Monitoring of photodynamic therapy results in age-related macular degeneration by means of preferential hyperacuity perimeter

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PURPOSE. *To describe changes revealed by Zeiss Preferential Hyperacuity Perimeter (PreView PHP) in age-related macular degeneration (AMD), before and after photodynamic therapy (PDT), and determine usefulness of such monitoring.*
METHODS. *Forty patients (40 eyes) with subfoveolar choroidal neovascularization (CNV) and 20 volunteers with cataract (40 eyes) were examined in a prospective study. Control group was screened for false positive results to evaluate reliability of the test. Subfoveolar CNV was confirmed by fluorescein angiography and optical coherence tomography (OCT). Best-corrected visual acuity (BCVA) and macular visual field in the PHP (area and intensity of distortion) were assessed 1 day before and 1 week and 4 weeks after PDT.*
RESULTS. *Four weeks after PDT there was improvement in PHP results in 20 eyes (50%), stabilization in 15 eyes (37.5%) and progression in 5 eyes (12.5%). At this time there was BCVA improvement in 9 eyes (22.5%), stabilization in 28 eyes (70%), and worsening in 3 eyes (7.5%). 1 week after PDT 30 eyes (75%) presented temporary progression in PHP but only 3 patients (7.5%) presented temporary decrease of visual acuity and progression in OCT. Correlation coefficient of BCVA and PHP results was low during whole study. There was no significant change in control group during observation. 17.5% false positive PHP results were obtained at baseline. In the PDT group no false negative results were noted.*
CONCLUSIONS. *Visual outcome after PDT cannot be predicted with use of PreView PHP. Temporary progression of changes in PHP 1 week after PDT can be expected in most cases. (Eur J Ophthalmol 2007; 17: 768-75)*

KEY WORDS. *Age-related macular degeneration, AMD, PDT, Photodynamic therapy, PHP, Preferential hyperacuity perimetry*

INTRODUCTION

Zeiss PreView PHP (Fig. 1) is a device used for qualitative evaluation of distortion areas in the macula based on interactive cooperation with a patient. PHP (Fig. 2) utilizes human ability to detect subtle misalignment of one object relative to another in space–hyperacuity or Vernier acuity. During the test a patient marks distortion areas in dotted lines displayed on a screen. Angle resolution of PHP is 3-6 angular seconds–10 times more than in standard visual acuity testing by Snellen (1), the sensitivity of this method is higher than in case of the Amsler test (2). Results of PHP tests are almost not affected by patient contrast sensitivity (3), age (4, 5), and optic media transparency (6). Currently this is the only device for monitoring age-related macular degeneration (AMD) progression approved by the Food and Drug Administration.
This method makes possible earlier detection of AMD

Fig. 1 - *PreView PHP (Zeiss).*

Fig. 2 - *Normal PHP results.*

metamorphopsias of neovascular membrane origin (Fig. 3) (7) than patient self-detection also by means of the Amsler test (2). PHP gives ophthalmologists the opportunity to evaluate metamorphopsia (area and intensity) within 14 degrees of the central field of vision and monitor changes during follow-up visits. Metamorphopsias in choroidal neovascularization (CNV) develop due to elevation of retinal pigment epithelium (RPE) and photoreceptors by neovascular membrane (8).

High PHP sensitivity enables observation of pathologic changes, early detection of metamorphopsias suggesting CNV (7), and referral of patients to other procedures for confirmation of CNV. These procedures include fluorescein angiography and optical coherence tomography that are used to qualify a patient for treatment, and in some cases indocyanine angiography for extended diagnostics.

