EXTENDED REPORT

Different transitions of multifocal electroretinogram recordings between patients with age-related macular degeneration and polypoidal choroidal vasculopathy after photodynamic therapy

H Imai, S Honda, Y Nakanishi, H Yamamoto, Y Tsukahara, A Negi

Br J Ophthalmol 2006;90:1524–1530. doi: 10.1136/bjo.2006.092783

See end of article for authors' affiliations

Correspondence to:
H Imai, Department of
Organ Therapeutics,
Division of
Ophthalmology, Kobe
University Graduate
School of Medicine, 7-5-2
Kusunoki-cho, Chuo-ku,
Kobe 650-0017, Japan;
h-i@excite.co.jp

Accepted 16 May 2006
Published Online First
6 July 2006

Aim: To compare and evaluate the transitions in retinal function after photodynamic therapy (PDT) between age-related macular degeneration (AMD) and polypoidal choroidal vasculopathy (PCV) using multifocal electroretinograms (mfERGs).

Methods: 10 eyes with choroidal neovascularisation (CNV) secondary to AMD and 11 eyes with CNV secondary to PCV were included in the study. mfERGs were recorded before PDT, and 1 week and 3 months after PDT. mfERG recordings were acquired by a Veris system (V.3.1.3) using a 103 hexagon stimulus. The first-order kernel was used to calculate amplitudes and latencies. Mean amplitudes and latencies from two central rings rated 0–4° of visual angle were analysed and compared with each disease.

Results: In AMD, the mean first negative peak (N1) amplitudes tended to decrease, and the mean first positive peak (N1P1) amplitudes reduced to significant levels ($p=0.047$) 1 week after PDT. 3 months after PDT, there were no significant differences in the mean N1 and N1P1 amplitudes compared with pre-PDT values. In PCV, there were no significant changes in the mean N1 and N1P1 amplitudes 1 week after treatment. However, 3 months after PDT, mean amplitudes showed significant increases in N1 ($p=0.008$) and N1P1 ($p=0.006$) amplitudes compared with pre-PDT values.

Conclusions: mfERG recording transitions are different between patients with AMD and those with PCV. In patients with AMD, these results may show transient impairments in retinal function 1 week after PDT, but in those with PCV, the efficacy of PDT is superior to the impairment after PDT.

In industrial countries, age-related macular degeneration (AMD) is the leading cause of central visual loss in elderly people.¹ The number of patients with AMD is gradually increasing, and almost one third (27.9%) of the population >75 years of age has AMD.² Polypoidal choroidal vasculopathy (PCV) has been described over the past two decades with a characteristic orange protrusion in fundoscopic examinations.^{3–6} In some cases, the distinction of PCV from AMD is difficult without indocyanine green angiographic (ICG) findings, which show polyp-like pooling of the dye.^{6–9} In about 8–13% of Caucasian patients, PCV has the clinical appearance of exudative AMD when re-examined with ICG.^{8, 10}

Photodynamic therapy (PDT) with verteporfin was shown to be beneficial and safe for the treatment of subfoveal choroidal neovascularisation (CNV) due to AMD,^{11–13} pathological myopia,^{14, 15} idiopathic CNV^{16, 17} and PCV.^{18–20} Most clinical studies have shown the beneficial effects of PDT. Some papers report that PDT for treating patients with PCV requires fewer repeat treatments than for patients with AMD, and PDT is also more effective in treating PCV.^{19, 20}

Multifocal electroretinography (mfERG) is a technique developed by Sutter and Tran,²¹ which allows the mapping of retinal function in the posterior pole through simultaneous stimulation of different areas of the retina. mfERG recordings can provide an objective assessment of retinal function, and its sensitivity in detecting functional abnormalities has been shown in various macular disorders.^{22–23} Several studies have also used mfERG to evaluate changes in retinal function after PDT, and have reported the usefulness of this technique.^{24–28}

The purpose of our study is to compare and assess changes in retinal function at the fovea using mfERG after PDT in patients with AMD and in those with PCV.

