Population based glaucoma screening

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Chapter 7

Supra-threshold perimetry compared to standard automated perimetry in glaucoma

SUPRA-THRESHOLD PERIMETRY COMPARED TO STANDARD AUTOMATED PERIMETRY IN GLAUCOMA

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Abstract

Purpose: To compare the severity of glaucomatous damage measured with supra-threshold perimetry (STP) to the severity measured with standard automated perimetry (SAP).

Design: Prospective, cross-sectional study.

Methods: One hundred thirty-one (131) glaucoma patients and glaucoma suspect patients scheduled for SAP (Humphrey Field Analyzer 24-2 SITA Standard) were invited to undergo two additional 52-points STP tests in one eye. Ninety-two (92) patients were included. Eyes with non-glaucomatous visual field loss were not eligible, as well as eyes with best corrected visual acuity <0.5 (20/40) except when caused by glaucoma. If both eyes were eligible, one eye was randomly selected. Test sequence was also randomized. The Mean Deviation (MD) of the SAP test was compared to the number of missed points on STP.

Results: There was a linear relationship between the number of missed points on STP and the SAP MD, with a correlation coefficient of -0.92. The MD can be estimated from the STP score by multiplying the number of missed points by -0.75. STP was nearly twice as fast as SAP.

Conclusion: STP appears to be a fast and reliable method for estimating the severity of glaucomatous damage.

7.1 Introduction

Standard Automated Perimetry (SAP) has become the most commonly used form of perimetry for glaucoma diagnosis and follow-up. Commonly used SAP devices are the Humphrey Field Analyzer (HFA, Carl Zeiss Meditec Inc., Dublin, CA, USA) and the Octopus perimeter (Haag-Streit AG, Koeniz, Switzerland), among others. In SAP, the threshold luminance of every test location in the visual field is determined by a staircase procedure: the stimulus luminance is either increased or decreased stepwise until a change occurs in the response of the subject.[1,2] Initially, the HFA employed a full-threshold strategy, wherein the staircase step size is 4dB until the threshold is crossed. After the first crossing, the step direction reverses and a second crossing is performed with a step size of 2dB. The second crossing occurs in either an ascending or descending direction, and threshold is designated as the last-seen stimulus luminance. Full-threshold testing accurately determines threshold luminance, but at the expense of a long examination duration (typically 15 minutes per eye).[3] In an effort to reduce test duration, FASTPAC was introduced around 1993, using 3dB steps and no reversals.[4,5] A more sophisticated algorithm was introduced in 1997, the Swedish Interactive Threshold Algorithm (SITA). It reduces test time by taking into account information from nearby test locations to estimate threshold luminance, as well as by optimized test pacing and several other optimizations.[6,7]

Despite these improvements, SAP remains a difficult and time-consuming task that can be too demanding for some patients. Alternatives are desirable. Goldmann kinetic perimetry is easier for the patient, but equally time-consuming and it relies, more than SAP does, on the perimetric skills of the examiner. SAP with a larger stimulus (size V) reduces test-retest variability, which may be an indication that the test is easier to perform,[8] but, since SITA is not available for unconventional stimulus sizes, testing time is inevitably long. Modern techniques such as Frequency Doubling Technology perimetry (FDT, Carl Zeiss Meditec Inc., Dublin, CA, USA) are also of interest. However, there are not enough longitudinal data available to decide whether FDT is suitable for glaucoma follow-up. Furthermore, FDT requires the purchase of an additional device. Yet another option is supra-threshold perimetry (STP), which will be explored in this study.

In STP, stimuli are presented at an intensity several decibels above the peer-average threshold luminance. If a stimulus is seen, then it is assumed that there is no significant defect at that particular location. If a stimulus is not seen, then there is either a relative or an absolute scotoma. By accepting the loss of information about scotoma depth, STP achieves a substantial reduction in test time. To what extent this loss of information compromises the applicability of STP in glaucoma care is largely unknown.

Besides being an interesting alternative to SAP from a clinical point of view, there is another reason why a more detailed knowledge of the performance of STP is mandatory. Several of the major population-based studies that reported on glaucoma incidence, the Rotterdam Study,[9-11] the Blue Mountains Eye Study,[12] the Baltimore Eye Survey,[13] and the Beaver Dam Eye Study,[14] used STP for visual field screening because of examination time constraints, especially since SITA was not yet available at that time. The interpretation of the results from these studies would also benefit from a detailed comparison of STP and SAP.

The aim of this study was to compare glaucomatous damage on STP and SAP. This was performed cross-sectionally, in a clinical setting. In STP, we used the number of missed test points as our outcome measure; in SAP, we used the Mean Deviation (MD). There are a few studies that have compared STP to SAP,[15-18] but these were aimed at the diagnostic performance of STP (presence or absence of abnormalities) and their data do not allow for a quantitative comparison of glaucomatous damage.

