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Comparison of Visual Field Results of Humphrey Matrix Perimetry and Standard Automated Perimetry with SITA Strategy in Glaucoma and Ocular Hypertension Subjects

Glokom ve Oküler Hipertansiyon Hastalarında Humphrey Matriks Perimetrisi ve Standart Otomatik Perimetrinin SITA Stratejisi ile Elde Edilen Görme Alanı Sonuçlarının Karşılaştırılması

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Summary

Purpose: To compare the results of Humphrey Matrix 30-2 full threshold test and standard automated perimetry (SAP) using the Swedish Interactive Threshold Algorithm (30-2 SITA standard strategy).

Material and Method: Test duration, mean deviation (MD), pattern standard deviation (PSD), number of depressed points on pattern deviation plot (PDP) at level of $p<0.05$ and $p<0.01$ were compared using the Wilcoxon signed-rank test. The correlations between MD, PSD and the number of depressed points were analyzed using Spearman's rank correlation coefficient. Kappa (κ) statistic was used to determine the strength of agreement between Matrix and SAP-SITA tests.

Results: PSD was higher in Matrix perimetry and the number of depressed points at level of $p<0.05$ was significantly higher in SAP-SITA test. MD ($r=0.48$), PSD ($r=0.58$) and the number of points depressed on PDP at the level of <0.05 and <0.01 ($r=0.48$ and $r=0.47$, respectively) showed moderate correlations between the two tests ($p<0.001$). The agreement between SAP and Matrix perimetry was found to be moderate ($\kappa=0.44$, $p<0.001$).

Discussion: Visual field indices and the number of depressed points on PDP of the two perimetries demonstrated only a moderate level of correlation. Therefore, a direct comparison of the global indices or individual test points should be avoided among Matrix perimetry and SAP. *(Turk J Ophthalmol 2011; 41: 98-103)*

Key Words: Frequency doubling technology, glaucoma, humphrey matrix perimetry, SITA strategy, standard automated perimetry

Özet

Amaç: Humphrey Matriks 30-2 tam eşik testi sonuçları ile İsveç interaktif eşik algoritmasını (30-2 SITA standart stratejisi) kullananan standart otomatize perimetri (SAP) sonuçlarını karşılaştırmak.

Gereç ve Yöntem: Test süresi, ortalama deviasyon (MD), patern standart deviasyon (PSD) ile patern deviasyon haritasında $p<0,05$ ve $p<0,01$ düzeyinde baskılanmış nokta sayıları Wilcoxon signed rank testi ile karşılaştırıldı. İki testteki MD, PSD ve baskılanmış nokta sayıları arasındaki korelasyon Spearman korelasyon katsayısı kullanılarak analiz edildi. Matriks ve SAP SITA testleri arasındaki uyumun değerlendirilmesinde kappa (κ) istatistiği kullanıldı.

Sonuçlar: PSD'nin matriks perimetride, $p<0,05$ seviyesinde baskılanmış nokta sayısının ise SAP-SITA testinde istatistiksel açıdan anlamlı oranda yüksek olduğu saptandı. İki test arasında MD ($r=0,48$), PSD ($r=0,58$) ve Patern deviasyon haritasında $p<0,05$ ve $p<0,01$ düzeyinde baskılanmış noktaların sayısı ($r=0,48$ and $r=0,47$, sırasıyla) arasında orta derecede korelasyon olduğu görüldü ($p<0,001$). SAP ve Matriks perimetri arasındaki uyumun orta düzeyde olduğu saptandı ($\kappa=0,44$, $p<0,001$).

Tartışma: İki perimetrideki görme alanı indeksleri ve patern deviasyon haritasındaki baskılanmış noktaların sayısı yalnızca orta düzeyde korelasyon göstermektedir. Bu nedenle Matriks perimetri ve SAP'da ki global indeksler ve test noktaları arasında doğrudan bir karşılaştırma yapılmamalıdır. *(Turk J Ophthalmol 2011; 41: 98-103)*

Anahtar Kelimeler: Frekans çiftleme teknolojisi, glokom, humphrey matriks perimetri, SITA stratejisi, standart otomatize perimetre