The aim of the study was to describe hyperacuity pattern changes after photodynamic therapy (PDT) and to determine usefulness of such evaluation by means of PreView PHP in monitoring patients undergoing PDT with Visudyne.
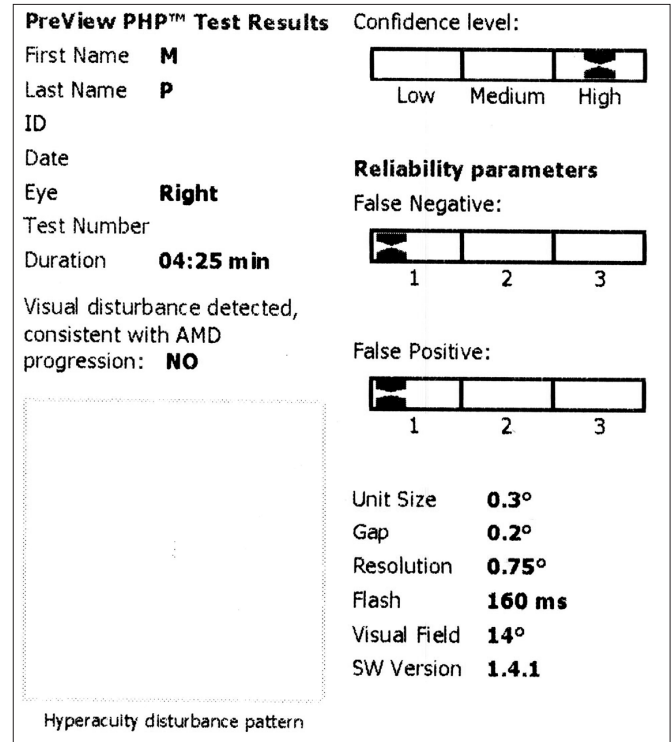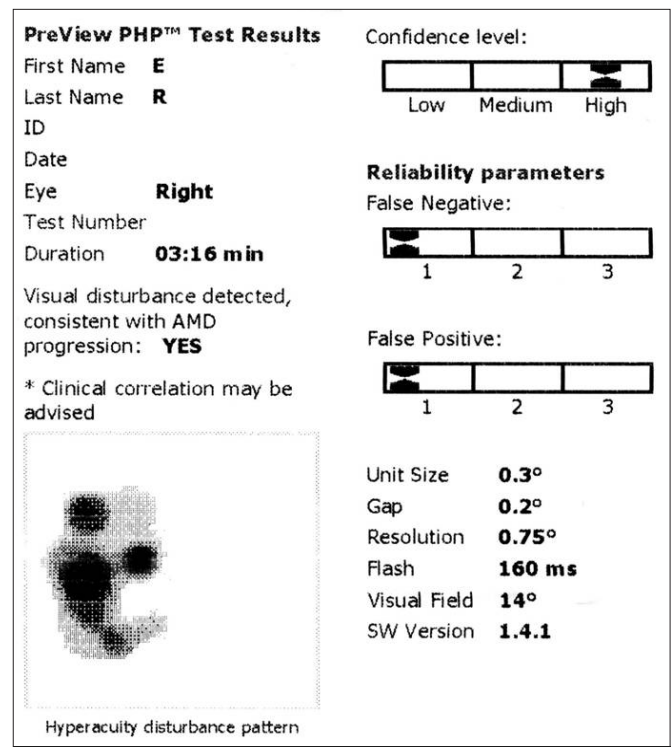

