A Comparison between the Pulsed Rising Amplitude Perimetry and the Normal Staircase Strategy in Standard Automated Perimetry

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Abstract

Background and scope: Pulsed rising amplitude perimetry (pulsed RAMP) is an improved strategy for automated static perimetry, developed to save examination time without accuracy loss. The aim of this study was to identify characteristic differences between the normal strategy (NS) and the pulsed RAMP strategy in standard automated perimetry, in order to evaluate the potential of the pulsed RAMP for threshold estimation.

Methods: Visual fields from 33 glaucoma patients, 11 controls and 4 patients with other pathology were statistically analysed. A G pattern test using the pulsed RAMP and the NS were performed in randomised order. The MD (mean defect), the sLV (square root of loss variance), the test duration and the point-wise accuracy, related to a calculated reference pre- and post-study visual fields of each patient, were evaluated.

Results: The mean examination time was 8.34 min (SD 2.02) for the pulsed RAMP, compared to 13.37 min (SD 2.67) for the NS. The Bland-Altman correlation plot for the MDs showed a trend (p=0.0018) towards higher MDs in the pulsed RAMP compared to the NS. The sLV of the pulsed RAMP was on average 1.49 dB higher than the sLV of the NS. The absolute mean local deviations, evaluated with the pulsed RAMP (r=0.38), deviated more from the references than those obtained with the NS.

Conclusion: The pulsed RAMP strategy was faster than the NS, but took longer than other established fast strategies like the SITA, TOP and Dynamic. The gain in time, compared to the NS, was paired with reduced local accuracy.

Keywords: Visual fields; Perimetry; Pulsed RAMP perimetry; Examination time; Temporal summation

Abbreviations: CLIP: Continuous Light Increment Perimetry; FOS-curves: Frequency-of-Seeing urves; MAP: Maximum a Priori; MD: Mean Defect; NS: Normal Staircase Strategy; RAMP: Rising Amplitude Perimetry; SAP: Standard Automated Perimetry; SITA: Swedish Interactive Threshold Algorithm; TOP: Tendency-Oriented Perimetry; sLV: Square root of Loss Variance; PSD: Pattern Standard Deviation; ast: Apostilb

Introduction

Standard automated perimetry (SAP) is the currently accepted gold standard for detection and monitoring of glaucomatous dysfunction [1]. The outcome of SAP as a psychophysical test, however, is subjective and variable [2,3]. In the normal strategy (NS) the stimulus luminance varies stepwise, in order to define thresholds. As published literature clearly demonstrates, in cases with advanced visual field disturbances, increasing the accuracy of the estimated threshold and its reproducibility require prolongation of the examination time. This, in consequence, results in increasing fatigue-related artefacts [2,3], which hinder a direct comparison of local threshold resolution.

New fast perimetric strategies, like Dynamic, Swedish Interactive Threshold Algorithm (SITA) and Tendency-Oriented Perimetry (TOP) aim at achieving a comparable high sensitivity and specificity for detection of disease and progression analysis, while taking considerably less time. Here, the examination time is decreased using the prior information about age-corrected normal thresholds values, frequency-of-seeing curves (FOS-curves) and correlations between different points, while the results of the already tested neighbouring points are taken into account, as well [4-9]. The significant gain in time in the TOP strategy, however, is producing a reduction in spatial resolution, making the test unsuitable for application in pathologies with very narrow, deep defects [8,9].

One further attempt in optimising the test duration, while keeping an accurate threshold determination, is the introduction of methods based on continuous luminance variation. The rising amplitude perimetry (RAMP) and its modification - the continuous light increment strategy (CLIP) [10,11], in contrast to the TOP strategy, is assessing every single test location independently. Here, the slow temporal onset algorithm starts from invisible (subthreshold) light and increases in luminance until the patient responds to the light.

In general, the determination of thresholds varies complexly and is dependent on several variables, including the effect of temporal summation, stimulus duration, speed of the light onset and wavelength of monochromatic light [12,13].