PATIENTS AND METHODS

Patients

We retrospectively recruited patients with subfoveal CNV due to AMD, and those with macular-type PCV, who were administered their first PDT. Additional inclusion criteria for the study required that patients have a minimal best-corrected visual acuity of 0.1 by the Landolt ring chart (worthy of the logarithm of the minimum angle of resolution of 1.0), so that they may maintain a steady fixation during mfERG recordings. Patients who had received previous treatments including PDT, direct laser photocoagulation or macular surgery, those who had other diseases that could influence visual acuity and those who had a dense subretinal haemorrhage beyond the fovea that could attenuate the effect of PDT were excluded from the study.

A total of 21 eyes from 21 patients (15 men and 6 women) were studied. The mean patient age was 72.9 (range 59–86) years. The mean diameter of the greatest linear dimension was 3350 (range 1400–6400) μm . Of the 21 patients, 10 were diagnosed with AMD (2 had predominantly classic CNV, 2 had minimally classic CNV and 6 had occult without classic CNV) and 11 with PCV. Table 1 summarises further

Abbreviations: AMD, age-related macular degeneration; CNV, choroidal neovascularisation; ICG, indocyanine green angiography; mfERG, multifocal electroretinography; PCV, polypoidal choroidal vasculopathy; PDT, photodynamic therapy

Table 1 Baseline details of patients before photodynamic therapy

Baseline data of patients	CNV with AMD (n = 10)	PCV (n = 11)	p Value
Women (n)	3	3	0.89
Age (years)	72 (6.75)	74 (6.20)	0.56
GLD (μ m)	3180 (1663)	3510 (1617)	0.65
Visual acuity	0.63 (0.18)	0.66 (0.26)	0.74
Parameters of mfERG			
Amplitude (nV/deg ²)			
N1	11.27 (5.64)	8.27 (4.34)	0.18
N1P1	31.13 (14.93)	21.75 (10.02)	0.10
Latency (ms)			
N1	15.25 (1.43)	16.29 (2.02)	0.19
P1	30.08 (2.75)	30.00 (2.55)	0.95

Values are mean (SD).

AMD, age-related macular degeneration; CNV, choroidal neovascularisation; GLD, greatest linear dimension; N1, first negative peak; N1P1, first positive peak; PCV, polypoidal choroidal vasculopathy. Statistically significant differences were calculated using the χ^2 test with a 2×2 contingency table for dichotomous and categorical variables, and Student's *t* test for continuous variables.

baseline demographic and clinical data. We found no significant differences in the baseline data between AMD and PCV groups.

All patients provided written informed consent after adequate explanations for the purpose and procedures of the study. Procedures used in this study conformed to the tenets of the Declaration of Helsinki.

Photodynamic therapy

PDT was given according to the Treatment of Age-related Macular Degeneration with Photodynamic Therapy and the Verteporfin in Photodynamic Therapy Studies.^{11–13} All patients received a 6 mg/m² infusion of verteporfin (Visudyne; Novartis AG, Bülach, Switzerland) over 10 min, followed by the application of a diode laser at 689 nm to the targeted treatment area 15 min after beginning the infusion. A total light energy of 50 J/cm² and a light dose rate of 600 mW/cm² for 83 s were delivered to the targeted area with an additional 500- μ m border surrounding the intended

Figure 1 Two central rings rated 0–4° of visual angle of 103 hexagons were used for the evaluation of multifocal electroretinography (mfERG) recordings to focus the analysis on changes in central macular function.

Table 2 Mean visual acuity transition in both groups

	Friedman's χ^2 test	Pre-PDT	1 w	3 m
AMD	0.775	0.63 (0.19)	0.52 (0.14)	0.61 (0.27)
PCV	0.746	0.66 (0.27)	0.63 (0.29)	0.57 (0.35)

Values are mean (SD).

AMD, age-related macular degeneration; PCV, polypoidal choroidal vasculopathy; PDT, photodynamic therapy; pre-PDT, before PDT; 1 w, 1 week after PDT; 3 m, 3 months after PDT.

