Article

Revisiting an Early Treatment for Wet AMD

Is there a role for thermal laser in the era of anti-VEGF therapy?

September 1, 2011

Revisiting an Early Treatment for Wet AMD

Is there a role for thermal laser in the era of anti-VEGF therapy?

Jaclyn L. Kovach, MD • Ingrid U. Scott, MD, MPH

Thermal laser photocoagulation of choroidal neovascularization associated with neovascular age-related macular degeneration (**Figure 1**) is a well-known technique that has been used since the 1970s and studied extensively in the decades that have followed. The success of the treatment, defined as a reduction of vision deterioration, is dependent on the location of the CNV and on the patient's pretreatment vision. The risks of laser-induced retinal damage and recurrent CNV, often culminating in severe vision loss consistent with the natural history of the condition, has led to the preferential use of anti-vascular endothelial growth factor agents or photodynamic therapy for lesions under and near the fovea. In the current era of vision stabilization and potential improvement following anti-VEGF therapy, is there a role for thermal laser photocoagulation in wet AMD?

Figure 1. Laser therapy was a mainstay of treatment for CNV secondary to AMD, but anti-VEGF therapies have swiftly replaced laser as a first-line treatment strategy.

EXTRAFOVEAL CNV

In 1982, results from the Senile Macular Degeneration Study (SMDS) were published by the Macular Photocoagulation Study (MPS) group. This randomized, controlled clinical trial sponsored by the National Eye Institute investigated the efficacy of argon laser photocoagulation in preventing severe visual loss in eyes with symptomatic CNV outside the fovea secondary to AMD. The eligibility criteria included CNV at a distance of 200-2500 µm from the center of the foveal avascular zone, best-corrected visual acuity of at least 20/100, and symptoms related to CNV (decreased acuity, distortion, monocular diplopia). Participants were assigned to either thermal laser treatment or observation.

Argon thermal laser treatment was performed after a retrobulbar block using 200-µm spots of 0.5-second duration to produce a white lesion that covered the entire neovascular complex (including adjacent blood, pigmentation or blocked fluorescence) and extended beyond the lesion by 100-125 µm on all sides. Patients were followed up at three and six months after enrollment and at six-month intervals thereafter with as needed retreatment.

Two hundred twenty-four patients were enrolled, and 113 were treated with laser. One hundred five patients were followed through one year and 20 through two years. After 18 months, 60% of untreated eyes, compared with 25% of treated eyes, had lost six or more lines of vision. Complica tions included retrobulbar hemorrhage in three patients, new subretinal hemorrhage in 31 eyes post-treatment, and Bruch's membrane perforation in one eye.

The SMDS demonstrated that thermal argon photocoagulation of symptomatic extra-foveal CNV reduces the risk of severe vision loss. These results did not apply to patients with serous or hemorrhagic detachments of the RPE.[1] Five-year results from the SMDS showed that mean baseline BCVA was approximately 20/40 for eyes with extrafoveal CNV and had de creased to 20/125 in treated eyes and 20/200 in observed eyes, with a mean loss of 5.2 and 7.1 Snellen lines, respectively.[2] At the time, thermal laser photocoagulation was the first and only proven treatment for CNV caused by AMD.

Busbee et al. conducted a cost-utility analysis of thermal laser photocoagulation of extra-foveal CNV using the five-year data from the SMDS and reported that laser treatment resulted in a mean gain of 0.0740 qualityadjusted life years (QALYs) per patient treated, as compared to observation alone. The mean cost of treatment for the average patient totaled $1,715. The cost per QALY ranged from $16,117 to $49,7663 for thermal laser and over $56,000 for ranibizumab.[4] As a potentially more cost-effective treatment option than ranibizumab, thermal laser photocoagulation of extrafoveal CNV secondary to AMD could be an attractive management alternative if the CNV is small, well defined, and distant from the fovea.

JUXTAFOVEAL CNV

In the 1990s, the MPS group evaluated the effectiveness of thermal laser photocoagulation for the treatment of

geometrical center of the fovea. After five years, almost no eyes with juxtafoveal CNV treated with laser had an improvement in vision compared to baseline. Twenty-five percent of treated eyes and 15% of untreated eyes maintained their baseline visual acuity. More than twice as many treated patients compared to observed patients retained a visual acuity of 20/40 or better, and 25% of laser-treated eyes had a BCVA of 20/400 or worse, compared to 40% of untreated eyes. Mean BCVA at baseline for all patients was approximately 20/60, and after five years, mean BCVA was 20/200 for treated eyes and 20/250 for observed eyes with losses of five and six lines, respectively.

