NeuroVision, Inc.

CLINICAL STUDY REPORT

EVALUATION OF THE AA-1 SYSTEM FOR THE TREATMENT OF AMBLYOPIA

(Protocol No. ISO2 Rev. 06)

July 2001

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1.0 INTRODUCTION

Amblyopia, also referred to as "lazy eye", is a defect in the visual acuity of an eye that is anatomically and functionally normal, which persists after refractive errors in the eye were corrected. The cause of amblyopia is generally believed to be an abnormality that occurred during a critical period in childhood and prevented the visual system from developing normally. Normally two identical images are transferred from both eyes to the brain, which fuses the two images into a composite, single image. However, sometimes the image arriving from one eye is significantly different than that arriving from the other eye. This can be caused by a variety of factors, such as the eyes not being parallel (strabismus or squint), one eye being more shortsighted than the other, or conditions that create abnormal images in one or both eyes.

Amblyopia in children is usually treated by occluding the non-amblyopic eye. The idea behind this method is to "force" the amblyopic eye to "strengthen", i.e., increase in visual acuity. Occlusion of the dominant eye is a long established method. However, it has many drawbacks, the most major being low compliance with the treatment. Furthermore, the method is only useful until the age of about nine, and beyond that age the method is basically useless. Even for children below this age there are several disadvantages, such as impaired visual function, social and emotional problems due to wearing an unsightly patch over one eye and, sometimes, skin irritation associated with the patch.

Other methods for treating amblyopia include optical penalization, in which lenses are used to blur rather than occlude the vision of the non-amblyopic eye and cycloplegic drugs that are also used to blur the vision of the non-amblyopic eye. However, these methods are not preferred and have limited success for various reasons, for example, blurring vision is taxing and annoying to the patient and drugs must be administered with caution.

In the absence of effective treatment for Amblyopia, NeuroVision has developed a new system that is based on repetitive learning sessions aimed to improve the visual acuity of the amblyopic eye. The performance of this new system was evaluated in this clinical study.

<u>Administration of the study</u>
The clinical study was sponsored by NeuroVision Ltd. (Tel-Aviv, Israel) and was conducted from August 2000 to June 2001. The principal investigator was Dr. Tova Ma-Naim from the Ophthalmic Department, Shiba Medical Center, Israel.
The study protocol and case report forms (CRFs) were approved by the Principal Investigator, the Sheba Medical Center Ethics Committee (IRB) and the Ministry of Health prior to the commencement of the study.

Patients were well informed and have signed informed consent forms prior to their enrollment.
The trial was conducted in accordance with all applicable national and international regulatory requirements, in particular the Good Clinical Practice (GCP) requirements of the FDA. Certified external auditors routinely monitor the trials for GCP compliance.

2.0 DEVICE DESCRIPTION

The AA-1 Adult Amblyopia Treatment System is indicated for the treatment of patients aged 9 and up, suffering from amblyopia.

The treatment is composed of a series of sessions, conducted at a clinic in a controlled environment. During every session, the patient is exposed to interactive visual stimulations, in which the patient should identify and indicate the right images to the treatment station computer.

The treatment station includes a standard (commercial) PC workstation and a standard monitor. The workstation is connected to the Internet.

The clinic administrator interacts with the treatment workstation via standard I/O devices: Mouse and Keyboard. The patient interacts with the treatment workstation via the computer mouse only.

During the treatment the patient is seated 5 feet away from the monitor, and wears headphones, which provide him with additional instructions and feedback.

AA-1 treatment consists of 20-30 interactive sessions lasting about 30 minutes each. Visits occur twice weekly and the treatment program is completed in about three months. Through the successive sessions, the patient completes increasingly demanding visual perception tasks.

AA-1, by remotely analyzing patients' performance and customizing their treatment parameters, provides to its points-of-care service that is tailored to each individual patient. This service is delivered to the treatment sites over the Internet.

3.0 PURPOSE AND OBJECTIVES

The purpose of the study was to evaluate the effective performance of the AA-1 system for the treatment of amblyopia.

In particular, the performance of the AA-1 System was addressed through the following objectives:

1) Effective performance of the AA-1 system in improving Best Corrected Visual Acuity (BCVA) of amblyopic subjects over their baseline BCVA.

2) Maintenance of the improved BACA

4.0 ENDPOINTS

4.1 PRIMARY ENDPOINT

Acuity improvement

- Improvement of a minimum of 2 lines in ETDRS chart of the BCVA over baseline in a minimum of 60% of completed subjects.

4.2 SECONDARY ENDPOINT

Persistence

- Maintenance of the improved visual acuity (+/- 50%) after 3 months post-treatment.