For CLIP methods, the summative phenomenon of the neighboring areas after exposure to light, that is the effect of temporal summation,
influences the threshold determination while presenting higher thresholds [10,11,13,14].

Another temporal processing factor, affecting thresholds for luminance determination, is the abruptness of the temporal onset and offset of the stimulus. With longer stimulus duration, compared to the usual 100 ms or 200 ms, the temporal summation in SAP results in an increase in threshold [2,10,11,13-16]. Therefore, here, the difference between abrupt- and continuous onset stimuli seems to be a key factor affecting thresholds. In an attempt to overcome these problems, we choose an abrupt (pulsed) RAMP instead of a continuous RAMP stimulus.

Of particular interest is the fact, that a CLIP like test has the characteristics of longer stimulus duration combined with slower onset, compared to the light pulses of the NS in standard perimeter. However, as clearly demonstrated in previous studies, the CLIP type methods are also strongly affected by the patient’s reaction time [15,17,18]. On a white 4 asb background (as the one featured in Octopus cupula perimeters), the critical integration of vision is shown to be less than 100 ms [2]. Thus, a measurement for threshold luminance applied in the conventional static visual field examinations requires flashes of 100 ms or longer [12].

Accordingly, in our study we applied a pulsed RAMP with a 100 ms pulse duration, which is below the critical time for temporal summation and is shorter than human reaction time. Each stimulus was followed by a 600 ms pause, which is longer than the usual reaction time for suprathreshold stimuli. The evaluation of the patient’s individual reaction time behavior should increase the accuracy within the discrete pulse intensities and yield an accurate threshold determination.

The aim of this study was to prove this hypothesis in a clinical setting, identifying the characteristic differences between the method with an abrupt temporal onset (the pulsed RAMP fast strategy) and the normal continuous bracketing strategy (NS), in order to judge the potential of the pulsed RAMP threshold estimation.

Materials and Methods

Subjects

The study was performed according to the tenets of the Declaration of Helsinki and was approved by the local Ethics Committee. All subjects signed their informed consent for participation in the study.

Inclusion criteria

A total of 53 right eyes of fifty-three subjects (of which 27 females and 26 males) were recruited. All participants underwent full ophthalmologic examination: clinical history, visual acuity, applanation tonometry, biomicroscopy of the anterior segment and ophthalmoscopy of the posterior pole. Control subjects (n=11) had an intraocular pressure below 21 mmHg, best corrected visual acuity 20/20, and anteroposterior orbitopathy, i.e. Graves’ orbitopathy, and idiopathic optic neuritis). For verification purposes we included four patients with pathology other than glaucoma (prolactinoma, optic disc drusen, Basedow’s orbitopathy, i.e. Graves’ orbitopathy, and idiopathic optic neuritis).

Visual field testing

A pulsed RAMP-strategy, phase 4 (pre-market) implementation and a G, normal strategy (NS), were performed, using the portable commercially available direct projection perimeter Octopus 300 (Haag-Streit AG, Kôniz). The maximum stimulus luminance was 4'800 asb and the background luminance was 31.4 asb, for both strategies. The pulsed RAMP-strategy runs as follows: in analogy to the G-program, stimuli of standard size (Goldmann III) are projected at 59 test locations within the central 30° of the visual field. Initially, the threshold is estimated at eight anchor points in eight regions of the visual field. The pulsed RAMP stimulus presents standard static stimuli of increasing luminance in the same location until the patient responds to the light (Figure1, B1-Bx). The stimulus duration is 100 ms (C) and is followed by 600 ms break (D) (for complete descriptions refer to Figure 1).

The true threshold is calculated according to the patient’s reaction time (measured in different locations), its relation to the frequency-of-seeing curves (FOS-curves) and the probability for every light pulse shown, to have triggered the given response. The reaction time was calculated using responses to negative catch trials (n=16). Negative catch trials were defined as single stimuli shown 8 dB brighter than previously perceived stimuli in the same locations. Negative catch trials, which were not responded to within 1700 ms, were evaluated as not perceived and therefore considered false-negative responses. Responses to (invisible) 40 dB stimuli within 1700 ms were considered false-positive (n=6).