7.2 Methods

Study population
Glaucoma patients and glaucoma-suspect patients, who were scheduled for SAP at our outpatient department in 2008, received a letter of invitation. We invited only one randomly selected patient per day in order to avoid long waiting times in our tightly booked department. The selected patients were requested to perform two additional STP tests in one eye. Glaucoma-suspect patients were subjects with ocular hypertension and/or a positive family history of glaucoma and/or glaucomatous optic neuropathy but no glaucomatous visual field loss at their latest visit. Ocular hypertension was defined as an intra-ocular pressure (IOP) >20 mmHg on at least two separate visits. Positive family history of glaucoma was defined as one or more first-degree relatives with glaucoma. Glaucomatous optic neuropathy was defined as a vertical cup-disc ratio of at least 0.7. Glaucoma patients were patients with glaucomatous visual field loss in their enrolled study eye. Glaucomatous visual field loss was defined using SAP (HFA 24-2 SITA standard, see next section) as either:
1. Glaucoma Hemifield Test outside normal limits, and/or
2. Pattern Standard Deviation $P<0.05$, and/or
3. a scotoma of three adjacent points $P<0.05$ in the pattern deviation probability plot in which at least one point $P<0.01$, with all points being on the same side of the horizontal meridian.
The field loss had to be reproducible, that is, it had to be present on at least two consecutive fields (not including the first field ever made) in the same hemifield and with at least one depressed test point having exactly the same location. Fields had to be reliable and the field loss had to be compatible with glaucoma

and without any other explanation. A test result was considered unreliable if false positives exceeded 10% or if both false negatives and fixation losses exceeded 10% and 20% respectively. All participants had perimetric experience. Patients with concurrent disease that might compromise the visual field were excluded. Eyes with best corrected visual acuity <0.5 (20/40) were also excluded, except when caused by glaucoma.

Perimetry

Visual fields (VF) were obtained with the Humphrey Field Analyzer (HFA 640; Carl Zeiss Meditec, Dublin, CA, USA). For STP, we used a test identical to the screening test used in the Rotterdam Study.[9] It has a 52-point grid covering the central field with a radius of 24°, and a threshold-related test strategy (see Appendix). In this strategy, a threshold sensitivity is determined in four "seed" locations, located at 10° eccentricity, one in each quadrant. The age-corrected average height of the hill of vision is then adjusted for each test subject based on the sensitivity of these four seed locations. This adjustment attempts to compensate for differences in media clarity, pupil size, and general responsiveness. The maximum amount of adjustment is restricted by the lower limit of the seed locations (26dB). The actual test is performed with stimuli that are 6dB brighter than the predicted sensitivity of each particular test point. Stimuli that are not seen will be presented for a second time, and only if missed twice are they reported as missed points on the test printout. We used the total number of missed points for quantifying the amount of visual field loss.

For SAP, the HFA 24-2 SITA Standard program was used. It has the same 52-point grid as our custom STP test field, but has two additional points nasally, extending its radius to 30° at that location. The global index Mean Deviation (MD) was used as a measure of glaucomatous damage on SAP.

If both eyes were eligible for the study, one eye was randomly selected. The selected eye underwent three consecutive VFs: two STP tests and one HFA 24-2, with five-minute breaks in between. Testing always started with STP, but the order of the second and third test was determined at random to avoid any systematic influence of diminishing concentration. Thus, the test sequence was either STP > STP > SAP, or STP > SAP > STP. Data from the second STP test were used for comparison with the SAP MD score; data from the first STP test were used only for calculating STP test-retest variability.

Analysis

We used the Student's t-test for continuous variables, and the chi-squared test for proportions (with Yates' correction where appropriate). Spearman's rho was used to determine correlation coefficients, since the data were not normally distributed. Test-retest variability was expressed as the coefficient of repeatability, which equals twice the standard deviation of the differences between the first and second STP tests, as described by Bland and Altman.[19] Calculations were performed in SPSS 16.0.2 for Windows, SPSS Inc. Chicago, IL, USA.

7.3 Results

Ninety-two out of 131 invited patients (70%) participated in the study. Participants and non-participants were similar with respect to age and gender. Table 7.3.1 presents the characteristics of the 92 participants, consisting of 20 glaucoma suspects and 72 glaucoma patients. In the group of glaucoma suspects, 9 had OHT, 9 had a positive family history for glaucoma, and 6 had glaucomatous optic neuropathy (several participants were classified as glaucoma suspect for more than one reason).