5.0 PROTOCOL SUMMARY

5.1 DESIGN

Prospective, randomized, single-blinded, controlled study. Independent clinicians performed all clinical visual tests in a double-blinded manner.

5.2 PATIENT POPULATION

The inclusion criteria included:

1. Monocular Refractive Amblyopia and/or Strabismic Amblyopia.

2. Age is between 9 and 55 years.
3. Cognitive intact, ability to follow multiple step instructions.
4. Ability and agreement to attend all study visits.
5. Best Corrected Visual Acuity is worse than 20/30, and better than 20/100.
6. A signed Informed Consent Form.

The exclusion criteria included:
1. Activity limitation due to medical disorder, medications, or emotional status.
2 Other eye disease or other causes for reduced visual acuity.
3. Migraines or Epilepsy.
4. Participation in other investigation that may directly or indirectly affect the results of this study.

5.3 STUDY GROUPS

Treatment Group
One study group (40 subjects) that underwent a series of treatment sessions with the system. Visual acuity testing was performed every 4 sessions.

Control Group
Ten control subjects, randomly selected, underwent treatment sessions provided in a non-specific sequence. Cross-over to the study group was performed when no improvement occurs after four sequential visual acuity tests.

5.4 ENROLLMENT PROCESS

Sixty-five patients were enrolled in the study. Enrollment procedure included:
- Complete Screening form
- Informed Consent.
- Subject's details
- Baseline information
- Comprehensive ocular examination including cycloplegic refraction evaluation, and dilated fundus examination performed by an independent licensed eye care practitioner (i.e., blinded from the timing of the examination).

5.5 MAPPING SESSIONS I AND II

- Baseline mapping.

5.6 TREATMENT SESSION 1 TO END OF STUDY

- A training/treatment session.
- Visual acuity assessment was performed every 4 Treatment Sessions.

5.7 POST-TREATMENT EXAMINATION (PTE)

Comprehensive ocular examination

5.8 PERSISTENCE EXAMINATION

Visual Acuity (VA) assessment was performed after 3 months from the Post-Treatment Examination, to verify the persistence of the visual acuity.

5.9 TREATMENT TERMINATION

When the following conditions are sustained during three sequential acuity tests (i.e. 12 treatment sessions), termination is to be considered:

- No improvement in visual acuity;
- No improvement in contrast sensitivity;
- No improvement in vernier acuity test;

Or 20/20 or better visual acuity is achieved;.

5.10 STUDY DURATION

The study last approximately 13 weeks of treatment for each patient. Additional visit was set three (3) months after the final session visit to assess treatment retention. Therefore, total study duration per patient was about six (6) months.

5.11 STATISTICAL CONSIDERATIONS

Subjects was evaluated for descriptive statistics and charting of outcomes on a stratified visual acuity basis giving percentages of improvement for total population, as well as for age decade (9-20; 21-30; 31-40; 41-55). The data was evaluated on the basis of relative improvement from each individual's baseline information, and broken

down as to lines of Snellen (ETDRS) visual acuity improvement, keeping in mind that the minimum level of improvement considered to be successful is a two lines improvement.

Secondary statistical analysis was developed to stratify varying types of amblyopic conditions treated in an attempt to determine whether patterns of amblyopic conditions respond to this treatment therapy more effectively than others.

5.12 DATA COLLECTION

Data collection occurred on an ongoing basis during the investigation. All data made on case report forms forwarded to the study coordinator after each subject visit. The coordinator entered the complete forms into a computerized CRF system using the Double Data Entry method. Data analysis began after all case report forms was received by the study coordinator, the data entered into a dedicated data base and forwarded to the data analysis center.

5.13 SAMPLE SIZE

Based on a pilot study done prior to the clinical trials, it was shown that the effect of the treatment is rather dramatic. In order to maintain confidence interval of 95% (α=0.05) and type II error of 20% (80% power), a sample size of 33 patients was needed. Allowing for loss to follow-up and other unexpected contingencies, and in order to analyze subgroup treatment efficacy 50 patients were recruited to this study. Keeping the population proportion at 4:1 (the controls are used to evaluate normal performance database), 40 patients were enrolled into the treatment group and additional 10 were enrolled into the control group.