If there was a significant change in the three follow-up periods by Friedman's χ^2 test, Wilcoxon's *t* test with Bonferroni's correction was carried out as a retrospective test.

treatment area. After treatment, patients were instructed to avoid direct sunlight or strong light over the next 5 days.

mfERG testing technique

Serial mfERGs were recorded in all patients before PDT, and 1 week and 3 months after PDT. mfERGs were recorded using the VERIS science V.3.1.3 system (Electro-Diagnostic Imaging, San Mateo, California, USA), with reference to guidelines from the International Society for Clinical Electrophysiology of Vision.²⁹ Multiple retinal areas were simulated using a stimulus array of 103 hexagons with a binary m-sequence length of 2. The overall stimulus pattern subtended an angle of approximately 25° on either side of the fixation. The luminance of the stimulus was 200 cd/m² for bright flashes and 1 cd/m² for dark flashes. The stimulus was displayed using a black-and-white monochrome cathode-ray tube monitor.

Before the mfERG recording, the maximum mydriasis was obtained using eye drops containing 0.5% tropicamide and 0.5% phenylephrine. All patients were kept in ordinary room light for 15 min for light adaptation before testing. Burien–Allen bipolar contact lens electrodes (Hansen Ophthalmic Laboratories, Iowa City, Iowa, USA) were used for mfERG recordings. Room lights were maintained throughout the recordings. Retinal signals were filtered with low-frequency and high-frequency cut-offs of 10 and 300 Hz, respectively, and amplified with a gain of 100 000.

Analysis of mfERG

First-order kernel mfERG responses were analysed. Two central rings rated 0–4° of the visual angle of the hexagon were applied (fig 1). As our purpose was to assess the influence of PDT on foveal function, the whole measurement area must be covered by the PDT irradiation area. The area of the central two rings almost matched the foveal area and was also fully covered by the PDT irradiation area in all patients in this study. The first negative peak (N1) and the first positive peak (N1P1) response amplitudes were then measured. The N1 response amplitude was measured from the starting baseline to the base of the N1 trough, and the N1P1 response amplitude from the N1 trough to the P1 peak. The N1 and P1 peak latencies were measured from the onset of the stimulus through the N1 trough and the P1 peak.

Statistical analyses

To confirm the dispersion of baseline data between patients with PCV and those with AMD, data were analysed using χ^2 tests with 2×2 contingency tables for dichotomous variables and Student's *t* tests for continuous variables.

To verify the transition of parameters in each group, visual acuity and averaged N1 and P1 mfERG response amplitudes and peak latencies of two central rings at different time intervals after PDT were compared with corresponding baseline pre-PDT value using Friedman's χ^2 test. When

significant differences were obtained, Wilcoxon's *t* tests with Bonferroni's correction were carried out as retrospective tests.

To compare the effect of PDT on N1 and N1P1 amplitudes between AMD and PCV groups, the amplitude at each time point after PDT was subtracted by the individual pre-PDT amplitude, and changes between pre-PDT and post-PDT amplitudes were collected for each patient, then Student's *t* test was used.

To analyse visual acuity, values of the logarithm of the minimum angle of resolution were calculated from the Landolt ring chart outcomes. All data were statistically analysed using StatView V.5; $p \leq 0.05$ was considered significant.

RESULTS

Complications and side effects

No general or ocular adverse event was observed during the course of the study, including severe subretinal haemorrhage, retinal pigment epithelial tears, vitreous haemorrhage or severe visual acuity loss.

Analysis of transitions of each parameter in AMD and PCV groups

Visual acuity

We found no statistically significant difference in mean visual acuity measured between AMD and PCV groups throughout the study period. The mean visual acuity tended to increase successively during the follow-up period in patients with PCV after PDT, but the increase was not significant ($p = 0.75$; table 2).