Fig. 3 - *PHP in age-related macular degeneration with choroidal neovascularization.*
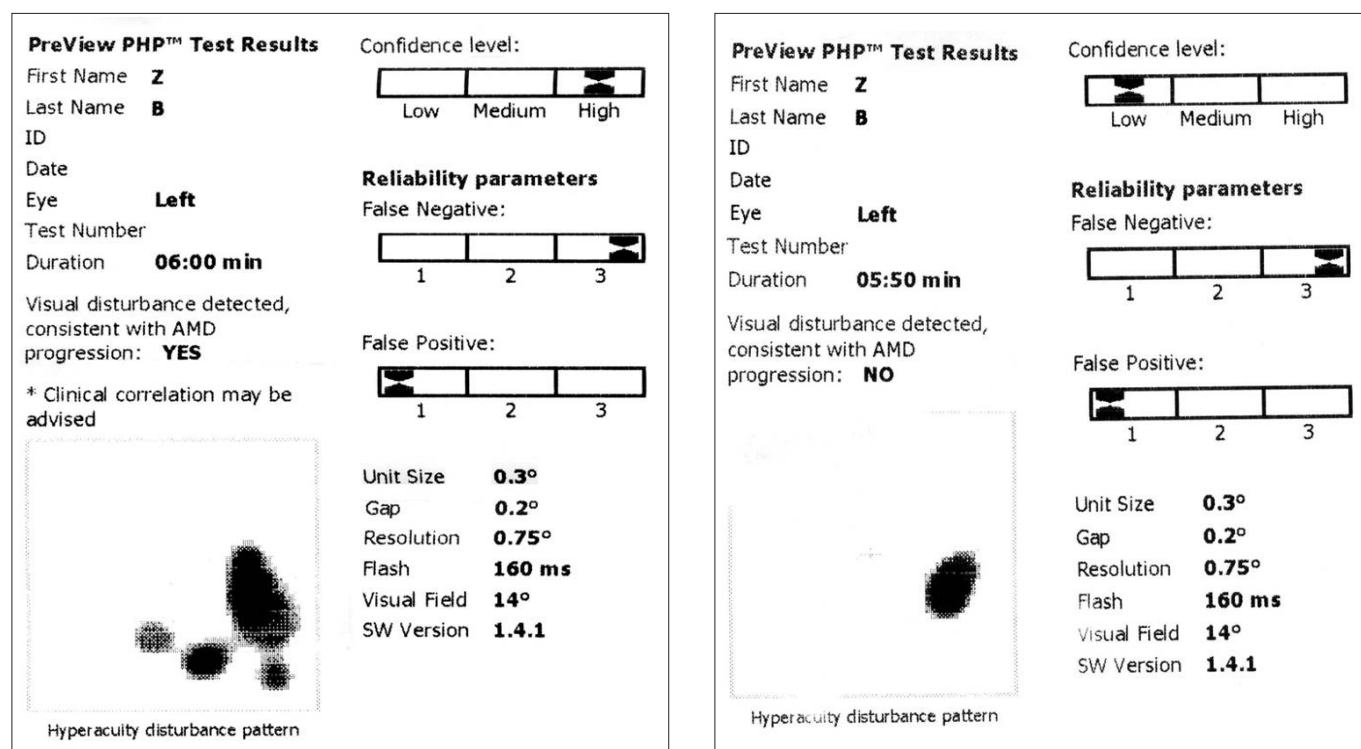
Fig. 4 - *Improvement in PHP after photodynamic therapy.*

METHODS

Forty eyes (40 patients) with wet form of AMD, subfoveolar neovascularization (confirmed by fluorescein angiography and optical coherence tomography), and best-corrected visual acuity (BCVA) between 0.3 and 0.7 (logMAR score, ETDRS charts) were examined. Forty eyes (20 volunteers) were examined as a control group to assess reproducibility and false positive results. Only patients with high confidence level in PHP at baseline were qualified for the study. A total of 68 patients were screened. Five patients with AMD and three volunteers had low confidence level and were excluded at baseline.

The study group consisted of 27 women, 13 men, age 52 to 80 (mean 71.3; SD 8.1). The control group consisted of 12 women, 8 men, age 50 to 79 (mean 69.6; SD 7.5) without macular pathology (confirmed with biomicroscopy and OCT), BCVA between 0.2 and 0.7 (logMAR score), lower visual acuity due to cataract.

Dynamics of hyperacuity pattern changes during treatment were evaluated on the basis of PHP macular vision area map comparison. PHP was done three times: 1 day before and 1 week and 4 weeks after PDT with Visudyne.

The same strategy was used in controls.

Pathologic changes before PDT were observed in all examined eyes in the study group.

RESULTS

BCVA by ETDRS charts before PDT in study group: 0.3–0.4 in 9 cases (22.5%), 0.42–0.5 in 6 cases (15%), 0.52–0.6 in 20 cases (50%), and 0.62–0.7 in 5 cases (12.5%).