6.0 RESULTS

6.1 CLINICAL STUDY SUMMARY

A total of 54 patients, 9-55 years of age, concluded the trials. The following table summarizes the general information of the patient groups, and the final results:

Table 1: Clinical Study Summary

SUBJECT	TREATMENT GROUP N=44	CONTROL GROUP N=10	P Value
AGE	33.4 ±14.1	36.7 ±9.2	0.892
GENDER Male Female	 29 15	 8 2	0.396
DIAGNOSIS Anisometropic Strabismic Monofixation Combination	 17 8 4 15	 5 1 0 4	0.547
VISUAL ACUITY BASELINE (logMAR)	0.42 ±0.14	0.41 ±0.12	0.942
Current VISUAL ACUITY (logMAR)	0.17 ± 0.14	0.41 ±0.12	
AVERAGE VA IMPROVEMENT at treatment end	2.5 lines	No Improvement	
AVERAGE VA IMPROVEMENT 3 months post treatment end.	2.6 Lines	Not Applicable	

6.2 CLINICAL STUDY RESULTS VS. SUCCESS CRITERIA

The success criterion for the treatment as established in the study protocol is:
2 lines of improvement achieved by more then 60% of the study patients.

The actual results were:
2 lines of improvement achieved by 70.5% of the study patients.

The success criterion for the VA persistence as established in the study protocol is:
Regression of less than 50% of the VA improvement achieved in the treatment.

The actual results were:
No patient had a regression of more then 50% of the achieved VA improvement.
Furthermore, the average VA of the study group has slightly improved during the 3 months retention period.

Conclusion: The study results passed the success criteria.

The following paragraphs detail and statistically analyze the study results**.**

6.3 THE CLINICAL STUDY POPULATION

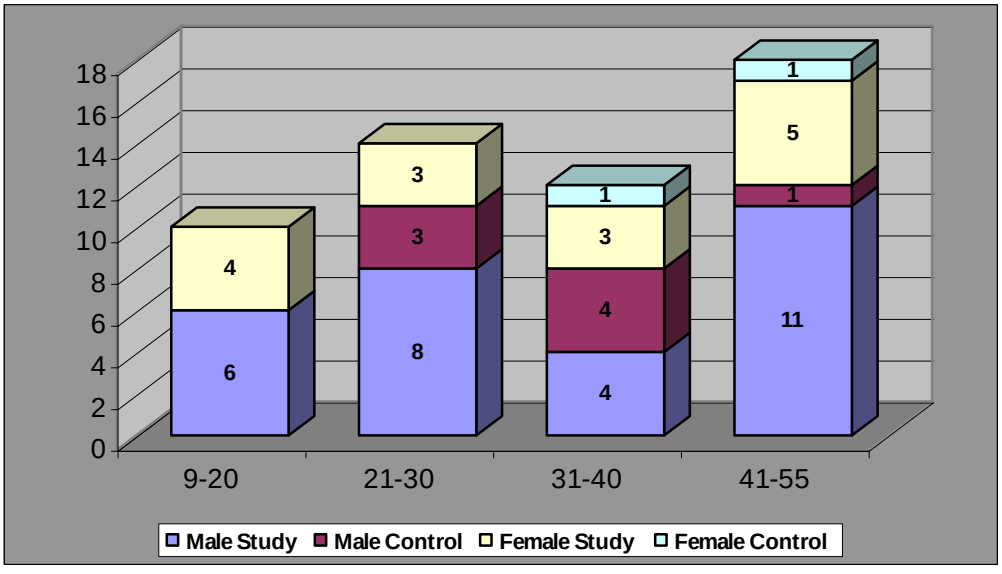
A total of 70 patients between the ages 9.5-54.8 years old (average age 33.7 and standard deviation of 13.30 years) were enrolled to this study in one center.

44 were recruited to the study group (average age of 33.4 and standard deviation of 14.06 years), and 10 were assigned to the control group (average age of 36.7 and standard deviation of 9.24 years).

Another 16 subjects were exit from the study. According to the reported reasons, 9 patients could not come on regular basis as the protocol requires; 4 patients stated that they were not interested to continue – and quit the study; 2 patients had to go through surgeries and 1 patient started military service and had to exit the study.

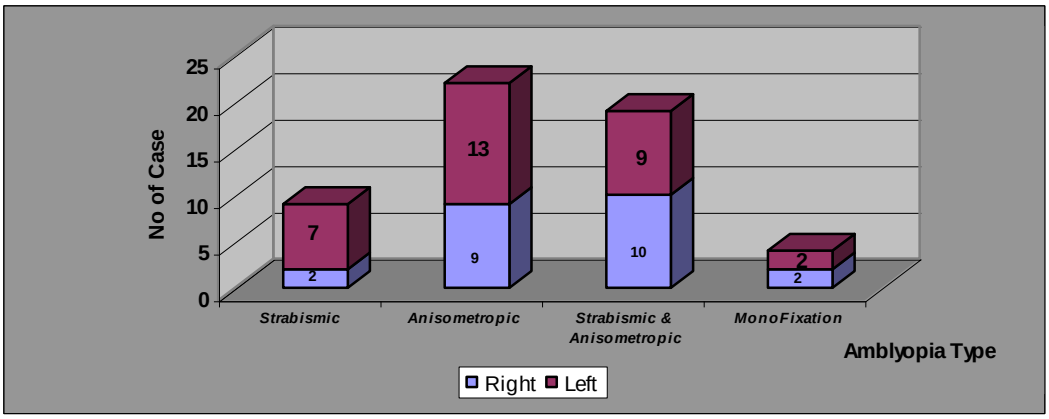
The distribution of the study and control groups according to the gender and the age group is presented in Graph 1.