In the present study, the pulsed RAMP-software was adjusted for testing the right eye. Therefore, for statistical analysis, the right eye of each subject was examined. The test order for subject examination, both for pulsed RAMP and NS, was randomised. Both tests were obtained at one visit with a 15 minutes break in between.

Analysis

In order to compare the pulsed RAMP to the NS, the RAMP
stimulus data were transformed into the PeriTrend format (Version 6.07, Haag-Streit AG, Koniz-Bern).

The mean defect (MD), the square root of loss variance (sLV) corresponding to the pattern standard deviation (PSD), the pointwise accuracy related to calculated reference fields, the test duration and the reaction time were evaluated.

We initially compared NS and pulsed RAMP strategy against each other, using a Bland-Altman plot. In order to evaluate the comparability of results, the individual thresholds and the global indices from a pulsed RAMP stimulus were compared to those of a NS, using an Interclass correlation. Also, we created a reference standard (at least for glaucoma patients who were followed up over a longer period of time) by averaging the prior- and post- study visual fields of each patient (G, Octopus 101). This way we could compare both the NS and the pulsed RAMP against reference data and see which test runs in a more stable way.

As the absolute number of the repeated stimuli varied, we calculated the false-positive and false-negative responses in percent for statistical analysis. The test was accepted as reliable, if less than 20% false-positive and less than 20% false-negative responses were reported.

In order to compare the results for the overall depression or elevation of the visual field of the NS or pulsed RAMP stimulus to a reference, we calculated the difference of MD (the Delta MD) to be the average MD derived from pre- and post- study visual fields.

To evaluate the influence of the location on the variation of the measured threshold, we calculated also the pointwise local deviation of the defect for the NS and of the pulsed RAMP stimulation compared to the reference (dB).

The G test procedure on the Octopus 101 is identical to the NS G program on the Octopus 300; both of them use 100 ms stimulus duration. The background luminance of the Octopus 101 is 4 asb, whereas the one of the Octopus 300 (NS, G program, as well as of the pulsed RAMP stimulus) is 31.4 asb. The intensities of the presented stimuli are scaled in a way that matches absolute sensitivity to one another. While the influence of the background luminosity on the defect depth in different pathologies has not been sufficiently studied yet, a deviation would influence both the comparison to the NS and the comparison to the pulsed RAMP in the same way. Hence, the comparison of the pointwise accuracy was still considered valid.

Results

Visual fields were obtained from fifty-three eyes (53 subjects: 27 females and 26 males). Visual fields from 20 eyes (4 controls, 14 glaucoma patients and 2 patients with other pathology) had to be excluded from further statistical analysis for the following reasons:

Four controls were excluded due to unreliable NS data: examination of the left eye (n=1), blepharochalasis (n=1), false program (TOP strategy instead of NS, n=1), and more than 20% false-negative results (n=1).

From the glaucoma group, five patients showed an unreliable NS examination with more than 20% false-positive answers (n=2) or a prolonged reaction time (mean 3.5 s/stimulus, n=3). Another six patients were excluded from the pulsed RAMP data due to program flaws, e.g. presentation of 82 instead of at least 89 stimuli (n=5). Another three glaucoma patients were excluded while defining our reference data, due to the significant visual field defect progression within the pre- and post- study period.

Concerning patients with other pathology, the prolactinoma patient was excluded due to a prolonged reaction time (2.6 s/stimulus, repetition of 286 of the 526 presented stimuli) and the patient with optic disc drusen - due to more than 20% false-positive results.