Four weeks after PDT there was PHP macular vision area improvement in 20 (50%) patients (Fig. 4), stabilization in 15 (37.5%) patients (Fig. 5), and worsening in 5 (12.5%) patients (Fig. 6). Changes in PHP 4 weeks after PDT are detailed in Figure 7.

BCVA was improved in 9 patients (22.5%)—by 16 letters in 1 (2.5%) patient, by 11–15 letters in 4 (10%) patients, and by 6–10 letters in 4 (10%) patients. Actual visual acuity stabilization (±5 letters) was observed in 28 (70%) patients. Visual acuity worsening was observed in 3 (7.5%) patients – by 6–10 letters in 2 (5%) patients and by 14 letters in 1 (2.5%) patient. Changes in visual acuity 4 weeks
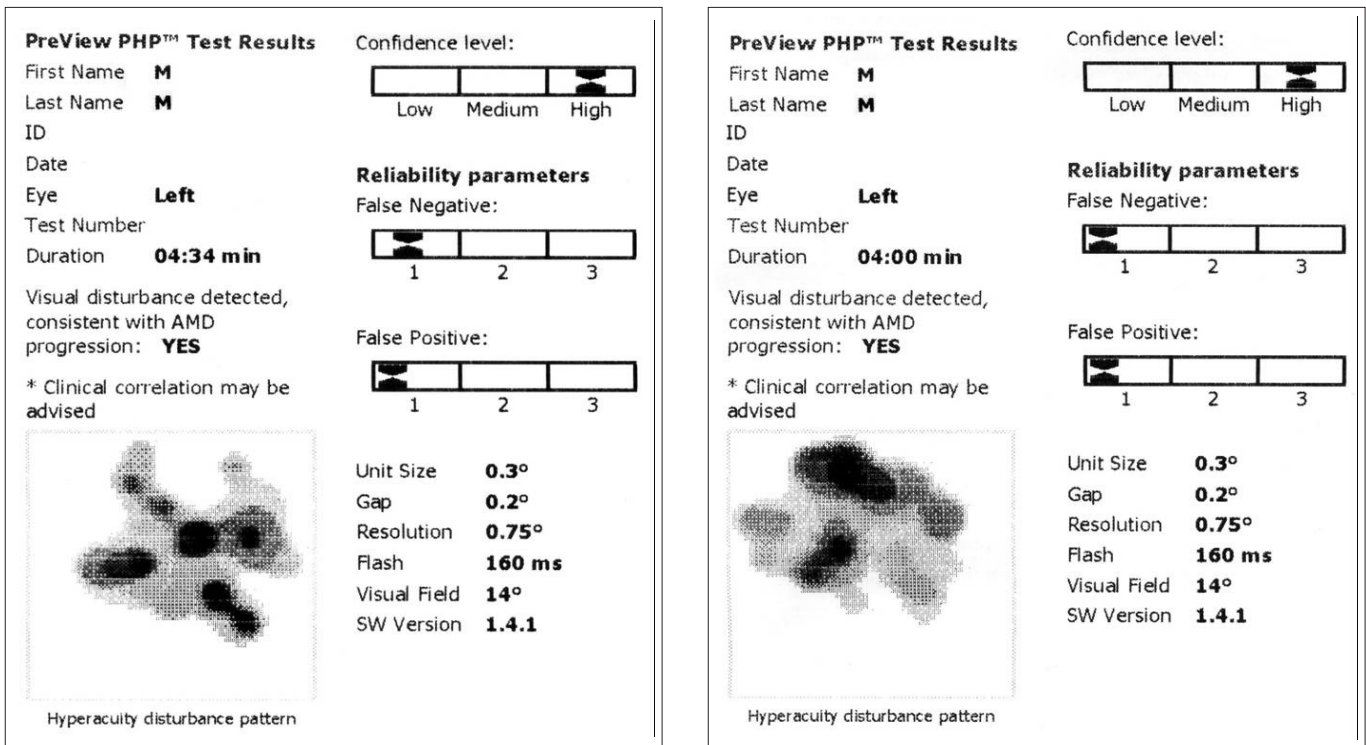
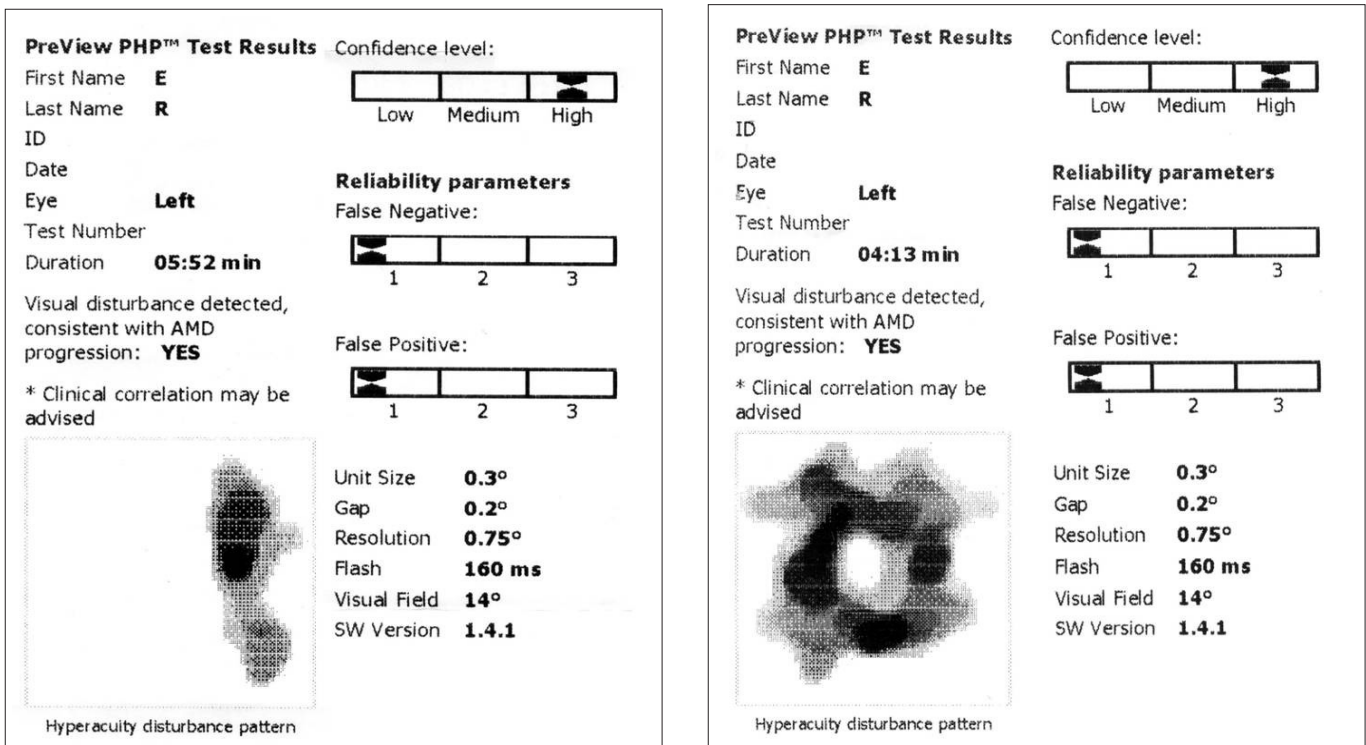**Fig. 5 -** *Stabilization in PHP after photodynamic therapy.*
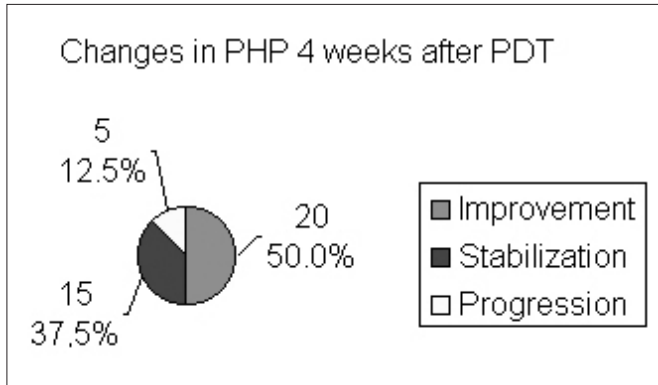