Graph 1: Study Population Distribution According to Gender and Age Group



From the graph it could be seen that proportions of the distribution of population in the study between the study and the control group is kept among most of the age groups.

Graph 2: Study Population Distribution According to Amblyopia Type and Amblyopic Eye



The graph above contains the summarized data of both groups, showing the distribution of the study population. A table that details the basic characteristics of the study patients is provided in attachment A.

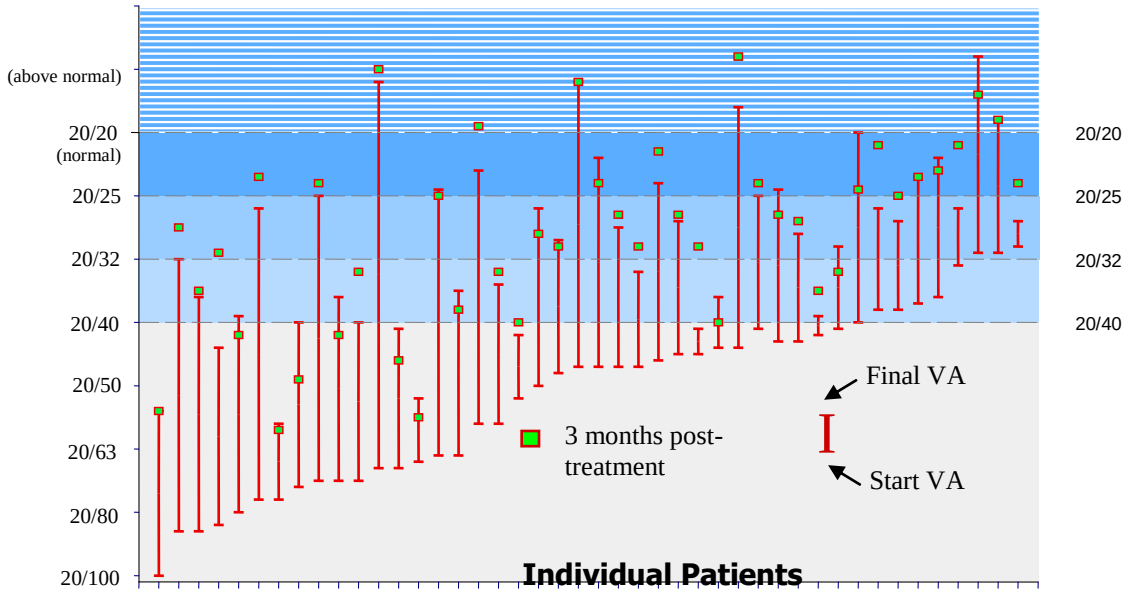
6.4 SAFETY ENDPOINT

No adverse event occurred throughout the study and all 54 patients completed the study. Therefore, it can be concluded that the treatment method proved to be safe for use.

6.5 EFFICACY ENDPOINTS

The following graph demonstrates the treatment group individual patients' Visual Acuity improvement and the Visual Acuity persistence 3 months after the treatment sessions end:

Graph 3: Treatment Group VA Improvement and Persistence



A table that details the VA improvement of all the study patients (treatment group + control group) is provided in attachment A.