At five years, both groups had lost vision, with severe vision loss occurring in 52% of laser-treated eyes and 61% of untreated eyes. The reason for poor long-term vision in the treated group was associated with the high frequency of persistent or recurrent CNV. Thirty-two percent of the treated group suffered persistent CNV, and 42% had recurrent CNV during the five years. This outcome translated to an estimated 78% five-year rate of persistent or recurrent CNV involving the center of the foveal avascular zone. Close followup was recommended, given the high rate of recurrent CNV.[5] Because both the thermal laser and untreated groups suffered a similar amount of vision loss, and treatment was associated with a high CNV recurrence rate, anti-VEGF therapy is generally favored for juxtafoveal CNV.

SUBFOVEAL CNV

The MPS also evaluated the efficacy of thermal laser photocoagulation for subfoveal CNV. The eligibility criteria included the presence of classic subfoveal CNV, welldemarcated boundaries, and a size of ≤ 3.5 MPS disc areas. Lesions were treated in their entirety with an outline of laser burns of 200-µm spot size and 0.5-second duration and were filled with overlapping laser burns to produce an intense, white laser lesion. Treatment extended 100 µm beyond the peripheral boundaries of all lesion components except for blood, in which case only the blood was covered with laser.

With regard to patients with new subfoveal CNV, mean BCVA was 20/125 for treated and control eyes at baseline and decreased to 20/320 and 20/500 with a mean loss of 3.5 and five lines, respectively, after four years. Forty-seven percent of untreated eyes and 22% of treated eyes lost six or more lines of visual acuity from baseline. Argon green laser and krypton red laser were found to be equivalent. Patients in the treatment group often noticed an immediate loss of visual acuity following treatment.[6-8]

The MPS also evaluated patients who had received prior laser treatment for an extrafoveal or juxtafoveal neovascular lesion and subsequently presented with recurrent CNV through the geometrical center of the foveal avascular zone. These eyes were assigned randomly to laser treatment or observation. Laser treatment was performed with coverage of all classic and occult CNV components and 100 µm beyond the lesion. Treatment extended at least 300 µm into the previous treatment scar and included visible feeder vessels.

At three years, the treated eyes had better visual acuity, but both groups had limited distance visual acuity. Baseline mean BCVA was 20/125 for treated and control eyes, with decreases to 20/250 and 20/320 and losses of three and four lines, respectively, after four years. At three years, 12% of treated eyes and 36% of untreated eyes had lost six or more lines of BCVA from baseline.[7]

Thermal laser photocoagulation can reduce the magnitude of vision loss secondary to subfoveal CNV associated with AMD. Anti-VEGF therapy has replaced this treatment modality for subfoveal lesions, given the potential for visual acuity recovery and stabilization with sustained anti-VEGF treatment. In patients with subretinal fibrosis, persistent leakage and poor visual prognosis, photodynamic therapy may be performed more commonly than thermal laser in an effort to reduce the anti-VEGF treatment burden.

OCCULT CNV

Given the often indistinct borders of occult CNV and the risk of retinal pigment epithelial tears if a pigment epithelial detachment (PED) is present, thermal laser of occult subfoveal CNV has not been widely pursued. Several small, prospective studies have investigated the usefulness of indocyanine green angiography (ICGA), which offers improved CNV and feeder vessel visualization, in guiding the treatment of extrafoveal or juxtafoveal CNV with thermal laser photocoagulation.

At least half of the patients in these studies had a stabilization or improvement in vision. The percentage dropped to 15% in patients with a PED.[9-11] ICGA-guided thermal photocoagulation of the hot spot of extrafoveal retinal

CNV using dynamic ICGA-guided focal thermal laser ablation of the perfusing afferent arteriole, subretinal fluid was eliminated, and small visual acuity improvements were achieved in 40% of patients studied.[13] Anti-VEGF agents are widely accepted as the first-line treatment for occult CNV secondary to AMD.