The remaining 33 subjects' fields were statistically analysed (20 female and 13 male; mean age: 59.21 years; SD: 12.96). The control subjects' age ranged from 26 to 74 years (n=7; mean age: 58.5 years; SD: 14.95). The glaucoma group (n=24 patients; mean age: 61.08 years; SD: 12.48) consisted of: 5 patients without visual field defects (group 1), 6 patients with early visual field defects (group 2), 7 patients with moderate visual field defects (group 3), and 6 patients with advanced visual field defects (group 4). There were no differences in age, gender, or for the test order between groups and/or glaucoma subgroups (p=0.36, p=0.13, p=0.27, p=0.37, p=0.69 and p=0.62, respectively; one-way ANOVA, Bonferoni correction).

Comparison of examination time

The pulsed RAMP stimulus allowed for much faster examination time when compared to the NS (Figure 2). The mean duration of examination was 8.34 (SD 2.02) minutes for the pulsed RAMP stimulus, compared to 13.37 (SD 2.67) minutes for the NS. Here, for the NS, as well as for the pulsed RAMP strategy, the examination time was longer in the glaucoma group compared to the other two groups (p=0.53; p=0.07, one-way ANOVA).

Comparison of global indices

On average, the pulsed RAMP stimulus thresholds were 1.0 dB higher than those of the G strategy. The Bland-Altman correlation plot (Figure 3) showed a significant trend (p=0.0018) for the MDs when the stimulus data were transformed into the PeriTrend format (Version 6.07, Haag-Streit AG, Koniz-Bern).

Figure 2: A linear diagram representing the relationship between the individual patient's examination time (min). The examination time duration for the NS is presented on the left and for the RAMP on the right. Each color indicates to which specific group the subject belongs to, as displayed on the mid-right, under methods.

Figure 3: A scatter plot showing the comparison between the pulsed RAMP and NS stimulation method.
difference with increasing average MDs: the MD values of the patients with severe visual field loss, when examined with the pulsed RAMP, seemed to be higher and showed more variations in comparison to the NS.

The overall mean sLV of the pulsed RAMP stimuli was 1.49 dB higher than that of the NS. The respective values for mean sLV were 6.32 dB (SD 3.34) for the pulsed RAMP and 4.94 dB (SD 3.26) for the NS. Regression results showed a significant intercept (p=0.017), indicating a systemic shift between both methods (Figure 4). Within the glaucoma group the sLV of the RAMP stimulus differed significantly from the NS, as well as from the reference. The sLV of the NS strategy did not differ from the sLV of the reference (p>0.05).

When comparing the two methods (the NS against the pulsed RAMP strategy) using the Interclass correlation, the correlation coefficient for the MD was 0.91 (95% C.I: 0.83-0.96) and for the sLV 0.84 (95% C.I: 0.70-0.92), indicating a strong correlation between both methods.

Neither for RAMP, nor for NS, did the Delta of the MD correlate significantly with the MD of the references. The distribution of the patients’ Delta MDs obtained with the RAMP and NS at different levels of the visual field sensitivity (-5,-3,-1, 0, +1, +3, +5 dB) showed a deviation of the pulsed RAMP shifted to the right from the reference and deviation of the NS to the left, which indicates higher MD levels obtained with the RAMP (Figure 5). In agreement with the results of Bland-Altman plots of the MD (Fig. 4), the Delta MD of the pulsed RAMP stimuli showed also a wider distribution around the median value (Figure 5).

**Local accuracy**

The absolute mean pointwise difference of the local thresholds of the pulsed RAMP (r=0.38) was larger than with the NS (r=0.67), when compared to the reference (Figure 6). Here, more values of the pulsed
RAMP are shifted to the zero-line, indicating more outliers. However, when the quadrant of the local deviation was calculated for the pulsed RAMP, as well as for the NS, the references’ MD correlated well with both stimuli applied (p=0.80, 95 % CI: 0.85-0.88; and p=0.87, 95% CI: 0.85-0.88, Interclass correlation). Here, the correlation between the local thresholds of the pulsed RAMP against the NS showed a highly significant difference (p<0.001). The mean rate of false-positive and false negative-responses for the pulsed RAMP group was 0.00%, (SD 0.00) and 1.12% (SD 3.81), whereas for the NS group it was 2.45% (SD 4.09) and 3.27% (SD 5.85), respectively. For both stimuli, the rate of the false-positive and false-negative test order, duration of the examination or reaction time. Age did not influence the results (p>0.05).