6.6 VA IMPROVEMENT AND SUCCESS CRITERIA

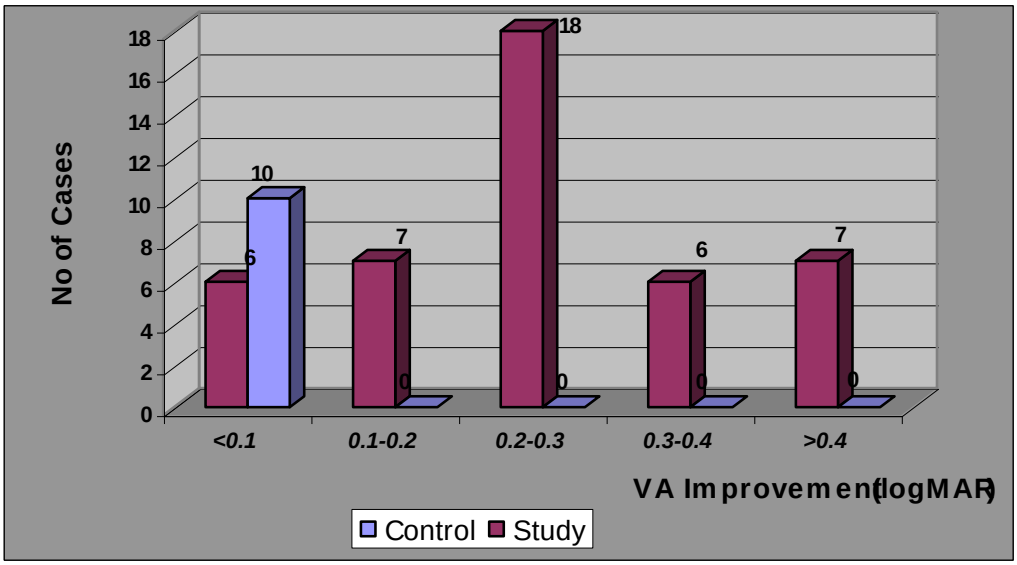
The study endpoints were defined as at least 2 lines of VA improvement or reaching 20/20.

Among the study group 31 patients (70.5%) succeeded in achieving at least the study endpoints.

All 10 patients (100%) of the control group failed to achieve the study endpoints and in fact there is no significant change between their baseline VA measurements and the final VA measurements.

The summary of the VA changes between baseline and endpoint measurements according to the study group is shown in Graph 4.

Graph 4: Summary of VA Changes (logMAR)



The graph represents the summary of the changes in VA, comparing the performances of the study and control groups. In can be seen that while all the control group patients are among the lowest VA improvement group (i.e., '<0.1'), the study group distributes with median improvement of 0.2-0.3.

To examine any statistically significant difference between the groups, Fisher's Exact test was performed.

The results of the Dynamometer grip strength test in the 2x2 matrix format are presented in Tables 2 & 3 below.

Table 2: Performance Analysis of the VA Test

		Succeeded	
		No	**Yes**
Group	**Study**	29.5%	70.5%
	Control	100%	0%

Table 3: Fisher's Exact Test Result

Chi-Square Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Fisher's Exact Test				0.00005	0.00005
N of Valid Cases	54				

According to the achieved improvement of both groups it can be concluded that there is a significant difference between them (P-value<0.05).

The secondary endpoint includes calculation of 95% confidence interval, of improvement percentage according to treatment groups.

The information is presented in Table 4.

Table 4: Confidence Interval of VA Change (logMAR)

	Distribution Data			95% C.I. of Differences	
	N	Mean	STD	Lower	Upper
Study	44	0.2482	0.128	0.2104	0.286
Control	10	0	5.44E-02	-0.034	0.0337

From the table above, it could be concluded that while the control's group confidence interval contains the zero (and the mean is also close to it), the study group shows significant improvement (of 0.25 lines in VA), without any relation to the zero.

The implication from this data is that the study group performed significant change in visual accuracy, where the control group showed no improvement.

Due to the fact that the 3rd VA check was set to be a midpoint in evaluating the performances of all patients in the study (all of the

control group was still received treatments), an ANOVA test was performed in order to find any significant differences in VA changes (including the exit patients group). Tables 5 through 7 present the results.

Table 5 presents the summarized changes in VA, according to study group.

Table 5: Confidence Interval of VA Changes After the 3rd Check (logMAR)

	Distribution Data			95% C.I. of Differences	
	N	Mean	STD	Lower	Upper
Study	44	0.1495	0.08556	0.1352	0.1638
Exit	12	0.1208	0.07280	0.1104	0.1312
Control	10	0.0070	0.05500	0.0011	0.0129

It can be seen, from the table above, that the average improvement of the study group was higher than improvement of the control group and with only minor difference from the exits group. In order to find whether this difference is statistically significant, two ANOVA test were performed, and presented in Tables 6 & 7 below:

Table 6: ANOVA Table Testing Significant Differences Between Study, Exit and Control Groups in VA Performances at the 3rd Check

		Sum of Squares	df	Mean Square	F	Sig.
VA Changes Vs. Study Group	Between Groups	.166	2	.083	13.033	.0000
	Within Groups	.400	63	.006		
	Total	.566	65			

(I) Type	(J) Type	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Control	Control					
	Study	-.1425*	.0279	.0000	-.1989	-.0862
	exit	-.1138*	.0341	.0014	-.1849	-.0427
Study	Control	.1425*	.0279	.0000	.0862	.1989
	Study					
	exit	.0287	.0260	.5913	-.0355	.0929
exit	Control	.1138*	.0341	.0014	.0427	.1849
	Study	-.0287	.0260	.5913	-.0929	.0355
	exit					

*. The mean difference is significant at the .05 level.