SUMMARY

For the past 40 years, thermal laser photocoagulation has been a treatment option in the armamentarium of neovascular AMD therapies. At the time of its publication, the MPS offered evidence-based justification for the use of thermal laser as the only proven treatment for classic CNV secondary to AMD. Occult CNV lesions were excluded from these clinical trials, with no proven alternative treatments available. For classic CNV that met the eligibility criteria, thermal laser photocoagulation could, at best, provide a reduction in vision loss, but it carried significant risks.

Even without large, prospective, randomized, controlled trials comparing anti-VEGF therapy to thermal laser, the improved visual potential offered by ranibizumab and bevacizumab has led to a drastic reduction in the use of thermal laser therapy, with its significant risks of visual acuity loss and recurrent CNV. PDT is used more commonly than thermal laser and is sometimes administered in an attempt to decrease the frequency of intravitreal injections in patients with wet AMD.

An argument can be made in favor of thermal laser photocoagulation for small, well-defined extrafoveal CNV, given its attractive cost and logistical burden profiles, but for the treatment of subfoveal and juxtafoveal CNV, either classic or occult, anti-VEGF therapy has been generally accepted as a more effective treatment option. **RP**

REFERENCES

1. Macular Photocoagulation Study Group. Argon laser photocoagulation for senile macular degeneration. *Arch Ophthalmol*. 1982;100:912-918.
2. Macular Photocoagulation Study Group. Argon laser photocoagulation for neovascular maculopathy. Five-year results from randomized clinical trials. *Arch Ophthalmol*. 1991;109:1109-1114.
3. Busbee BG, Brown MM, Brown GC, Sharma S. CME review: A cost-utility analysis of laser photocoagulation for extrafoveal choroidal neovascularization. *Retina*. 2003;23:279-287.
4. Hodge W, Brown A, Cruess A, et al. Pharmacologic management of neovascular age-related macular degeneration: systematic review of economic evidence and primary economic evaluation. *Can J Ophthalmol*. 2010;45:223-230.
5. Macular Photocoagulation Study Group. Laser photocoagulation for juxtafoveal choroidal neovascularization: five-year results from randomized clinical trials. *Arch Ophthalmol*. 1994;112:500-509.
6. Macular Photocoagulation Study Group. Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration. *Arch Ophthalmol*. 1991;109:1220-1231.
7. Macular Photocoagulation Study Group. Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration:updated findings from two clinical trials. *Arch Ophthalmol*. 1993;111:1200-1209.
8. Macular Photocoagulation Study Group. Visual outcome after laser photocoagulation for subfoveal choroidal neovascularization secondary to age-related macular degeneration:the influence of initial lesion size and initial visual acuity. *Arch Ophthalmol*. 1994;112:480-488.
9. Weinberger AW, Knabben H, Solbach U, Wolf S. Indocyanine green guided laser photocoagulation in patients with occult choroidal neovascularisation. *Br J Ophthalmol*. 1999;83:168-172.
10. Donati G, Kapetanios AD, Pournaras CJ. ICG-guided laser photocoagulation of juxtafoveal and extrafoveal occult choroidal neovascularization. *Graefes Arch Clin Exp Ophthalmol*. 1999;237:881-886.
11. Da Pozzo S, Parodi MB, Ravalico G. A pilot study of ICG-guided laser photocoagulation for occult choroidal neovascularization presenting as a focal spot in age-related macular degeneration. *Int Ophthalmol*. 2001;24:187-194.
12. Gupta B, Jyothi S, Sivaprasad S. Current treatment options for retinal angiomatous proliferans (RAP). *Br J Ophthalmol*. 2010;94:672-677.
13. Cousins SW, Bearelly S, Reinoso MA, et al. Dynamic indocyanine green angiography-guided focal thermal laser treatment of fibrotic choroidal neovascularization. *Graefes Arch Clin Exp Ophthalmol*. 2008;246:1677-1683.

Jaclyn L. Kovach, MD, is assistant professor of clinical ophthalmology at the Bascom Palmer Eye Institute of the University of Miami Medical Center. **Ingrid U. Scott, MD, MPH**, is professor of ophthalmology and public health sciences at the Penn State Hershey Eye Center. Dr. Scott received minimal financial compensation as a

Scott can be reached via email at iscott@psu.edu.

Retinal Physician, Issue: September 2011
Table of Contents
Archives