Clinical progression, associated indices

Within the glaucoma group we evaluated which patient’s MD worsened at a 5% probability level, using the same pre- and post- study data, which were used to calculate the reference data.

In four of eighteen patients (22%) the disease progressed within the study time. Here, the sLV, as well as MD values of the RAMP stimulus, were more pathologic than those of the standard visual field (Figure 7).

The mean number of stimuli presented for the pulsed RAMP strategy was 93.0 (SD 4.6) in the glaucoma group, compared to 89.9 (SD 1.2) in controls. For the NS much more stimuli were used in the glaucoma group (mean 323.0, SD 32.8) compared to controls (mean 286.6, SD 24.8).

Discussion

This study was performed in clinical settings, in attempt to test whether the improved pulsed RAMP strategy provides a time saving alternative to the NS threshold without loss of accuracy.

Previous studies, concerning the RAMP and its modification - the CLIP -, show the influence of a stimulus duration longer than 200 ms on the temporal summation, and thus on the scotoma depth, when compared to the regular short stimulus pulse [10,11,13-16]. In this study, we tested a new RAMP strategy using discrete stimuli of increasing luminance with a stimulus duration of 100 ms and an inter stimulus interval of 600 ms.

As expected from our preliminary analysis (Palmowski-Wolfe AM, ARVO 2005; E-Abstract 4318) the pulsed RAMP stimulus resulted in a 37% reduced test duration compared to the NS. The time saving was generally more pronounced in the control group, and less pronounced in the glaucoma group with advanced visual field loss. However, when compared to the fast strategies available on the market, like Dynamic, SITA, and TOP algorithms, the pulsed RAMP is still slower than their average test durations [6-9,19,20].

Threshold values were comparable between the pulsed RAMP, the NS and the reference data. The control subjects were well differentiated in the pulsed RAMP data from patients with glaucoma and other pathology. In general, the pulsed RAMP strategy produced an MD that correlated well, not only with the NS, but also with the references (r=0.92; r=0.86, respectively), thus indicating a good correlation between measurements. However, applying a pulsed RAMP strategy, we found the threshold values to be more pathologic in some cases with advanced visual field loss, compared to the NS. This is in agreement with the previously reported difference in higher intensity levels of the short-duration strategies [5,21].

The sLV of the pulsed RAMP was on average 1.49 dB higher than that of the NS and tended to be even higher in cases with advanced visual field loss, thus making subtle defects more visible and prominent. To exclude the effect of visual fatigue, which is expected to be related to the higher local thresholds [21], in our study both examinations were obtained in a random order. Both data sets from the patients’ testing
were compared to the references. The patients included in the study, were experienced with the visual field examination.

Local threshold variations have been reported to be higher in glaucoma patients with advanced visual field loss and, for instance, in cases of disease progression are more frequent in areas of relative scotomata [3,22]. This was the reason to evaluate also the pointwise accuracy, related to calculated reference fields. Here, the absolute mean local deviation of the defects, evaluated with the pulsed RAMP (r=0.38), differed considerably and in cases with more advanced visual field defects was more pronounced and showed more outliers than with the NS. Therefore, and in analogy to previously reported results on CLIP strategy [10,11], we assume the higher sLV of the pulsed RAMP to be related more to the difficulty of estimating the thresholds, using patient’s reaction times, compared to either continuous RAMPs or pulsed RAMPs with step sizes of 4 dB threshold evaluation.