Mean N1 and N1P1 response amplitudes

Table 3 lists the mean N1 and N1P1 retinal response amplitudes before PDT, and 1 week and 3 months after PDT in patients with AMD. The mean N1 response amplitude tended to decrease 1 week after PDT, but the decrease was not significant ($p = 0.070$). For mean N1P1 response amplitudes, we found a significant reduction in retinal response amplitudes 1 week after PDT ($p = 0.047$). Three months after PDT, the mean N1 and N1P1 retinal response amplitudes were equivalent to those before PDT.

Table 4 lists the mean N1 and N1P1 retinal response amplitudes in patients with PCV before PDT, and 1 week and 3 months after PDT. We found no significant reduction in retinal response amplitudes (mean N1, $p = 0.412$; N1P1, $p = 0.362$) 1 week after PDT. Three months after PDT, the mean N1 and N1P1 retinal response amplitudes showed significant increases for both the N1 ($p = 0.008$) and N1P1 ($p = 0.006$) responses (compared with corresponding pre-PDT values).

Mean N1 and P1 peak latencies

Tables 3 and 4 list the mean N1 and P1 peak latencies before PDT, and 1 week and 3 months after PDT. We found no statistically significant change in mean peak latencies for both mean N1 and P1 in any of the analysed groups from either disease.

Figures 2 and 3 show the typical mfERG transitions in patients with AMD and in those with PCV, respectively.

Difference in mean N1 and N1P1 response amplitudes between two groups

One week after PDT, the mean change in N1 and N1P1 response amplitudes in the AMD group seemed lower than that in the PCV group, but the difference was not significant (N1, $p = 0.050$; N1P1, $p = 0.057$; fig 4).

Three months after PDT, the mean change in N1 response amplitudes in the PCV group seemed higher than that in the AMD group, but the difference was not significant ($p = 0.061$). The mean change in N1P1 response amplitudes was significantly higher in the PCV group than that in the AMD group ($p = 0.01$; fig 5).

DISCUSSION

In this study, we found no significant change in visual acuity by PDT in AMD and PCV groups, whereas there was a difference in mfERG outcomes between the two groups. In AMD, we found transient decreases in N1P1 amplitudes at 1 week, and a recovery to pre-PDT levels 3 months after PDT. However, N1 and N1P1 amplitudes increased continuously during the follow-up period in patients with PCV. Changes in N1 and N1P1 amplitudes 1 week after PDT tended to worsen, although the worsening was not significant in the AMD group compared with the PCV group. The change in the N1 response amplitude seemed better in the PCV group than in the AMD group 3 months after PDT, and the change in the N1P1 amplitude was significantly better in the PCV group when compared with AMD.

The natural course of AMD with CNV is often progressive and the final visual prognosis is poor. PDT is reported to be an effective treatment for CNV secondary to AMD for the stabilisation of visual acuity compared with the natural course.¹⁻³ Recently, several studies reported the efficacy of PDT for patients with PCV.¹⁸⁻²⁰ For example, Chan *et al*¹⁹ reported the early improvement in clinical findings and the regression of polypoidal lesions in the angiographic findings shortly after PDT, and the visual acuity was stable or improved in 95% of patients at a 1-year follow-up in patients with PCV. The number of treatments necessary to inactivate the PCV lesion was lower than the PDT sessions necessary to treat CNV secondary to AMD. These results indicate that PCV is more suitable for PDT than it is for AMD.

Table 3 Mean amplitude and latency transitions in patients with age-related macular degeneration

Amplitude	Friedman's χ^2 test	Pre-PDT (nV/deg ²)	1 w (nV/deg ²)	3 m (nV/deg ²)
N1	$p = 0.045$	11.27 (5.10)	8.64 (3.68) ($p = 0.070$)	11.99 (4.16) ($p = 0.324$)
N1P1	$p = 0.02$	31.13 (15.53)	24.74 (9.37) ($p = 0.047$)	30.69 (11.72) ($p = 0.399$)
Latency	Friedman's χ^2 test	Pre-PDT (ms)	1 w (ms)	3 m (ms)
N1	0.139	15.25 (1.30)	15.43 (1.55)	16.25 (1.51)
P1	0.723	30.08 (2.48)	29.74 (1.38)	29.65 (2.84)

Values are mean (SD).