Fig. 6 - *Progression in PHP after photodynamic therapy.*

Fig. 7 - *Changes in PHP 4 weeks after photodynamic therapy.*

Fig. 8 - *Changes in visual acuity 4 weeks after photodynamic therapy.*
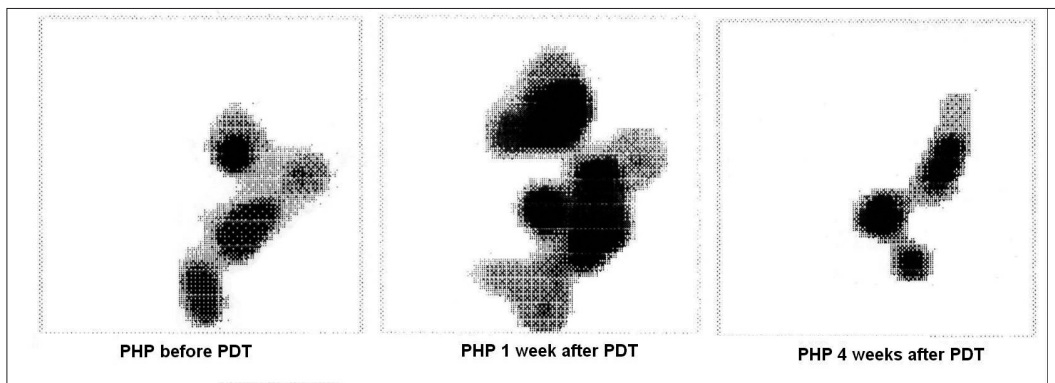

Fig. 9 - *Temporary progression in PHP 1 week after photodynamic therapy.*

after PDT are detailed in Figure 8.

One week after PDT there were temporary PHP determined changes in progression in 30 patients (75%) which regressed after 4 weeks (Fig. 9). Stabilization was observed in 10 patients (25%).

Visual acuity improved in 3 patients (7.5%) – by 6–10 letters in 2 (5%) patients and by 11–15 letters in 1 (2.5%) patient.

No change in visual acuity (±5 letters) was observed in 33 (82.5%) patients.

Visual acuity worsening was observed in 4 (10%) patients – by 6–10 letters in 2 (5%) patients and by 11–15 letters in 1 (2.5%) patient.