It is also important to keep in mind, that from the pulsed RAMP data none of the control subjects was excluded, while six glaucoma patients and two patients with other pathology were excluded from statistical analysis, due to a program flaw, prolonged reaction time or higher false-positive results. From the remaining glaucoma patients the disease showed progression over time in 22% of cases. For these patients with glaucoma progression, the sLV and the MD of the pulsed RAMP stimulus often were more pathologic when compared to the NS. Since the pulsed RAMP perimetry, similarly to the normal staircase perimetry, is a white-on-white perimetry, this observation raises the question whether a pulsed RAMP is acting more like a stress test.

Using a RAMP strategy to find the threshold means that the FOS curve is always approached from the dim side. Therefore, the chance of receiving sensitivities below the 50% point of the FOS curve – the true threshold as defined in perimetry – is higher than receiving sensitivities above that point. An optimal threshold strategy would approach the 50% point of the FOS curve the same number of times from above as from below. A mean to ensure implementation of that strategy during a test, is to use already established thresholds nearby to calculate starting values, based on the average deviation of nearby points. If previous test results are known and under the hypothesis, that no true change has taken place, the previously established thresholds could be used, in the original form or modified with a randomly assigned deviation, chosen from a symmetric range of deviations. Although there are some concerns – as there is the statistical problem of the regression to the mean – it helps to approach the thresholds from both sides. Furthermore, perimetry aims for more stable results where random deviations are reduced in favor of detecting true change. A regression to the mean in this sense might even be a desirable measure to reduce variability induced by threshold testing algorithms that start far from the patient’s effective local sensitivity.

However, by definition, this is not possible, if a RAMP stimulus is applied. While the tested algorithm used anchor points to start the RAMP stimuli intensity closer to the expected thresholds, a RAMP stimulus had to be repeated, if seen immediately. One would expect a sensitivity shift towards higher thresholds in that case. To counteract this effect, we calculated a correction based on the tested normal subjects and applied this correction to all subjects. Knowing about the flattening of the FOS curve with increased defect depth [23] we would expect that a correction based on normal threshold levels would not completely correct the deviation in areas with defects. However, in our study we could not observe the defects being shallower on average, compared to the NS strategy; a fact, we did not find an explanation for.

A possible reason for the increased sLV and for the average lower pointwise accuracy may be found in the step size of the pulsed RAMP strategy. Evaluating and including the patient’s reaction time was supposed to refine the step size of 4 dB to become comparable to the 2 dB in the NS. First, the average reaction time to negative catch-trials, displayed 8 dB brighter than previously established local sensitivities, was calculated. Then, the local threshold was estimated from the reaction time prolongation compared to the average suprathreshold reaction time. Based on the individual subject’s reaction time distribution, this appeared to work reasonably well in normal visual fields. The reaction time distribution displayed a somewhat Gaussian-like function. However, in affected visual fields, the reaction time often showed a discontinuous distribution around two dominant reaction times. In one patient for example, the average reaction time on negative catch-trials was approximately 600 ms. The reaction times to RAMP stimuli were grouped around 600 ms and around 1000 ms. One explanation for this outcome would be, that the second peak – 1000 ms – corresponds with the reaction time to stimuli close to threshold, which were recognized and responded to. The 600 ms responses were responses to anticipated “next” RAMP pulse and rather suprathreshold responses. Following this interpretation, the reaction time information is not useful to calculate an estimated threshold between the two stimulus pulses. Consequently, the advantage of reduced test duration, that partially comes from a larger step size of 4 dB compared to the NS, would be lost through use of narrower step sizes, if the characteristic of the RAMP strategy should match the NS results closer.

In summary, the pulsed RAMP stimulus allows for shorter test duration than the NS. The RAMP strategy produces an MD, which is comparable to the NS and to the references and is, therefore, suitable for use in a follow-up. The gain in time, however, goes along with a reduction in the accuracy of the local defect depths. The pulsed RAMP thus shows no advantage over other already accepted alternative test strategies. Therefore, we recommend choosing established fast strategies, rather than the pulsed RAMP strategy.

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Conflict of Interest

Matthias J. Monhart was employed by Haag-Streit AG, Koeniz-Berne, during the period of data collection and initial evaluation. Any financial interest or conflict is disclosed.

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