N1, first negative peak; N1P1, first positive peak; PDT, photodynamic therapy; Pre-PDT, before PDT; 1 w, 1 week after PDT; 3 m, 3 months after PDT.

If there was a significant change in the three follow-up periods by Friedman's χ^2 test, Wilcoxon's *t* test with Bonferroni's correction was carried out as a retrospective test.

Table 4 Mean amplitude and latency transitions in patients with polypoidal choroidal vasculopathy

Amplitude	Friedman's χ^2 test	Pre-PDT (nV/deg ²)	1 w (nV/deg ²)	3 m (nV/deg ²)
N1	$p=0.035^*$	8.27 (3.97)	8.55 (4.49) ($p=0.412$)	11.75 (4.23) ($p=0.008^+$)
N1P1	$p=0.007^*$	21.75 (9.15)	22.55 (11.23) ($p=0.362$)	32.14 (11.26) ($p=0.006^+$)
Latency	Friedman's χ^2 test	Pre-PDT (ms)	1 w (ms)	3 m (ms)
N1	0.328	16.29 (1.84)	17.59 (2.15)	16.37 (1.63)
P1	0.239	30.00 (2.33)	30.98 (1.73)	29.85 (1.91)

Values are mean (SD). N1, first negative peak; N1P1, first positive peak; PDT, photodynamic therapy; Pre-PDT, before PDT; 1 w, 1 week after PDT; 3 m, 3 months after PDT.
If there was a significant change between the three follow-up periods by Friedman's χ^2 test, Wilcoxon's t test with Bonferroni's correction was carried out as a retrospective test.

In our study, the N1 amplitudes tended to decrease and the decreases in N1P1 amplitudes were statistically significant at 1 week, and then recovered to pre-PDT levels at 3 months in patients with AMD. By contrast, the decrease in amplitudes at 1 week was not found in patients with PCV. Furthermore, the N1 and N1P1 amplitudes increased significantly at 3 months in patients with PCV.

Several studies have used mfERGs to evaluate the changes in retinal function after PDT.^{24–28} However, previous reports showed the effect of PDT in the retinal function only at short term or at long term after PDT. In this study, we aimed to compare the effect of PDT between these diseases both at short term and at long term after PDT. PDT is usually administered every 3 months if needed, but the retina, including the retinal pigment epithelium, and choriocapillaries are likely to be damaged gradually as PDT is repeated. For these reasons, 3 months after PDT should be the most appropriate term to evaluate the late-phase effect of a single PDT. In addition, as mfERG was carried out at 4 days according to previous reports,²⁸ or at 3 and 7 days,²⁷ to evaluate a short-term effect of PDT, we also carried out mfERG at 1 week after PDT to compare our results with those of previous reports.

Lai *et al*²⁸ and Liang *et al*²⁷ showed a transient reduction in retinal function using mfERG on short-term results after

PDT. Previous studies have documented that probable causes for transient impairments in retinal function during early phases after PDT are due to acute inflammatory responses or ischaemic changes evaluated with optical coherence tomographies, fluorescein angiographies, ICGs and animal models. These phenomena may be related to transient visual fluctuations and disturbances commonly experienced by patients during the first week after PDT.^{30–36} Lai *et al*²⁸ showed decreases in N1 and N1P1 amplitudes and increases in P1 latency 4 days after PDT, and recovery 1 month after PDT, in three central rings of 103 hexagons. They suggested that the transient impairment of retinal function causes the common adverse event of subjective visual outcome early after PDT. On the other hand, Liang *et al*²⁷ measured and compared all six rings of 103 hexagons before PDT, and 3 or 7 days after PDT. Their results showed that N1 and P1 latencies and amplitudes in all rings remained unchanged at 3 or 7 days, and they concluded that there was no considerable evidence to suggest an adverse effect of PDT during early stages of treatment, as detected by mfERG recordings. One of the reasons for this discrepancy may be because of the dissimilarity of diagnoses between the two studies. Lai *et al*²⁸ included three patients with AMD, four with PCV, four with myopic CNV, four with idiopathic CNV and two with CSC. Liang *et al*²⁷ included 12 patients with AMD, two with myopic

