detachment.

Six months after membrane ablation, the best-corrected VA in the operated eye was 6/20. The clinical and angiographic appearance of the scar was generally unchanged from those found two months after ablation (Figure 3). The size of the window defect hyperfluorescence was reduced in size.

A more careful comparison between pre- and postoperative fundus color photography and FA disclosed that a 200 µm retinal translocation with a shift of the foveal sensory retina to a more superior position had taken place during the subsequent retinal detachment surgery.

Case 2

A 78-year-old male was diagnosed as having a subfoveal choroidal neovascular membrane secondary to AMD in his left eye. Best-corrected VA was reduced to counting fingers from a distance of 1 meter. FA (Figure 4) performed three weeks before the operation disclosed a well-defined subfoveal membrane of approximately 1.5 disc areas. A pars plana vitrectomy was performed as described earlier, and after introducing the endoscope into the subretinal space, the fibrovascular membrane was clearly visualized. However, its borders could not be distinctly identified. Instead, the periphery of the membrane was covered by what seemed to be a layer of mottled retinal pigment epithelium that gradually regained a healthier appearance farther away from the center of the membrane. Blood vessels, possibly feeder vessels, approximately 80 µm thick, were seen arranged in a radial pattern at the circumference of the membrane.

Laser treatment was applied to the identified membrane area to obtain the desired moderate whitening effect (energy ranged from 2 to 2.5 mJ). The surgery was then completed as described earlier without complications. On FA performed six weeks later (Figure 5), the membrane appeared somewhat larger compared to that documented three weeks before the procedure, but was exhibiting considerably less leakage. Surrounding the membrane, an area of speckled hyperfluorescence was seen with characteristics of window defect the size of approximately 3x4 disc diameters. This corresponded roughly to the area of retinal detachment induced during the operation. Three months after membrane ablation, the best corrected VA improved to 6/30; and on the FA (Figure 6), the membrane was unchanged in size and showed only mild late staining. The size of the window defect surrounding the membrane reduced in size.

DISCUSSION

Traditional laser photocoagulation of subfoveal neovascular membranes, as practiced by the MPS group, involves passage of laser energy through the retina on its way to the neovascular membrane. This energy is partly absorbed by retinal xanthophyll, causing retinal coagulative damage. Additional damage is caused by heat diffusion from the target tissue to the overlying photoreceptors. Using laser systems emitting wavelengths greater than 530 nm preclude retinal damage by xanthophyll energy absorption, but does not prevent damage by the latter mechanism. Furthermore, because of deeper tissue penetration by longer wavelengths, more damage is caused to the choroidal vasculature underlying the neovascular membrane. The end result of these factors is irreversible foveal photoreceptor damage with loss of visual function.

To avoid retinal damage by laser energy, Thomas and Ibanez have examined the efficacy of subretinal endophotocoagulation in the treatment of AMD-related choroidal neovascular membranes in 3 eyes. Following pars plana vitrectomy, a retinotomy was created along the horizontal raphe, and a small foveal detachment was created by subretinal fluid infusion. A specially designed endolaser probe was then introduced into the subretinal space, and following the landmarks seen on a projected fluorescein angiogram,
endophotocoagulation was performed. The authors did not mention the wavelength of the laser system used. The treatment was angiographically successful, but postsurgical visual outcome was disappointing. This was related to presumed accompanying coagulative damage to the choriocapillaris and RPE underlying the treated membrane.

ElDirini et al\(^2\) have found that inadvertent coagulative necrosis of photoreceptors occurred in rabbits when using subretinal laser energy greater than 1.0 Watts. Thomas and Ibanez did not exclude such a damage as a possible factor influencing the visual outcome of their patients, but found it unlikely, considering the fact that laser energy applied was 500 mW or lower in all three patients.