Mean change between BCVA before PDT and 1 week and 4 weeks after PDT was not statistically significant. Correlation between BCVA and PHP results was rather low both 1 and 4 weeks after PDT. However, only one patient who gained >5 letters had hyperacuity pattern progression and there was no patient who lost >5 letters and had PHP result improvement.
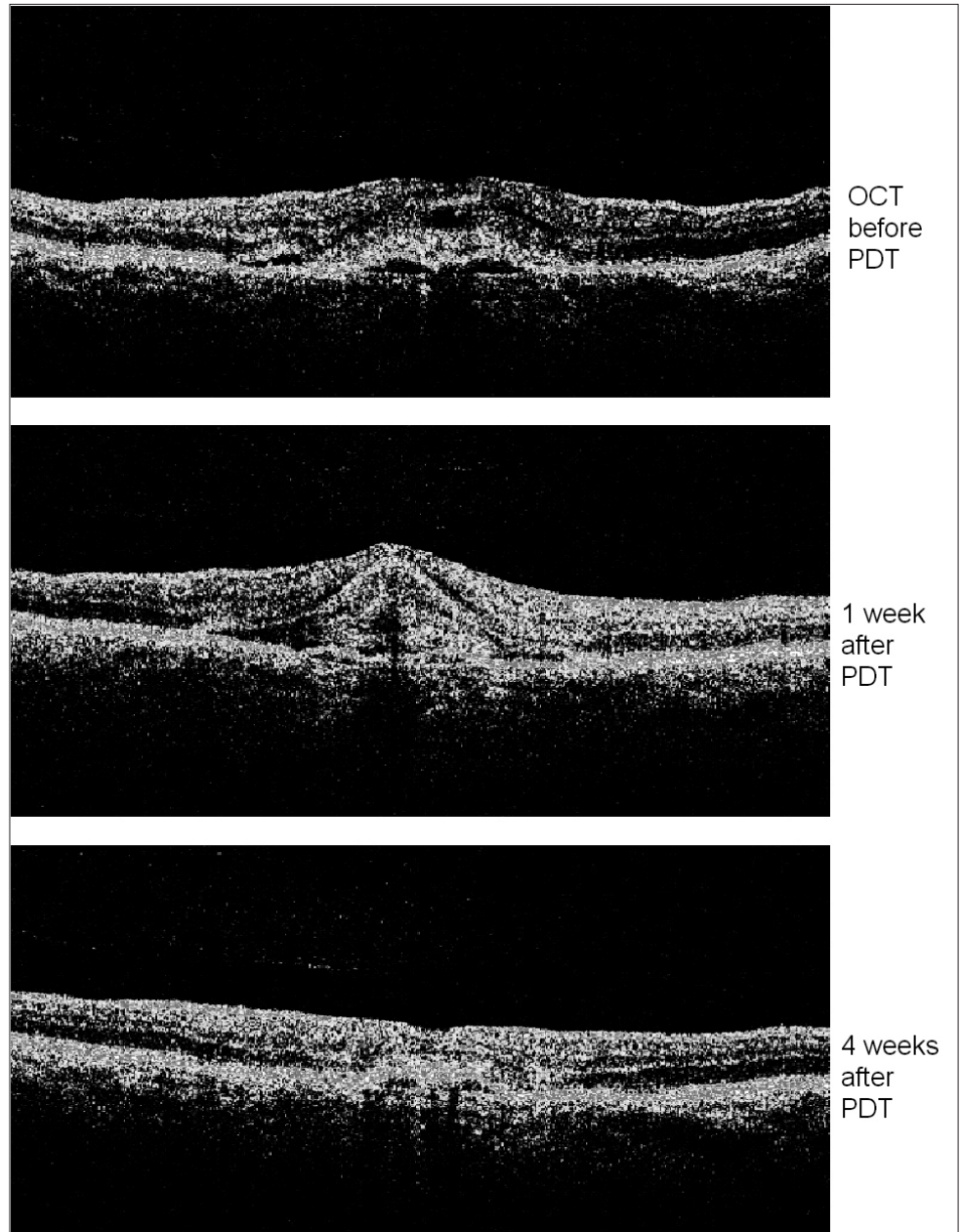
Tables I through III present correlation between BCVA and PHP results.

TABLE I - CORRELATION BETWEEN BCVA AND PHP RESULTS 1 WEEK AFTER PDT

1 week after PDT coefficient	PHP progression	PHP improvement	PHP stabilization	PHP-BCVA correlation
Patients who gain >5 letters	0	0	3 (7.5%)	0.17283
Patients who lose >5 letters	3 (7.5%)	0	1 (2.5%)	
Patients with VA stabilization	27 (67.5%)	0	6 (15%)	

PDT = Photodynamic therapy; BCVA = Best-corrected visual acuity

Fig. 10 - *Temporary progression in OCT 1 week after photodynamic therapy.*

OCT before PDT

1 week after PDT

4 weeks after PDT

TABLE II - CORRELATION BETWEEN BCVA AND PHP RESULTS 4 WEEKS AFTER PDT

4 weeks after PDT	PHP progression	PHP improvement	PHP stabilization	PHP-BCVA correlation coefficient
Patients who gain >5 letters	1 (2.5%)	6 (15%)	2 (5%)	0.25663
Patients who lose >5 letters	2 (5.0%)	0	1 (2.5%)	
Patients with VA stabilization	2 (5.0%)	14 (35%)	12 (30%)	