Figure 2 Data from a patient who was diagnosed with age-related macular degeneration. The peak amplitude decreased 1 week after photodynamic therapy (PDT; 1 w), but returned to pre-PDT levels 3 months after PDT (3 m). (A) three-dimensional density plot; (B) trace array.

Figure 3 Data from a patient who was diagnosed with polypoidal choroidal vasculopathy. The peak amplitude remained 1 week after photodynamic therapy (PDT; 1 w) and significantly increased 3 months after PDT (3 m). (A) three-dimensional density plot; (B) trace array. Pre-PDT, pre-PDT level.

CNV and three with idiopathic CNV. In our study, we found a difference in the transition of N1 and N1P1 amplitudes between patients with AMD and those with PCV 1 week after PDT, suggesting a disease-dependent effect of PDT on retinal function during the early phase after PDT. Results from mfERG recordings in patients with PCV 1 week after treatment may include a recovery effect for the disease. In other words, the better electrophysiological responses after PDT might have outweighed the side effects of photoreceptor depression in PCV. Grouping and averaging methods for mfERG recordings may provide another reason for the

different results in the two studies. In our study, we used two central rings of 103 hexagons for analysis, to focus strictly on foveal function.

In another study that focused on long-term results after PDT, Moschos *et al*²⁶ showed an increase in retinal response densities 6 months after PDT in patients with myopic CNV. In our study, 3 months after PDT, N1 and N1P1 amplitude responses remained unchanged in patients with AMD, but increased markedly in patients with PCV. The previous result suggests the difference of efficacy between each disease and the advantage of PDT to treat PCV over AMD.

Figure 4 Change in the response amplitude between 1 week after photodynamic therapy (PDT) and pre-PDT. First negative peak (N1;A) and first positive peak (N1P1;B) response amplitudes seemed lower in patients with age-related macular degeneration (AMD) than in those with polypoidal choroidal vasculopathy (PCV), but there was no significance (NS).

Figure 5 Change in response amplitude between 3 months after photodynamic therapy (PDT) and pre-PDT. First negative peak (N1;A) response amplitudes seemed higher in patients with polypoidal choroidal vasculopathy (PCV) than in those with age-related macular degeneration (AMD), but there was no significance (NS) (right). For first positive peak (N1P1;B) response amplitudes, there was a significant increase in the PCV group compared with that in the AMD group. *, significant

At 3 months in PCV, functional improvements in mfERG were shown, but not in visual function by visual acuity. We consider that mfERG detecting the electrophysiological changes at the photoreceptors is more sensitive to evaluate the effect of PDT than visual acuity measurements.

Of course, limitations to this study must be considered. Firstly, a selection bias may have occurred, as we included only patients with a best-corrected visual acuity of 20/200 or better; patients with poorer vision were excluded from the study. This inclusion criterion was applied to ensure that patients could maintain good fixation throughout the mfERG recordings to increase the accuracy of serial comparisons. Alternatively, a fundus camera-guided mfERG system may enable a more precise monitoring of the recording. Secondly, there was no control group for comparison and the follow-up period was relatively short to evaluate the treatment effects. A randomised controlled clinical trial with a longer follow-up period may be needed to confirm the benefit of mfERG to analyse the retinal function after PDT.

In conclusion, mfERG recordings may be a good source to compare the functional outcome after PDT between patients with AMD and those with PCV.

Authors' affiliations

H Imai, S Honda, Y Nakanishi, H Yamamoto, Y Tsukahara, A Negi, Department of Organ Therapeutics, Division of Ophthalmology, Kobe University Graduate School of Medicine, Kobe, Japan

Competing interests: None.