Another factor that may have contributed to the visual outcome is the compromised view of the subretinal tissues through the detached retina. When detached, the retina is not transparent, but translucent, thereby making identification of the membrane difficult. Laser treatment following topographic landmarks seen on a projected fluorescein angiogram harbor potential inaccuracy, since the landmarks are usually retinal, and when the retina is detached, parallax error is introduced. These factors may lead to inaccurate laser treatment with potential damage to healthy choroidal tissue neighboring the membrane. Inadvertent damage to healthy tissues surrounding the membrane by instrument manipulation is another factor potentially influencing surgical outcome. This is more difficult to control because as mentioned previously, the retina overlying the working space is not transparent.

Our new surgical technique includes several innovative components aimed to achieve an efficient membrane ablation while minimizing inadvertent healthy tissue damage by the aforementioned mechanisms.

**Viscoelastic Macular Detachment**

Detachment of the macula was induced by subretinal injection of the commercially available viscoelastic substance, Healon GV\(^*\) (Pharmacia & Upjohn, Peapack, NJ), which was previously shown to be nontoxic when injected to the subretinal space of Yucatan pigs.\(^7\) Because of the material's high viscosity, it does not easily dissect under the attached retina. A relatively high pressure is consequently built in the expanding subretinal space, stretching the overlying retina to form a high, confined, and stable detachment. This provides a safe space for instrument manipulation, diminishing the risk of inadvertent tissue damage. Furthermore, the viscous property of the substance may theoretically reduce tissue damage once instrument touch has occurred, analogous to corneal endothelial cells protection during anterior segment surgery. The high detachment also theoretically lowers the risk of photoreceptors thermal damage by heat energy emitted from the treated membrane. However, the stretching of the retina during substance injection caused the retinotomies in both patients to stretch and attain a final size of approximately 1 mm. Although useful in the setting of our study, since the large retinotomies allowed the introduction of both endoscope and laser probes without the need to create
a second retinotomy, such a large retinotomy creates a large pericentral scotoma and may influence postoperative VA. The scotoma may further enlarge if laser treatment is to be applied to the retinotomy circumference to decrease the risk of postoperative retinal detachment. In the future, the laser system probe will be adapted to the instrument channel built in the Grin endoscope probe, thereby obviating the need for a large retinotomy or the creation of two separate ones. Detaching the retina by fluid previous to the injection of the viscoelastic substance will probably allow the creation of the desired high detachment, yet avoiding the retinotomy stretching. Other substances, such as low viscosity viscoelastic substances or heavy liquids, may also be found helpful in achieving this.

Subretinal Endoscopy

Imaging the subretinal space through the semi-transparent retina compromises the accuracy of tissue manipulation, as discussed earlier. For the ablation of choroidal neovascular membranes by the erbium:YAG system, the use of an endoscopic system is even more crucial, since a very gradual and controlled removal of tissue layer is needed if underlying tissue damage is to be avoided. Koch et al. has previously demonstrated the ability of the gradient index technology-based endoscope (Insight-4000 Micro-Endoscope: Insight Instruments Inc. Sanford, FL) to provide high-resolution images of the suprachoroidal and subretinal spaces. Using this system, a clear detailed image of the subretinal tissues was seen in both treated cases. In the first patient, a round subretinal fibrovascular membrane, its full extent easily defined, surrounded by healthy appearing RPE cell layer, was seen laying beneath the neurosensory retina. In the second patient, although a fibrovascular membrane was also clearly seen, its borders could not be identified. The membrane seemed to be covered at its periphery by a zone of mottled RPE layer that gradually attained a healthier appearance as distance from the center of the membrane increased. Blood vessels, possibly feeding the fibrovascular membrane, were arranged in a radial pattern at the circumference of the membrane and could theoretically be treated selectively by a laser system with a suitable wavelength. In both cases, the endoscopic image was detailed enough to allow membrane treatment precise in extent and depth.