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Introduction

Standard automated perimetry (SAP) is currently the most common method for detection of visual field defects in glaucoma. SAP uses a differential contrast stimulus that consists of a small spot of white light presented on a white background. However, most of the retinal ganglion cells (RGC) can respond to this stimulus and a considerable amount of RGCs has to be lost before the detection of functional damage by SAP.[1,2] The inability of SAP to detect early functional damage led to investigation of selective perimetric tests that target specific ganglion cell subpopulations. These tests are originally developed on the basis of selective ganglion cell loss hypothesis, which assumes that the RGCs with larger cell bodies may be damaged early in the glaucomatous process.[3,4] However, some histological studies have shown that the degree of damage was approximately the same across all ganglion cell types[5-7]. This resulted in a second hypothesis that would explain the earlier detection of visual field damage with these selective tests. According to this hypothesis, the inadequacy of SAP to detect early functional damage might be due to overlapping ganglion cell receptive fields, therefore, frequency-doubling technology (FDT) perimetry and short-wavelength automated perimetry (SWAP) that target RGC subpopulations with lower levels of redundancy may improve the detection of early visual field damage.[8]

Among these newer psychophysical tests, FDT perimetry uses a stimulus of low spatial with high temporal frequency which preferentially stimulates the magnocellular RGCs.[9] The first version of FDT perimetry used a maximum of 19 targets (10º) extending from the fixation. Although several studies have shown that FDT perimetry could detect glaucomatous visual field loss reliably, small scotomas could be skipped due to this large target size.[10-12] The Humphrey Matrix perimetry, the latest version of FDT perimetry, uses a smaller (5º) stimulus, which allows testing of approximately the same number of points as SAP and, therefore, enhances the diagnostic ability of FDT perimetry. The Humphrey Matrix perimetry uses a threshold determination procedure based on Bayesian statistics known as ZEST (zippy estimation by sequential testing).[13] It is similar to the Swedish Interactive Threshold Algorithm (SITA) found in the Humphrey Field Analyzer (HFA). This algorithm was shown to reduce the test time (by about 50%) and had greater efficiency, lower intra- and intertest variability, and similar levels of accuracy.[14,15]

In this study, we aimed to compare the results of Humphrey Matrix 30-2 full threshold perimetry and SAP-SITA (30-2 SITA standard strategy) in patients with glaucoma and ocular hypertension (OHT).

Materials and Methods

One hundred twenty patients with OHT or glaucoma were included in this study. The study protocol was designed according to the Declaration of Helsinki and approved by the institutional review board of Hacettepe University School of Medicine. Informed consent was obtained from all participating patients.

All subjects underwent a comprehensive eye examination by a glaucoma specialist (Mİ), including slit-lamp biomicroscopy, applanation tonometry, gonioscopy, fundoscopy, perimetry (both SAP-SITA 30-2 and FDT-Matrix 30-2), ultrasound pachymetry and optic nerve head topography. Patients with best corrected visual acuity less than 20/40, refractive error> 5.00 spherical diopters (D) and/or 2 D of cylinder, corneal opacity or cataract were excluded from the study.

Patients were classified as having OHT, if they had intraocular pressure (IOP) ≥22 mmHg on at least 3 separate occasions, normal visual field with SAP 30-2 full-threshold test, normal optic nerve head (ONH) and retinal nerve fiber layer (RNFL) appearance on clinical examination. Patients were classified as having primary open-angle glaucoma (POAG), when they had ONH or RNFL structural abnormalities (diffuse thinning, focal narrowing, or notching of the optic disc rim, especially at the inferior or superior poles, documented progression of cupping of the optic disc, diffuse or localized abnormalities of the peripapillary RNFL, especially in the inferior or superior poles, disc rim or peripapillary RNFL hemorrhages, neural rim asymmetry of the two eyes consistent with loss of neural tissue) and/or visual field damage (in SAP 30-2 full threshold test) consistent with RNFL damage (nasal step, arcuate field defect, temporal wedge or paracentral/midperiphery depression in clusters of neighbouring test points), visual field loss in the upper hemifield that is different compared with the lower hemifield {(abnormal glaucoma hemifield test (GHT)}, not explained by any other disease and open-angle at gonioscopy. Exfoliative glaucoma patients had exfoliative material on the pupillary ruff or anterior lens capsule visible with or without pupillary dilation.