REFERENCES

- Segato T, Midena E, Blazino MC. Age-related macular degeneration. *Aging (Milano)* 1993;5:165-76.
- Leibowitz HM, Krueger DE, Maunier LR, et al. The Framingham Eye Study monograph: an ophthalmological and epidemiological study of cataract, glaucoma, diabetic retinopathy, macular degeneration, and visual acuity in a general population of 2631 adults, 1973-1975. *Surv Ophthalmol* 1980;24(Suppl):335-610.
- Yannuzzi LA, Sorenson J, Spaide RF, et al. Idiopathic polypoidal choroidal vasculopathy (IPCV). *Retina* 1990;10:1-8.
- Kleiner RC, Brucker AJ, Johnston RL. The posterior uveal bleeding syndrome. *Retina* 1990;10:9-17.
- Stern RM, Zakov ZN, Zegarra H, et al. Multiple recurrent serous anguinous retinal pigment epithelial detachments in black women. *Am J Ophthalmol* 1985;100:560-9.
- Uyama M, Matsubara T, Fukushima I, et al. Idiopathic polypoidal choroidal vasculopathy in Japanese patients. *Arch Ophthalmol* 1999;117:1035-42.
- Kwok AK, Lai TY, Chan CW, et al. Polypoidal choroidal vasculopathy in Chinese patients. *Br J Ophthalmol* 2002;86:892-7.
- Yannuzzi LA, Ciardella A, Spaide RF, et al. The expanding clinical spectrum of idiopathic polypoidal choroidal vasculopathy. *Arch Ophthalmol* 1997;115:478-85.
- Spaide RF, Yannuzzi LA, Slakter JS, et al. Indocyanine green videoangiography of idiopathic polypoidal choroidal vasculopathy. *Retina* 1995;15:100-10.
- Ciardella AP, Donsoff IM, Huang SJ, et al. Polypoidal choroidal vasculopathy. *Surv Ophthalmol* 2004;49:25-37.
- Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin. One-year results of 2 randomized clinical trials: TAP report 1. *Arch Ophthalmol* 1999;117:1329-45.
- Treatment of Age-related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin. Two-year results of 2 randomized clinical trials: TAP report 2. *Arch Ophthalmol* 2001;119:198-207.
- Verteporfin in Photodynamic Therapy Study Group. Verteporfin therapy of subfoveal choroidal neovascularization in age-related macular degeneration: two-year results of a randomized clinical trial including lesions with occult with no classic choroidal neovascularization: verteporfin in photodynamic therapy report 2. *Am J Ophthalmol* 2001;131:541-60.
- Verteporfin in Photodynamic Therapy Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in pathologic myopia with verteporfin: 1-year results of a randomized clinical trial. VIP report no. 1. *Ophthalmology* 2001;108:841-52.
- Blinder KJ, Blumenkranz MS, Bressler NM, et al. Verteporfin therapy of subfoveal choroidal neovascularization in pathologic myopia: 2-year results of a randomized clinical trial. VIP report no. 3. *Ophthalmology* 2003;110:667-73.
- Spaide RF, Martin ML, Slakter J, et al. Treatment of idiopathic subfoveal choroidal neovascular lesions using photodynamic therapy with verteporfin. *Am J Ophthalmol* 2002;134:62-8.
- Chan WM, Lam DS, Wong TH, et al. Photodynamic therapy with verteporfin for subfoveal idiopathic choroidal neovascularization: one-year result of an uncontrolled, prospective case series. *Ophthalmology* 2003;110:2395-402.