Table 7.3.1 Characteristics of participants

	glaucoma suspects (n=20)	glaucoma patients (n=72)	all participants (n=92)
age (yrs; mean (SD))	67 (11)	59 (12)	65 (12)
gender (% male)	50	49	49
right eye selected (%)	55	47	49
test sequence STP > SAP > STP (%)	60	47	50

SD = Standard Deviation; STP = Supra Threshold Perimetry custom test; SAP = Standard Automated Perimetry

Table 7.3.2 presents the amount of visual field loss and testing time of STP and SAP. The STP test was almost twice as short as the SAP test ($P<0.001$).

Table 7.3.2 Visual field loss and test time of STP and SAP

	glaucoma suspects (n=20)	glaucoma patients (n=72)	all participants (n=92)
HFA MD (dB; mean (SD))	-1.5 (1.7)	-11.8 (7.6)	-9.5 (8.0)
STP1 (missed points; mean (SD))	1.5 (1.1)	13.2 (10.5)	10.7 (10.5)
STP2 (missed points; mean (SD))	1.5 (1.0)	14.7 (11.8)	11.9 (11.8)
STP test time (s; mean (SD))	184 (15)	233 (42)	223 (43)
HFA test time (s; mean (SD))	305 (37)	407 (63)	385 (72)

HFA = Humphrey Field Analyzer 24-2 SITA Standard programme; MD = Mean Deviation; SD = Standard Deviation; STP = Supra Threshold Perimetry custom test; 1= first test, 2= second test

Figure 7.3.1 shows the relationship between SAP MD and the number of missed points on STP. The coefficient of determination (R2) of the linear regression line was 0.89. The regression line is described as MD = -0.72*STP – 0.68; when forcing the line to go through the origin, we found MD = -0.75*STP. The residuals of the fit followed a normal distribution. The Spearman's rho correlation coefficient was -0.92 (P<0.001).

Figure 7.3.2 presents a scatter plot of the first versus the second STP test. The regression line was almost equal to the line of equality (y=x). Slightly more points were missed on the second STP test (11.9, SD 11.8 points) than on the first test (10.7, SD 10.5; P=0.001). The coefficient of repeatability was 7.0 missed points. Subgroup analysis revealed that patients with test sequence STP > STP > SAP had a trend towards a better coefficient of repeatability (5.9 missed points) than patients with test sequence STP > SAP > STP (7.9 missed points), but this difference was not significant (P=0.118).

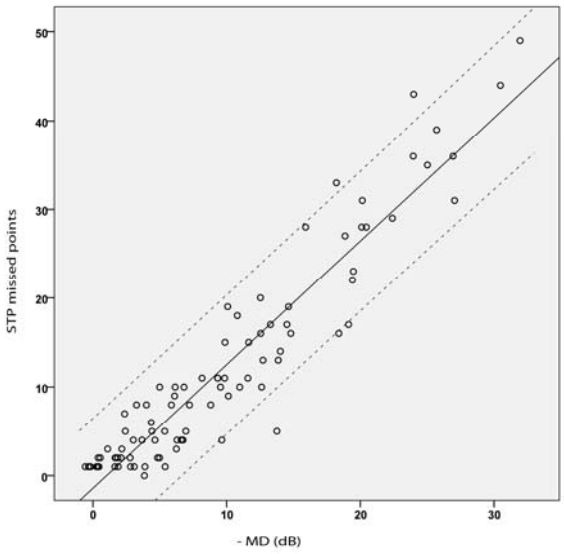

Figure 7.3.1 Scatter plot showing the (minus of the) HFA 24-2 MD plotted against the number of missed points on STP. Lines show the regression line and corresponding 95% confidence interval.

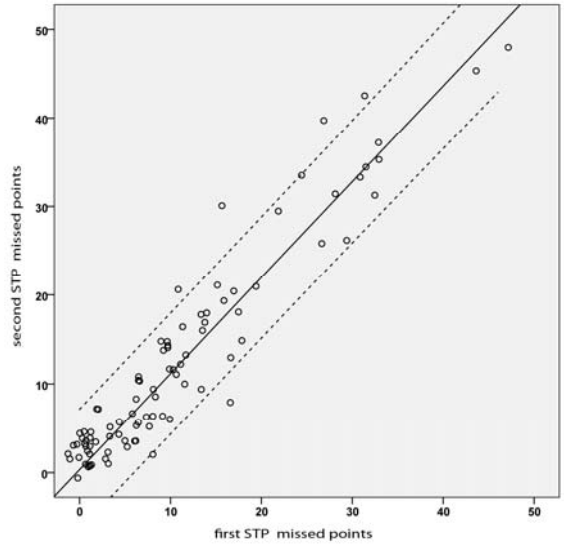

Figure 7.3.2 Scatter plot of the first versus the second STP test. Lines show the regression line and corresponding 95% confidence interval.