According to the ANOVA table, there is a significant difference ($p<0.05$) in the VA improvement between the study, the exit and the control groups at the 3rd check measurements.

It can be concluded that even at this stage, a significant difference in VA performances can be seen.

6.7 VA IMPROVEMENT - ANALYSIS ACCORDING TO AMBLYOPIA TYPE

In order to analyze the average improvement in VA (presented in logMAR units), several data group profiles were examined.

The summarized information of the data, according to Amblyopia type group, is presented in Table 7.

Table 7: Summarized Data of Improvement According to Amblyopia Type (logMAR)

Amblyopia Type		Chage (logMAR)
Strabismic	N	8
	Mean	.2275
	Std. Deviation	.1201
Anisometropic	N	17
	Mean	.2747
	Std. Deviation	.1608
Strabismic & Anisometropic	N	15
	Mean	.2280
	Std. Deviation	.1090
MonoFixation	N	4
	Mean	.2525
	Std. Deviation	2.500E-02
Total	N	44
	Mean	.2482
	Std. Deviation	.1280

The table demonstrates some minor differences in the average improvement. The highest average improvement was in the Anisometropic and the Monofixation groups, while the Strabismic group performances were the lowest.

The percentage of "achieved success" case, according to Amblyopia type, is presented in Table 8.

Table 8: Percentage of Success According to Amblyopia Type Group

			Amblyopia Type				
			Strabismic	**Anisometropic**	**Strabismic & Anisometropic**	**MonoFixation**	**Total**
Success	**No**	**No.**	2	6	5		13
		% of Total	25.00%	35.30%	33.30%		29.50%
	Yes	**No.**	6	11	10	4	31
		% of Total	75.00%	64.70%	66.70%	100.00%	70.50%

In order to determine any significant difference between the groups, an Chi-Square test was performed. The results are presented in Table 9 below:

Table 9: Chi-Square Test for Significant Differences Between Amblyopia Type Groups

	Value	**df**	**Asymp. Sig. (2-sided)**
Pearson Chi-Square	2.130	3	.546
N of Valid Cases	44		

According to the calculated data, no significant difference between Amblyopia type groups was found (P-value > 0.05).

6.8 VA IMPROVEMENT - ANALYSIS ACCORDING TO GENDER GROUP

The summarized information of the data, according to Gender group, is presented in Table 10.

Table 10: Summarized Data of Improvement According to Gender (logMAR)

Gender		Change (logMAR)
Female	N	15
	Mean	.2247
	Std. Deviation	.1158
Male	N	29
	Mean	.2603
	Std. Deviation	.1342
Total	N	44
	Mean	.2482
	Std. Deviation	.1280

The table shows that both the total average change is slightly higher among the male study group.

The percentage of "achieved success" case, according to gender, is presented in Table 11.

Table 11: Percentage of Success According to Gender

			Gender		
			Female	**Male**	**Total**
Success	**No**	**No.**	5	8	13
		% of Total	33.33%	27.60%	29.50%
	Yes	**No.**	10	21	31
		% of Total	66.67%	72.40%	70.50%

In order to determine any significant difference between the groups, a Chi-Square test was performed. The results are presented in Table 12 below:

Table 12: Chi-Square Test for Significant Differences Between Gender Groups

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.157	1	.692
N of Valid Cases	44		

According to the calculated data, no significant difference, between Gender groups, was found (P-value > 0.05).

6.9 VA IMPROVEMENT - ANALYSIS ACCORDING TO AGE GROUP

The summarized information of the data, according to Age group, is presented in Table 13.

Table 13: Summarized Data of Improvement According to Age Group (logMAR)

Age Group		Change (logMAR)
9-20	N	10
	Mean	.2650
	Std. Deviation	.1304
21-30	N	10
	Mean	.2550
	Std. Deviation	.1091
31-40	N	8
	Mean	.2238
	Std. Deviation	.1746
41-55	N	16
	Mean	.2456
	Std. Deviation	.1219
Total	N	44
	Mean	.2482
	Std. Deviation	.1280

From the data presented in the table above, it can be seen that there is no relation between age group and VA improvement.

The percentage of "achieved success" case, according to age group, is presented in Table 14.

