

# Photodynamic Therapy *versus* Thermal Laser Photocoagulation for the Treatment of Recurrent Choroidal Neovascularization due to AMD

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**Abstract.** *The aim of this study was to compare the effectiveness of thermal laser photocoagulation (TLP) to that of photodynamic therapy (PDT) for the treatment of recurrent choroidal neovascularization (CNV) in patients with age-related macular degeneration (AMD). Patients and Methods: We prospectively studied 38 patients (40 eyes) with AMD presented with recurrent CNV after TLP. The study eyes were assigned to one of the two groups according to their treatment (repetition of TLP or PDT). PDT was performed according to the standard protocol. The follow-up time ranged from 9 months to 9 years. Results: The mean best-corrected visual acuity (VA) was statistically significantly lower compared to that of the baseline in both groups of the study. There were no statistically significant differences between the two groups with regard to the stabilization, improvement or decline of the best-corrected VA. Conclusion: According to our results TLP and PDT are equally ineffective for the treatment of recurrent CNV in patients with AMD.*

Age-related macular degeneration (AMD) is the leading cause of central visual loss among individuals 65 years of age and older in developed countries (1, 2).

AMD can be identified into two types: dry or non-neovascular, which accounts for 80% of cases and results in chorioretinal atrophy leading to slow progressive, usually bilateral but non-symmetrical visual loss; and exudative or neovascular, which is characterized by the development of choroidal neovascularization (CNV) that is expanded inwards, subretinally (type I) or intraretinally (type II). This latter type of the disease results in subretinal exudation, hemorrhage, neurosensory retinal detachment and fibrosis

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leading to profound loss of central vision in the vast majority of the patients in a short period of time (usually a few months). The diagnosis of AMD can be made biomicroscopically and confirmed with the use of fluorescein angiography (FA), digital indocyanine angiography (ICGA) and optical coherence tomography (OCT).

For a long time, thermal laser photocoagulation (TLP) was the treatment of choice for patients with exudative AMD. The laser treatment was performed directly on the CNV in order to destroy it. However, a high percentage of the treated patients presented recurrences of the CNV after the TLP treatment. According to the results from previous studies the recurrence rate varied from 25-50% within the first five years after TLP (3-8).

The treatment of the recurrences of CNV is performed either by repetition of TLP (3-5, 9, 10) directly on the recurrent CNV, or, more recently, by photodynamic therapy (PDT) with verteporfin activated by a diode-laser source (11). The main advantage of PDT is that as it is activated by light levels far lower than those used for TLP, it causes minimal damage to healthy tissues. Consequently, it can be used to treat subfoveal lesions.

The purpose of this prospective study was to compare the results of TLP to those of PDT in the treatment of CNV recurrences in patients with exudative AMD. To our knowledge, there is no published study to date comparing the efficacy of these two treatment modalities in the management of CNV recurrence due to exudative AMD.

## Patients and Methods

Thirty-eight consecutive patients with recurrent CNV due to exudative AMD who were referred to the Retina Service of the First Athens University Eye Clinic for evaluation and treatment between 1999-2004 were prospectively included in the study. The recurrence of the CNV was documented by FA and ICGA within the first six weeks after the TLP.

All eyes of the patients in the study were treated either by repetition of the TLP or by PDT. The choice of treatment was decided based on the location of the CNV lesion and its distance from the foveola. According to this criterion the CNV lesion was

Table I. Gender and age of the patients in the study.

	Number of patients			P-value
	PDT	Laser	Total	
Gender				0.836
Males	6	13	19 (50%)	
Females	6	13	19 (50%)	
Age of recurrence (year)				0.791
Mean (±SD)	70.7 (±6.8)	71.1 (±9.9)	71.0 (±9.0)	

classified as extrafoveal (margin more than 200 µm from the center of the foveal avascular zone), juxtafoveal (margin less than 200 µm from the center of the foveal avascular zone, but not under it), and subfoveal (CNV under the center of the foveal avascular zone). All eyes with extrafoveal CNV were treated by TLP, while those with juxtafoveal and subfoveal CNV by PDT.

Exclusion criteria were as follows: age less than 50 years, Snellen visual acuity better than 7/10 or worse than 1/10, any other pathology leading to CNV (e.g. angioid streaks, high myopia, presumed ocular histoplasmosis syndrome, choroidal rupture), as well as a history of more than one recurrence.

After the TLP or PDT all patients were re-evaluated at two weeks, six weeks and every three months for the first two years, and thereafter every six months for the remainder of the follow-up time.

At the initial visit, as well as at every re-examination, all patients underwent a general ophthalmological and retinal assessment including indirect ophthalmoscopy and slit-lamp biomicroscopy with an area centralis contact lens. Best-corrected visual acuity was recorded on standard Snellen charts. Improvement or decline of visual acuity was defined as a change of at least two lines of Snellen acuity. Color and red-free photography, FA and ICGA were performed on all patients at every examination.