Although IOP measurements were not modified according to the pachymetric results, central corneal thickness values affected our treatment approach and decision-making in differentiating preperimetric glaucoma and OHT patients.

All patients had previous experience with SAP and FDT perimetries. Within 2 weeks period after clinical examination, the subjects underwent SAP and FDT tests on the same day in random order with a 15-minute or

more break between the two tests. SAP was performed using the Humphrey Field Analyzer II 750 (Carl Zeiss Meditec, Dublin, California, USA) with a 30-2 SITA standard strategy. A conventional size III white stimulus on a white background was used. Optimal lens correction for near was placed before the tested eye and the other eye was patched. FDT perimetry was performed with Humphrey Matrix Visual Field Instrument (Carl Zeiss Meditec, Dublin, Ca; Welch-Allyn, Skaneateles, NY) using the Matrix 30-2 full threshold program. The patients' habitual correction was worn during the examination. One eye of each patient with reliable SAP (false-positive and false-negative results less than 33% and fixation losses <20%) and FDT (fixation losses, false-positive and false-negative results <20%) was randomly used for the statistical analysis, when both eyes satisfied the inclusion criteria. For both perimetric methods, abnormal visual field was defined as a GHT outside normal limits, pattern standard deviation (PSD) with $p<5\%$ and presence of a cluster of 3 or more contiguous non-edge points in a location typical for glaucoma with $p<5\%$ with at least one point having $p<1\%$ on pattern deviation plot (PDP).

Statistical Analysis

The statistical package for the social sciences (SPSS) version 11.5 (SPSS Inc., Chicago, Illinois, USA) was used in the analysis of the data. Test duration, mean deviation (MD), PSD, number of depressed points on PDP at level of $p<0.05$ and $p<0.01$ were compared between SAP-SITA and Matrix 30-2 full threshold perimetry using Wilcoxon signed-rank test. The correlations between visual field indices (MD and PSD) and number of abnormal points on PDP were analyzed using Spearman's rank correlation coefficient and, kappa (κ) statistic was used to determine the strength of agreement between Matrix and SAP-SITA tests. A κ value >0.8 was accepted as almost perfect, 0.6 to 0.8 as substantial, 0.4 to 0.6 as moderate, 0.2 to 0.4 as fair, and <0.2 as slight.

Results

Forty-four OHT subjects and 76 glaucoma patients were enrolled in this study. Glaucoma group included 57 POAG and 19 exfoliative glaucoma patients. Patient characteristics are given in detail in Table 1. All visual field tests were reliable according to the criteria described above.

Test duration of SAP-SITA was statistically significantly longer than that of Matrix perimetry (451.34±58.02 vs. 384.36±15.29 seconds, respectively; $p<0.001$) (Table 1). The mean values of MD and PSD as well as the number of depressed points at level of $p<0.05$ and $p<0.01$ are given in Table 2. There were no differences in MD values of SAP-SITA and FDT Matrix in the OHT and glaucoma groups ($p=0.14$ and $p=0.85$, respectively), whereas PSD values of FDT Matrix were found to be statistically higher than those of SAP-SITA in both OHT ($p<0.001$) and glaucoma groups ($p=0.006$). The number of depressed points at level of $p<0.05$ was higher in SAP-SITA than in FDT Matrix in both OHT ($p=0.002$) and glaucoma groups ($p<0.001$), however, no differences could be found in the number of depressed points at level of $p<0.01$.

In the entire group, SAP-SITA MD demonstrated a significant positive correlation with Matrix MD ($r=0.48$, $p<0.001$) and SAP-SITA PSD exhibited a significant positive correlation with Matrix PSD ($r=0.58$, $p<0.001$) (Figure 1A and 2A, respectively). Number of points depressed at level of $p<0.05$ and $p<0.01$ showed a moderate correlation between the two tests ($r=0.48$, $r=0.47$, respectively; $p<0.001$) (Table 2). In OHT group, we failed to find a significant correlation between SAP-SITA and FDT-Matrix global indices (Table 2). In glaucoma group, SAP MD and PSD were found to be significantly correlated with Matrix MD and PSD ($r=0.53$, $r=0.60$, respectively; $p<0.001$) (Figure 1B and 2B). A similar correlation between the two tests was also demonstrated in the number of depressed points at level of $p<0.05$ and $p<0.01$ ($r=0.49$, $r=0.53$, respectively; $p<0.001$) (Table 2). When only patients with perimetric glaucoma were included in the analysis, the correlation coefficients for MD ($r=0.65$, $p<0.001$) and the number of depressed points at level of $p<0.01$ ($r=0.62$, $p<0.001$) were found to be slightly higher (Table 3).