Table 14: Percentage of Success According to Age Group

			Age Group				
			9-20	**21-30**	**31-40**	**41-55**	**Total**
Success	**No**	**No.**	2	2	3	6	13
		% of Total	20.00%	20.00%	37.50%	37.50%	29.50%
	Yes	**No.**	8	8	5	10	31
		% of Total	80.00%	80.00%	62.50%	62.50%	70.50%

In order to determine any significant difference between the groups, an Chi-Square test was performed. The results are presented in Table 15 below:

Table 15: Chi-Square Test for Significant Differences Between Age Groups

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	1.605	3	.658
N of Valid Cases	44		

According to the calculated data, no significant difference, between Age groups, was found (P-value > 0.05).

6.10 VA IMPROVEMENT - ANALYSIS ACCORDING TO VA BASE-LINE GROUP

The summarized information of the data, according to VA Baseline group, is presented in Table 16.

Table 16: Summarized Data of Improvement According to VA in Baseline (logMAR)

VA Baseline Group		Change (logMAR)
Base<20/40	N	8
	Mean	.17
	Std. Deviation	8.357E-02
20/40<=Base<20/50	N	16
	Mean	.22
	Std. Deviation	.117
20/50<=Base<=20/100	N	20
	Mean	.30
	Std. Deviation	.130
Total	N	44
	Mean	.25
	Std. Deviation	.128

From the data presented in the table above, it can be seen that improvement is depended on the VA baseline performances, showing better improvement on worst cases.

The percentage of "achieved success" case, according to VA baseline, is presented in Table 17.

Table 17: Percentage of Success According to Baseline VA Group

			VA Base-Line			
			Base<20/40	**20/40<=Base<20/50**	**20/50<=Base<20/100**	Total
Success	**No**	No.	4	6	3	13
		% of Total	50.00%	37.50%	15.00%	29.50%
	Yes	No.	4	10	17	31
		% of Total	50.00%	62.50%	85.00%	70.50%

The table presents higher percentage of successful cases for patients starting with a worse baseline VA. In order to determine any significant difference between the groups, an F-test was performed. The results are presented in Table 18 below:

Table 18: Chi-Square Test for Significant Differences Between VA Base-Line Groups

	Value	**df**	**Asymp. Sig. (2-sided)**
Pearson Chi-Square	4.127	2	.127
N of Valid Cases	44		

According to the calculated data, no significant difference was found in the VA improvement between the VA baseline groups (P-value < 0.05).

In Table 19, the Visual Acuity endpoint reached by the patients is presented according to the VA baseline group.

Table 19: VA Endpoint According to Baseline Group

VA Baseline group	No. of patients	Patients reaching 20/40 and better	Patients reaching 20/32 and better	Patients reaching 20/25 and better	Patients reaching 20/20 and better
Base < 20/40	8	N/A	N/A	4 (50%)	2 (25%)
20/40<=Base<20/50	16	N/A	12 (75%)	7 (43.7%)	3 (18.7%)
20/50<=Base<20/100	20	14 (70%)	7 (35%)	4 (20%)	1 (5%)

6.11 CONTRAST SENSITIVITY

Contrast sensitivity improvement was measured by comparing the contrast sensitivity value before and after the treatment.

The summary of the basic characteristics of the performances compared before and after the treatments is presented in Table 20.

Table 20: Summarized Data of Average Performance

		Mean	Std. Deviation	Std. Error Mean
Pair 1	***1.5 after***	48.98	2.317	1.135
	1.5 before	29.51	2.489	1.148
Pair 2	***3 after***	79.43	1.746	1.088
	3 before	41.69	2.938	1.176
Pair 3	***6 after***	57.54	2.421	1.143
	6 before	19.05	3.999	1.232
Pair 4	***12 after***	11.22	4.529	1.256
	12 before	3.63	4.276	1.245
Pair 5	***18 after***	3.09	3.342	1.200
	18 before	1.86	2.897	1.174

According to the presented data, in all 5 pairs, the patients achieved average higher scores in all measurements.

The correlation between the performances before and after treatment is presented in the following table.

Table 21: Correlation Between Performance (before Vs. after)

		N	Correlation	Sig.
Pair 1	**1.5 after & 1.5 before**	44	.369	.0138
Pair 2	**3 after & 3 before**	44	.348	.0208
Pair 3	**6 after & 6 before**	44	.520	.0003
Pair 4	**12 after & 12 before**	44	.366	.0144
Pair 5	**18 after & 18 before**	44	.486	.0008

The table shows that all calculated correlations are statistically significant ($p<0.05$) with high positive correlation.

A Paired Sample T-Test was performed in order to determine whether there are significant improvements in performances. The data is shown in Table 22.