BCVA = Best-corrected visual acuity; PDT = Photodynamic therapy

TABLE III - CORRELATION BETWEEN BCVA 4 WEEKS AFTER PDT AND PHP RESULTS 1 WEEK AFTER PDT

4 weeks after PDT	PHP progression (1 week)	PHP improvement (1 week)	PHP stabilization (1 week)	PHP-BCVA correlation coefficient
Patients who gain >5 letters	4 (10%)	0	5 (12.5%)	0.274
Patients who lose >5 letters	2 (5%)	0	1 (2.5%)	
Patients with VA stabilization	24 (60%)	0	4 (10%)	

BCVA = Best-corrected visual acuity; PDT = Photodynamic therapy

There were 7 (17.5%) false positive PHP results in the control group with no significant change during observation. After 1 and 4 weeks 6 (15%) false positive results were obtained.

DISCUSSION

PHP tests carried out 1 and 4 weeks after PDT enable monitoring of functional PDT results. One week after PDT there is progression in PHP: metamorphopsias area enlargement and/or deepening of some degree. This worsening disappears in most cases in 4 weeks, which can be a reflection of inflammation process in neovascularization area. It seems to be most intensive during the first week after treatment and probably gradually declines during following weeks.

It should be proven that changes observed in PHP during the first 12 weeks after PDT can facilitate making a decision to repeat therapy. Figure 10 provides an example of OCT image obtained 1 week after PDT corresponding with PHP temporary changes.

Satisfactory sensitivity of PHP in retinal diseases is related to lower specificity. In a multicenter clinical trial all cases of neovascular AMD were confirmed with PHP but the rate of false positive results was high – 18% in patients with no AMD (9).

CONCLUSIONS

PHP seems to be a useful tool only for monitoring hyperacuity pattern after PDT. It does not predict visual outcome. Low BCVA and PHP result correlation suggests that PHP can reveal more subtle changes than visual acuity testing. RPE elevation causes metamorphopsia but probably it does not necessarily decrease VA substantially. It is also possible that positive effect of resolving macular edema on BCVA can be partially masked by increased RPE disturbance and subsequent hyperacuity pattern worsening. Alterations in many retinal layers can be expected after PDT, which is why focusing on RPE elevation only seems not to be useful. Furthermore, patients and ophthalmologists can be alarmed by PHP results, especially early after treatment. Therefore it is important to be aware of possible temporary progression. Patients should be informed that improvement can be expected over a longer period of time.

Proprietary interest: None.

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REFERENCES

1. Enoch JM, Williams RA, Essok EA, Barricks M. Hyper-acuity perimetry: assessment of macular function through ocular opacities. Arch Ophthalmol 1984; 102: 1164-8.
2. Loewenstein A, Malach R, Goldstein, et al. Replacing the Amsler grid: a new method for monitoring patient with age-related macular degeneration. Ophthalmology 2003; 110: 996-70.
3. Westheimer G. Spatial frequency and light-spread descriptions of visual acuity and hyperacuity. J Opt Soc Am 1977; 67: 207-12.
4. Kline DW, Culham JC, Bartel P, Lynk L. Aging effects on vernier hyperacuity: a function of oscillation rate but not target contrast. Optom Vis Sci 2001; 78: 676-82.
5. Lakshminarayanan V, Enoch JM. Vernier acuity and aging. Int Ophthalmol 1995; 19: 109-15.
6. Enoch JM, Essock EA, Williams RA. Relating vernier acuity and Snellen acuity in specific clinical populations. Doc Ophthalmol 1984; 58: 71-7.
7. Preferential Hyperacuity Perimetry Study Group. Preferential Hyperacuity Perimeter (PreView PHP) for detecting choroidal neovascularization. Ophthalmology 2005; 112: 1758-65.
8. Hirose H, Enoch JM, Tuan KM. Quantification of prism induced metamorphopsia as a model for clinical retinal (and other) distortions. Ophthalmic Physiol Opt 1997; 17: 239-47.
9. Goldstein M, Loewenstein A, Barak A, et al. Preferential Hyperacuity Perimeter Research Group. Results of a multicenter clinical trial to evaluate the preferential hyperacuity perimeter for detection of age-related macular degeneration. Retina 2005; 25: 296-303.