We detected visual field defects in 38 patients with SAP and in 42 patients with FDT-Matrix. Sixty-five patients (54.2%) had normal and 25 patients (20.8%)

Table 1. Patient and visual field characteristics

	Total (n=120)	OHT (n=44)	Glaucoma (n=76)
Age (years)	57.75±11.88 (23-81)	53.04±10.73 (23-76)	60.47±11.72 (28-81)
Gender			
Men	42 (35%)	5 (11.4%)	37 (48.7%)
Women	78 (65%)	39 (88.6%)	39 (51.3%)
Test Duration (seconds)			
SAP-SITA	451.34±58.02	422.39±45.45	468.10±58.14
FDT-Matrix	384.36±15.29	381.89±12.74	385.79±16.50

FDT: Frequency doubling technology
OHT: Ocular Hypertension
SAP: Standard automated perimetry
SITA: Swedish interactive threshold algorithm

had abnormal visual field with both perimetric methods and the agreement between the two tests was found to be moderate (κ=0.44, p<0.001).

Discussion

Humphrey Matrix perimetry is a second-generation FDT perimetry that permits examination of larger number of visual field locations compared to the first-generation FDT. The FDT-Matrix 30-2 threshold program uses 68 stimuli (5ºx5º square test targets) and one 5º circular target arranged in a 30-2 like pattern. It has been shown that Humphrey Matrix perimeter offers improved spatial distribution similar to SAP.[11]

In agreement with the previous studies,[16,18] we found the test duration of FDT-Matrix to be significantly shorter than that of SAP-SITA. This difference may be explained by the different algorithms used by these tests. FDT-Matrix uses the ZEST algorithm for threshold estimation and each point is tested by a constant number of 4 stimuli at various thresholds.[19,20] This algorithm is computationally simpler than the SITA standard strategy, which uses variable number of stimulations at each

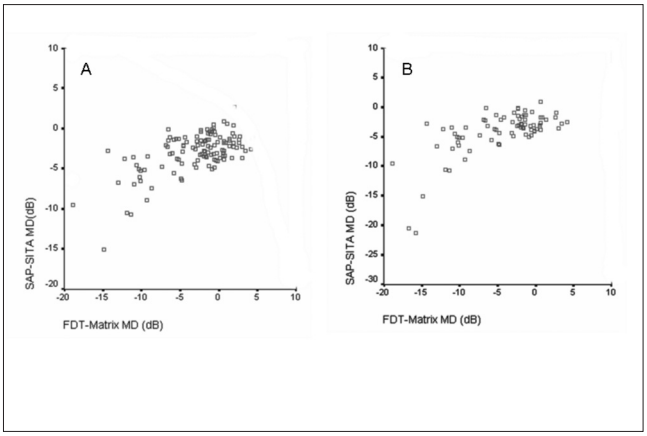

Figure 1. A graph showing the correlation between SAP-SITA and FDT-Matrix mean deviation (MD)
(A) In the entire group (0.48; p<0.001)
(B) In the glaucoma group (0.53; p<0.001)

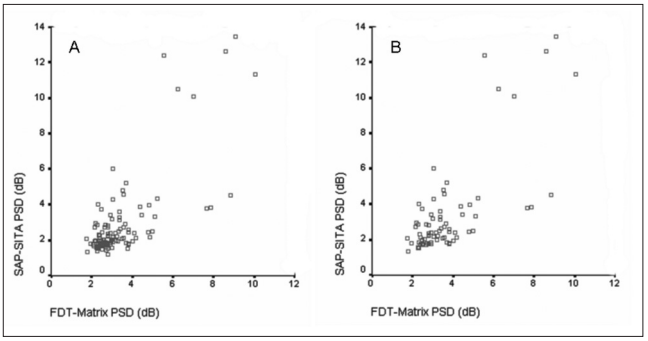

Figure 2. A graph showing the correlation between SAP-SITA and FDT-Matrix pattern standard deviation (PSD)
(A) In the entire group (0.58; p<0.001)
(B) In the glaucoma group (0.60; p<0.001)