During the follow-up, every new extrafoveal recurrence of the CNV after TLP was treated by repetition of the TLP as on the previous occasion. PDT was performed according to the standard protocol (12, 13).

Numerical data in the text and the tables are presented as mean (±SD). The two-tailed paired *t*-test, the Mann-Whitney and the non-parametric Wilcoxon tests were used for the statistical analysis of the data. A *p*-value less than 0.05 was considered statistically significant.

## Results

Thirty-eight patients (40 eyes) met the inclusion-exclusion criteria. Twenty-eight eyes with extrafoveal CNV were treated by TLP, whereas the remaining 12 eyes with juxtafoveal or subfoveal CNV were treated with PDT. The gender and age of the patients in the study are presented in Table I. No statistically significant difference was found between the two groups of patients.

The follow-up time was 2.5 years (±1.4 years) for the PDT-treated patients and 5.0 years (±1.4 years) for the TLP-treated patients (Table II).

Table II. Duration of follow-up.

Follow-up (years)	PDT	Laser	Total
Mean (±SD)	2.5 (±1.4)	5.0 (±1.4)	4.2 (±1.8)
Range	2.3 (0.9-5.0)	5.1 (2.4-9.0)	4.6 (0.9-9.0)

Table III. Initial and final visual acuity compared.

Visual acuity	PDT	Laser	Total	P-value
Initial VA*				
Mean (±SD)	0.37 (±0.20)	0.33 (±0.16)	0.34 (±0.17)	0.541
Final VA**				
Mean (±SD)	0.14 (±0.17)	0.19 (±0.19)	0.17 (±0.18)	0.388
P-value	0.003	0.005	0.004	

\*VA at treatment of the first recurrence; \*\*VA at the last treatment.

Table IV. Change in visual acuity experienced.

Visual Acuity	Number of patients		
	PDT (N)	Laser (N)	Total N (%)
Decline*	10	22	32 (80)
Stabilization or improvement*	2	6	8 (20)
Total	12	28	40 (100)

\*Improvement or decline defined as a change of at least two lines of Snellen acuity.

The mean final best-corrected visual acuity (VA) was statistically significantly lower compared to that of the initial one in both treatment groups (Table III).

The mean initial best-corrected VA of the eyes treated by PDT was 0.37 (±0.20) compared to that of the eyes treated by TLP which was 0.33 (± 0.16) (*p*=0.541). The mean final best-corrected VA of the same groups of patients were 0.14 (±0.17) and 0.19 (±0.19), respectively (*p*=0.388). It is obvious that no statistically significant difference either of the mean initial or the mean final best-corrected VA was found between the two study groups.

Finally, there was no statistically significant difference between the two groups as regards the stabilization or improvement/decline of the best-corrected VA (*p*=0.4655) (Table IV).

## Discussion

Treatment modalities for CNV due to exudative AMD include TLP, PDT, eye surgery and intravitreal injections of anti-VEGF factors (14, 15). TLP has been the mainstay of therapy for the past few decades. However, it does result in a high percentage of recurrences. The MPS group using an Argon green laser reported a percentage of recurrence as high as 54% in eyes with extrafoveal CNV during a 5-year follow-up period (8). Most of the recurrences occurred in the first 2 years after TLP and were on the foveal side of the original CNV. During the same follow-up period of five years, the MPS group reported a recurrence rate of 43-47% among eyes with extrafoveal CNV and 37% among eyes with subfoveal CNV (16). Sorrenson *et al.* (4) using a red krypton laser reported a recurrence rate of 39% during a 1-year follow-up period; most of the recurrences occurred during the first three postoperative months (75%). The CNVs closest to the center of the foveal avascular zone had a higher recurrence rate.

The MPS group studying the efficacy of the TLP in eyes with recurrent CNV (3, 16) found that during the first two years after TLP the recurrence rate was 60% among the eyes with juxtafoveal, 48% among those with extrafoveal and 25% among those with subfoveal recurrences. Our results are in agreement with the disappointing findings of the above mentioned studies, concerning the effectiveness of TLP in the treatment of the recurrences of the CNV due to exudative AMD.

PDT, which was introduced in 2001, presented an alternative treatment for subfoveal CNV lesions which could not be treated adequately with TLP. The effectiveness of PDT in the treatment of subfoveal CNVs due to exudative AMD were studied in two multicenter, prospective, randomized studies known as TAP (12, 13) and VIP (17). At the end of a follow-up period of two years, the results of these studies were very satisfactory, especially for those cases with predominantly classic subfoveal CNV lesions. However, patients with recurrent CNV after TLP were excluded from the study.