Erbium:YAG Laser System

The midinfrared (2.94-μm) erbium:YAG laser system (VersaPulse Select Erbium: Coherent, Palo Alto, CA) was found to be capable of a very precise, gradual, and controlled tissue ablation, including that of epiretinal membranes, in laboratory settings, and a clinical trial, followed by a multicenter study. Histologically, the laser energy applied to a tissue surface creates a well defined crater surrounded by a thermal coagulative zone only 10-60 μm wide by a process known as photothermal ablation (described in more details earlier in the article). The lateral coagulative zone extent was shown to further be reduced to a size of up to 12-μm by using the laser in a high-repetition (200 pulses per minute) mode, and by holding the laser probe tangential to the treated surface (personal communication, Dr DJ D’Amico). Blood vessels within this zone were found to thrombose. These
laser properties potentially enable one to gradually ablate choroidal neovascular membranes and coagulate the membrane vessels immediately surrounding the crater, while reducing the risk of inflicting thermal damage to the underlying choriocapillaris. Reducing the thickness of the membrane fibrous component may alleviate its barrier effect and improve outer retinal metabolism. The additional vascular coagulative effect may decrease the risk of bleeding from the treated surface, which in the presence of viscoelastic media may severely interfere with further treatment, and also increase the probability that any membrane remnants will be devoid of active blood vessel. Thus, in order to minimize the risk of physical and thermal damage to the choroidal vessels underlying the only 4-μm thick Bruch’s membrane, one may choose not to ablate the full thickness of the choroidal membrane, but to leave a thin avascular portion of it in place.

First used for the ablation of choroidal neovascular membranes, in this study we chose not to physically ablate the full thickness of the membranes. Instead, treatment was applied to the membrane to achieve uniform moderate whitening of its surface. This effect does not imply thermal coagulation as is does when using lasers with other wavelengths (eg, argon laser), but rather the accumulation of tissue debris on the treated surface and the dehydration of the underlying tissue. If this treatment mode was found to be safe for the underlying choriocapillaris, then a future attempt would be to achieve a more thorough, deep, possibly optic coherent tomography (OCT)-controlled membrane ablation.

The treatment of both patients in our trial resulted in significant improvement in VA. The best-corrected VA of the first patient treated improved from 6/90 to 6/20. This was accompanied by an apparent clinically reduction in the membrane thickness and cessation of the vascular activity within it. No choroidal ischemia could be detected postoperatively on FA. However, the small translocation of the neurosensory retina that occurred following the retinal detachment surgeries may be responsible for this improvement in VA. Best-corrected VA in the second patient treated improved from counting fingers from a distance of 1 meter to 6/30 three months after treatment. Change in membrane thickness could not be judged in this case, but FA showed significant decrease in vascular activity six weeks after treatment and only mild staining six weeks later. The increase in membrane size seen six weeks after treatment compared to its size three weeks before treatment, and the evidence of some post-treatment vascular activity, can imply that no laser effect has been achieved, and that final clinical and angiographic stabilization were instead caused by the natural evolution of the disease. However, the lack of evidence of any increase in membrane size thereafter, and the impressive improvement in post-treatment VA, which is unusual in the natural course of the disease, favor the possibility that the increase in the membrane size, occurred during the preoperative period.

In both patients, postoperative FA showed speckled window defect hyperfluorescence at the general area of the macular detachment induced during the operation. The defect extent diminished during follow up in both cases. This may imply that some damage had been inflicted to the RPE during the surgery, either by laser energy or by the viscoelastic material. Healon GV®, although shown to be nontoxic when injected into the subretinal space in Yucatan pigs, may be responsible to such damage in humans. Another possibility is that the damage was caused not by substance toxicity, but by the relatively high pressure built inside the subretinal space during the substance injection. In this case, detaching the retina by fluid prior to the viscoelastic substance injection may prove to prevent this damage.

Our preliminary results demonstrate that subretinal, viscoelastic assisted endoscope-guided photothermal ablation of choroidal neovascular membranes, is a feasible surgical technique that warrants further investigation.
REFERENCES