Table 2. The comparison and correlation of visual field indices and number of depressed points on pattern deviation plot between SAP-SITA and FDT-Matrix

	Patients	SAP-SITA	FDT-Matrix	P*	Spearman's Correlation Coefficient (rho)
MD (dB)	Total	-3.26±3.38	-3.19±4.83	0.48	0.48 (<0.001)
	OHT	-1.48±1.33	-0.84±2.79	0.14	0.12
	Glaucoma	-4.30±3.77	-4.55±5.23	0.85	0.53 (<0.001)
PSD (dB)	Total	2.82±2.25	3.31±1.53	<0.001*	0.58 (<0.001)
	OHT	1.84±0.32	2.64±0.49	<0.001*	0.18
	Glaucoma	3.40±2.65	3.69±1.78	0.006*	0.60 (<0.001)
Number of depressed points with p<0.05	Total	11.06±10.78	7.42±8.71	<0.001*	0.48 (<0.001)
	OHT	5.36±3.73	3.27±3.64	0.002*	0.23
	Glaucoma	14.35±12.10	9.83±9.83	<0.001*	0.49 (<0.001)
Number of depressed points with p<0.01	Total	4.31±8.83	3.69±6.76	0.45	0.47 (<0.001)
	OHT	0.68±1.09	1.00±1.90	0.69	-0.07
	Glaucoma	6.41±10.53	5.25±7.98	0.27	0.53 (<0.001)

MD: Mean deviation
OHT: Ocular Hypertension
PSD: Pattern standart deviation.
*P value for Wilcoxon signed ranks test comparing SAP-SITA and FDT-Matrix
SAP: Standard automated perimetry
SITA: Swedish interactive threshold algorithm

point with a gradual increase in the threshold level until the threshold of each location is determined.[15] The test-retest variability of FDT-Matrix is uniform over the measurement range of the instrument.[19]

In our study, MD values of SAP-SITA and FDT Matrix were similar with no statistically significant differences, whereas PSD values of FDT Matrix were higher than those of SAP-SITA in both OHT and glaucoma groups. In PDP, the number of depressed points at level of $p<0.05$ was higher in SAP-SITA, which lost its significance at level of $p<0.01$. In the study by Patel et al.,[17] MD was significantly lower with Matrix compared to SITA (-5.34+/-5.42 dB, -4.14+/-5.29 dB, respectively; p=0.03), whereas no significant difference was found in PSD between the two devices (p=0.78). Matrix delineated significantly smaller and deeper defects than those found with SITA.

We observed a moderate correlation between the global indices of Matrix 30-2 full threshold program and SAP 30-2 SITA standard tests in the entire study group (r=0.47 for MD and r=0.58 for PSD). This correlation was slightly stronger when only glaucoma (r=0.53 and 0.60, respectively) or perimetric glaucoma (r=0.65 and 0.60, respectively) patients were included in the analysis. A similar correlation was also seen between the total number of defects at the significance level of <0.05 and <0.01 on PDP (r=0.48 and r=0.47, respectively, in the entire study group) (r=0.49 and r=0.53, respectively; in the glaucoma group) (r=0.50 and r=0.62, respectively; in the perimetric glaucoma group). Artes et al.[19] compared the results of Humphrey Matrix perimetry with SAP and reported a strong correlation for MD and PSD of FDT-2 24-2 program and SAP-SITA standard 24-2 test in glaucoma patients with early to moderate visual field loss ($r>0.8$, $p<0.001$). Total deviation plots of Matrix may slightly underestimate the visual field loss apparent with SAP. However, the pattern-deviation maps of both instruments were shown to agree well with each other. In a study by Leeprachanon et al., MD and PSD indices of SAP with 24-2 SITA standard algorithm and FDT Humphrey Matrix 24-2 full threshold tests showed significant correlations in patients with glaucoma (r=0.75 and r=0.80, respectively), but not in the normal group. In the study by Zarkovic et al.,[21] a good correlation was reported between MD values of SITA standard 24-2 and FDT-Matrix 24-2 threshold tests (r=0.69) (18). Sakata et al. found significant correlations between global indices (r=0.75 for MD and r=0.83 for PSD) and number of depressed points in the total deviation plot and PDP (r=0.80 and r=0.78, respectively; p<.001) of SAP-SITA 24-2 and FDT-Matrix 24-2 programs (22). In a previous study with a smaller number of subjects (n=85), FDT Matrix MD and PSD parameters were found to be highly correlated with those of SAP (r=0.66 and 0.69, respectively) and the κ value was 0.6 for SAP and