In international literature, there is only one retrospective study which examines the effectiveness of PDT in the treatment of subfoveal CNV recurrences after TLP in 19 patients (20 eyes) with exudative AMD (11). The follow-up period of study was one year for the group as a whole, while 16 of them completed a second year of follow-up. At the end of the second year, deterioration of VA greater than 2 Snellen lines was avoided in 7 of the 16 eyes (44%). The conclusion of the study was that PDT could be an indication for the treatment of recurrent subfoveal CNV after prior TLP in patients with exudative AMD.

No prospective study has been published so far comparing the effectiveness of PDT to that of the TLP in the management of CNV recurrences. In our prospective study, we compare the effectiveness of these two treatment modalities in patients with recurrent CNV due to exudative AMD followed-up for a long period of time. Our results for the effectiveness of both treatments could not be characterized as satisfactory.

In conclusion, according to our results, TLP and PDT are equally ineffective for the treatment of recurrent CNV in patients with exudative AMD.

## References

- 1 Macular Photocoagulation Study Group: Laser Photocoagulation of subfoveal recurrent neovascular lesions in age-related macular degeneration. *Arch Ophthalmol* 109: 1232-1241, 1991.
- 2 Macular Photocoagulation Study Group: Recurrent choroidal neovascularization after argon laser photocoagulation for neovascular maculopathy. *Arch Ophthalmol* 104: 503-512, 1986.
- 3 Macular Photocoagulation Study Group: Persistent and recurrent neovascularization after krypton laser photocoagulation for neovascular lesions of age-related macular degeneration. *Arch Ophthalmol* 108: 825-831, 1990.
- 4 Sorenson JA, Yannuzzi LA and Shakin JL: Recurrent subretinal neovascularization. *Ophthalmology* 92: 1059-1074, 1985.
- 5 Monahan PM, Gitter KA, Eichler JD and Cohen G: Evaluation of persistence of subretinal neovascular membranes using digitized angiographic analysis. *Retina* 13: 196-201, 1993.
- 6 Macular Photocoagulation Study Group: Argon laser photocoagulation for senile macular degeneration: results of a randomized clinical trial. *Arch Ophthalmol* 100: 912-918, 1982.
- 7 The Moorfields Macular Study Group: Treatment of senile disciform macular degeneration: a single blind randomized trial by argon laser photocoagulation. *Br J Ophthalmol* 66: 745-753, 1982.
- 8 MPS Group: Argon laser photocoagulation for neovascular maculopathy: five-year results from randomized clinical trials. *Arch Ophthalmol* 109: 1109-1114, 1991.
- 9 Olk RJ and Burgess DB: Treatment of recurrent juxtafoveal subretinal neovascular membranes with krypton red laser photocoagulation. *Ophthalmology* 92: 1035-1046, 1985.
- 10 Regillo CD, Blade KA, Custis PH and O'Connell SR: Evaluating persistent and recurrent choroidal neovascularization. The role of indocyanine green angiography. *Ophthalmology* 105: 1821-1826, 1998.
- 11 Gabel-Ptisterer, Wehner A, Heimann H, Foerster MH and Wachtlim J: Photodynamic therapy with verteporfin for recurrent choroidal neovascularisation (CNV) following prior argon laser coagulation. *Ophthalmologie* 102: 592-596, 2005.
- 12 TAP Study Group: PDT of subfoveal choroidal neovascularization in AMD with verteporfin. Two-year results of 2 randomized clinical trials. *Arch Ophthalmol* 119: 198-207, 2001.
- 13 TAP Study Group: PDT of subfoveal choroidal neovascularization in AMD with verteporfin. Three-year results of an open-labeled extension of 2 randomized clinical trials. *Arch Ophthalmol* 120: 1307-1314, 2002.

- 14 Krzystolic MG, Afshari MA, Adamis AP, Gragoudas ES, Connolly E, O'Neill CA and Miller JW: Prevention of experimental choroidal neovascularization with intravitreal anti-VEGF antibody fragment. *Arch Ophthalmol* 120: 338-346, 2002.
- 15 The Eyetech Study Group: Anti-vascular endothelial growth factor therapy for subfoveal choroidal neovascularization secondary to AMD. Phase II Study Results. *Ophthalmology* 110: 979-986, 2003.
- 16 Macular Photocoagulation Study Group: Persistent and recurrent neovascularization after laser photocoagulation for subfoveal choroidal neovascularization of age-related macular degeneration. *Arch Ophthalmol* 112: 489-499, 1994.
- 17 Verteporfin in PDT Study Group: Verteporfin therapy of subfoveal CNV in AMD: two-year results of a randomized clinical trial including lesions with occult with no classic CNV. Report 2, *Am J Ophthalmol* 131: 541-560, 2001.
- 18 Macular Photocoagulation Study Group: Persistent and recurrent neovascularization after krypton laser photocoagulation for neovascular lesions of ocular histoplasmosis. *Arch Ophthalmol* 107: 344-352, 1989.

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