- 18 **Quaranta M**, Mauget-Faysse M, Coscas G. Exudative idiopathic polypoidal choroidal vasculopathy and photodynamic therapy with verteporfin. *Am J Ophthalmol* 2002;**134**:277–80.
- 19 **Chan WM**, Lam DSC, Lai TYY, et al. Photodynamic therapy with verteporfin for symptomatic polypoidal choroidal vasculopathy. *Ophthalmology* 2004;**111**:1576–84.
- 20 **Spaide RF**, Donsoff I, Lam DL, et al. Treatment of polypoidal choroidal vasculopathy with photodynamic therapy. *Retina* 2002;**22**:529–35.
- 21 **Sutter EE**, Tran D. The field topography of ERG components in man—I. The photopic luminance response. *Vision Res* 1992;**32**:433–46.
- 22 **Apostolopoulos MN**, Koutsandrea CN, Moschos MN, et al. Evaluation of successful macular hole surgery by optical coherence tomography and multifocal electroretinography. *Am J Ophthalmol* 2002;**134**:667–74.
- 23 **Marmor MF**, Tan F. Central serous chorioretinopathy: bilateral multifocal electroretinographic abnormalities. *Arch Ophthalmol* 1999;**117**:184–8.
- 24 **Palmowski AM**, Allgayer R, Heinemann-Vernaleken B, et al. Influence of photodynamic therapy in choroidal neovascularization of focal retinal function assessed with the multifocal electroretinogram and perimetry. *Ophthalmology* 2002;**109**:1788–92.
- 25 **Rüther K**, Breidenbach K, Schwartz R, et al. Testing central retinal function with multifocal electroretinography before and after photodynamic therapy. *Ophthalmologie* 2003;**100**:459–64.
- 26 **Moschos MN**, Panayotidis D, Moschos MM, et al. A preliminary assessment of macular function by MF-ERG in myopic eyes with CNV with complete response to photodynamic therapy. *Eur Ophthalmol* 2003;**13**:461–7.
- 27 **Liang L**, Jin C, Wen F, et al. The changes of multifocal electroretinography in the early stage of photodynamic therapy for choroidal neovascularization. *Doc Ophthalmol* 2003;**107**:165–70.
- 28 **Lai TY**, Chan WM, Lam DS. Transient reduction in retinal function revealed by multifocal electroretinogram after photodynamic therapy. *Am J Ophthalmol* 2004;**137**:826–33.
- 29 **Marmor MF**, Hood DC, Keating D, et al. Guidelines for basic multifocal electroretinography (mfERG). *Doc Ophthalmol* 2003;**106**:105–15.
- 30 **Costa RA**, Farah ME, Cardillo JA, et al. Immediate indocyanine green angiography and optical coherence tomography evaluation after photodynamic therapy for subfoveal choroidal neovascularization. *Retina* 2003;**23**:159–65.
- 31 **Michels S**, Schmidt-Erfurth U. Sequence of early vascular events after photodynamic therapy. *Invest Ophthalmol Vis Sci* 2003;**44**:2147–54.
- 32 **Husain D**, Kramer M, Kenny AG, et al. Effects of photodynamic therapy using verteporfin on experimental choroidal neovascularization and normal retina and choroid up to 7 weeks after treatment. *Invest Ophthalmol Vis Sci* 1999;**40**:2322–31.
- 33 **Moshfeghi DM**, Kaiser PK, Grossniklaus HE, et al. Clinicopathologic study after submacular removal of choroidal neovascular membranes treated with verteporfin ocular photodynamic therapy. *Am J Ophthalmol* 2003;**135**:343–50.
- 34 **Flower RW**, von Kerczek C, Zhu L, et al. Theoretical investigation of the role of choriocapillaris blood flow in the treatment of subfoveal choroidal neovascularization associated with age-related macular degeneration. *Am J Ophthalmol* 2001;**132**:85–93.
- 35 **Wachtlin J**, Behme T, Heimann H, et al. Concentric retinal pigment epithelium atrophy after a single photodynamic therapy. *Graefes Arch Clin Exp Ophthalmol* 2003;**241**:518–21.
- 36 **Rogers AH**, Martidis A, Greenberg PB, et al. Optical coherence tomography findings following photodynamic therapy of choroidal neovascularization. *Am J Ophthalmol* 2002;**134**:566–76.