Table 3. The comparison and correlation of visual field indices and number of depressed points on pattern deviation plot between SAP-SITA and FDT-Matrix in preperimetric and perimetric glaucoma patients

	Patients	SAP-SITA	FDT-Matrix	P*	Spearman's Correlation Coefficient (rho)
MD (dB)	Total	-3.26±3.38	-3.19±4.83	0.48	0.48 (<0.001)
	OHT	-1.48±1.33	-0.84±2.79	0.14	0.12
	Glaucoma	-4.30±3.77	-4.55±5.23	0.85	0.53 (<0.001)
PSD (dB)	Total	2.82±2.25	3.31±1.53	<0.001*	0.58 (<0.001)
	OHT	1.84±0.32	2.64±0.49	<0.001*	0.18
	Glaucoma	3.40±2.65	3.69±1.78	0.006*	0.60 (<0.001)
Number of depressed points with p<0.05	Total	11.06±10.78	7.42±8.71	<0.001*	0.48 (<0.001)
	OHT	5.36±3.73	3.27±3.64	0.002*	0.23
	Glaucoma	14.35±12.10	9.83±9.83	<0.001*	0.49 (<0.001)
Number of depressed points with p<0.01	Total	4.31±8.83	3.69±6.76	0.45	0.47 (<0.001)
	OHT	0.68±1.09	1.00±1.90	0.69	-0.07
	Glaucoma	6.41±10.53	5.25±7.98	0.27	0.53 (<0.001)

MD: Mean deviation
OHT: Ocular Hypertension
PSD: Pattern standart deviation.
*P value for Wilcoxon signed ranks test comparing SAP-SITA and FDT-Matrix
SAP: Standard automated perimetry
SITA: Swedish interactive threshold algorithm

Matrix.[23] Different correlations among previous studies can be explained by the characteristics of the patient population with variable visual defects ranging from early to severe, patient age and number of the studied subjects.

Sixty-five patients (54.2%) had normal visual fields with both tests, whereas 25 patients (20.8%) had abnormal visual field with both perimetric methods and the agreement between the two tests was moderate ($K=0.44$, $p<0.001$). Leeprachanon et al. evaluated the agreement between the two tests with the GHT and PSD criteria in patients with early to moderate visual field loss and found a substantial agreement between FDT-Matrix 24-2 and SAP with SITA standard 24-2 (83% agreement, $\kappa=0.66$ for GHT criteria and 86% agreement, $\kappa=0.70$ for PSD criteria).[21] The location of defects within 12 hemifield clusters found with FDT agreed moderately well with those detected with SAP (kappa=0.48). Sakata et al.[22] used the same criteria as in our study for definition of abnormal visual field and reported a moderate agreement between the two perimetric methods similar to our finding ($\kappa=0.49$). The moderate agreement between these two tests might be again explained by the different psychophysical properties and algorithms used in these tests. SAP employs differential light stimulus, which is nonspecific for ganglion cell type, whereas FDT perimetry measures contrast sensitivity and targets magnocellular cells.[8,12,24]

In conclusion, Humphrey Matrix is a quicker test than SAP-SITA. Visual field indices and the number of depressed points on PDP of the two perimetries are only moderately correlated. Therefore, a direct comparison of the global indices or individual test points should be avoided among Humphrey Matrix 30-2 full threshold perimetry and SAP perimetry with 30-2 SITA standard strategy.

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