As mentioned in the introduction, several population-based studies relied on STP for visual field screening. In the Rotterdam Study, for example, STP visual field loss was considered present when there was a scotoma that consisted of three or more contiguous missed points in two consecutive screening tests.[10] Fifty-five out of our 72 glaucoma patients (76%) would have been classified as having visual field loss according to the Rotterdam criterion. All 20 glaucoma suspects would be classified correctly as not having visual field loss. The average MD of the 17 missed glaucoma patients was -4.4dB (SD 2.5dB, range -1.1 to -9.6dB). Sensitivity of the Rotterdam criterion (using glaucomatous visual field loss on SAP as the gold standard) was 28% for early glaucoma (MD better than -6dB; 5 out of 18 patients), 83% for moderate glaucoma (MD between -6dB and -12dB; 20 out of 24 patients), and 100% for severe glaucoma (MD worse than -12dB; 30 out of 30 patients).

7.4 Discussion

In this study, we quantitatively compared glaucomatous damage on STP and SAP. We found a sound association between both types of perimetry. Severity of glaucomatous damage on SAP expressed in MD can be estimated from STP test results by multiplying the number of missed points by -0.75. Most patients with glaucomatous visual field loss on SAP also had STP abnormalities, except for patients with early glaucoma.

A study by Mills et al.[18] concerning 87 early glaucoma patients (defined as MD better than -7dB) used an STP test identical to ours. Their criterion for visual field loss was three or more missed points. They reported a sensitivity of 23%, which is similar to the sensitivity of 28% for early glaucoma patients as found in our study using the Rotterdam criterion. Based on these figures, STP does not seem suitable for identifying early glaucoma. Topouzis et al.[15] compared a 76-point STP test to HFA 30-2 full-threshold SAP in 29 glaucoma patients of unspecified severity. They reported a sensitivity of 74%, which is similar to the overall sensitivity of 76% as found in our study.

Several studies report on test-retest variability of SAP. Many of those compare the threshold sensitivity of individual test locations between consecutive tests, which is incompatible with STP output. A direct comparison can only be made with three studies. First, a study by Bjerre et al.[20] concerning 74 glaucoma patients that underwent two HFA 24-2 SITA Standard tests. They counted the number of depressed points at P<5% as a global index of visual field loss, and then compared the first with the second test. The resulting coefficient of repeatability was 9.9 points. Second, a study by Smith et al.[21] concerning 192 glaucoma patients that underwent several full threshold HFA tests. They used the MD as a measure of visual field loss and expressed test-retest variability as a variance. They

found a variance of 4.6 dB2, which equals a coefficient of repeatability of 4.3 dB. The latter value can be converted to STP format by dividing it by 0.75, yielding 7.0 missed points. Finally, we re-analyzed data collected in the Groningen Longitudinal Glaucoma Study.[22,23] Two consecutive HFA 30-2 SITA fast VF's were selected to determine the MD test-retest variability of 221 glaucoma patients. The coefficient of repeatability was 4.0dB, that is, 6.6 missed points. All three of the above-mentioned figures are comparable to the coefficient of repeatability of 7.0 missed points as found for STP in this study, suggesting that the test-retest variability of SAP and STP are similar.

There are some advantages of STP over SAP. Subjects find STP easier because test duration is a lot shorter, but also because – unlike in SAP – the majority of the stimuli are not close to threshold luminance. Furthermore, because we used a threshold-related STP test strategy (see methods), the number of missed points on STP was less affected by cataract and other media opacities than the global index MD. However, unlike the Pattern Standard Deviation (PSD) global index in SAP, the number of missed points on STP does not return to normal in end-stage disease, since the amount of adjustment for overall sensitivity loss is limited. Existing progression detection algorithms like the Glaucoma Progression Analysis (GPA; Carl Zeiss Meditec Inc., Dublin, CA, USA) and the AGIS criterion[24] cannot be used with STP, but the recently introduced and evaluated Nonparametric Progression Analysis (NPA) algorithm[25,23] can be applied to any continuous visual field loss measure, including the number of missed points on STP. The major drawback of STP is its lack of information about scotoma depth. This might be relevant in progression detection, since glaucoma progression has been shown to be a mixture of increase in both scotoma size and depth.[26,27] Given the obvious linear relationship between the number of missed points on STP and SAP MD, however, STP appears to be a viable alternative to SAP for obtaining a general impression of glaucomatous damage. Since SAP can be too demanding, especially for elderly patients, further longitudinal studies to evaluate the role of STP in progression detection would seem worthwhile.

Appendix

For the test used in this study, access "System Setup" and then "Additional Setup" on your HFA device. Select "Custom Test", then select "Create Screening Test". Coordinates of each of the 52 test points can now be entered consecutively. The test is identical to the HFA 24-2 grid without the two nasal points. Spacing between the test points is 6°. Upon completion, the default test parameters are shown. "Test Mode" needs to be set to "Threshold Related".

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