Table 22: Paired Sample T-Test for Significant Improvement in Performances

		Paired Differences			95% Confidence Interval of the Difference		t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	*Lower*	*Upper*			
Pair 1	***1.5 after - 1.5 before***	19.47	2.679	1.160	14.21	24.72	3.36	43	0.0016
Pair 2	***3 after - 3 before***	37.75	2.793	1.168	32.27	43.22	4.08	43	0.0002
Pair 3	***6 after - 6 before***	38.49	3.304	1.197	32.01	44.96	6.14	43	0.0000
Pair 4	***12 after - 12 before***	7.59	5.309	1.286	-2.82	17.99	4.54	43	0.0000
Pair 5	***18 after - 18 before***	1.23	3.184	1.191	-5.01	7.47	3	43	0.0045

The presented T-Test shows that all the performance improvements are significant ($p<0.05$).

The average contrast sensitivity improvement according to the Amblyopia type is presented in Table 23.

Table 23: Summarizes data of Average Improvement According to Amblyopia Type

Amblyopia Type		1.5 Improve	3 Improve	6 Improve	12 Improve	18 Improve
Strabismic	N	8	8	8	8	8
	Mean	14.00	29.25	40.25	42.75	4.88
	Std. Deviation	34.715	67.001	57.911	47.602	11.969
Anisometropic	N	17	17	17	17	17
	Mean	4.18	16.18	29.29	17.53	2.76
	Std. Deviation	25.048	37.236	60.715	41.805	8.235
Strabismic & Anisometropic	N	15	15	15	15	15
	Mean	46.40	49.87	58.00	8.40	1.20
	Std. Deviation	53.173	51.515	50.225	17.262	4.178
MonoFixation	N	4	4	4	4	4
	Mean	34.00	20.25	23.25	10.75	5.00
	Std. Deviation	52.485	29.239	26.247	18.319	6.272
Total	N	44	44	44	44	44
	Mean	23.07	30.41	40.52	18.39	2.82
	Std. Deviation	43.587	48.912	54.508	35.924	7.690

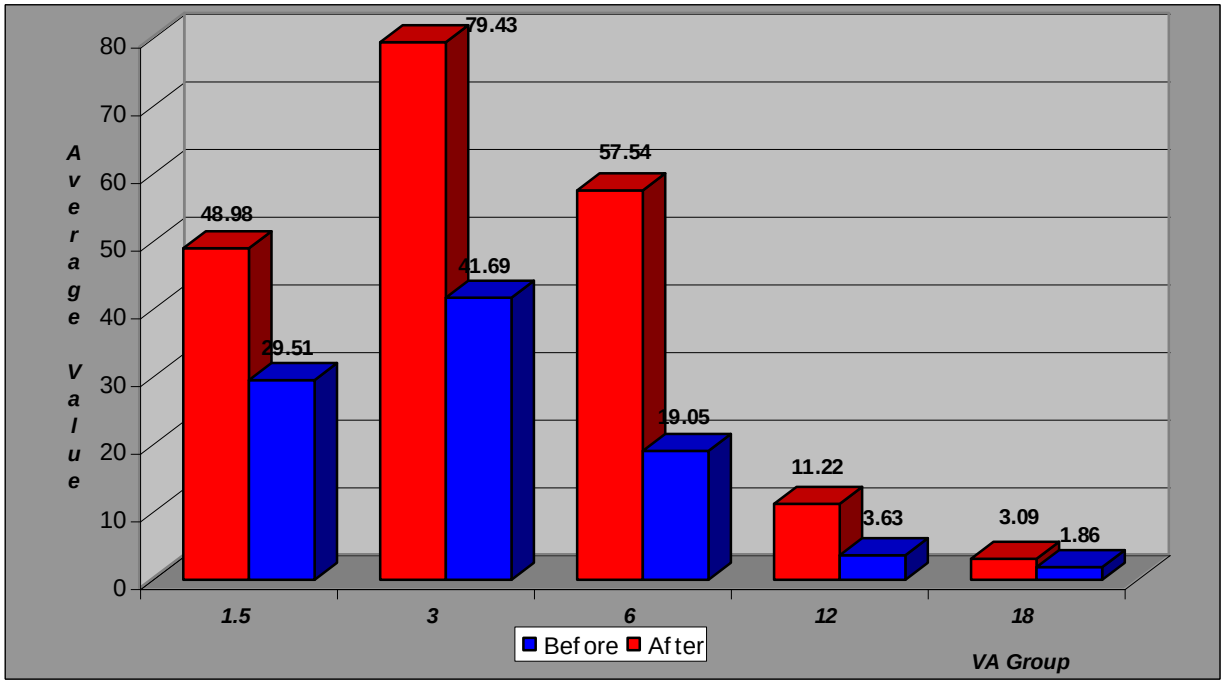
Minor differences can be seen at the average improvement in each Amblyopia type. ANOVA at Table 24 summarizes the test of statistically significant differences between the Amblyopia type groups.

Table 24: ANOVA of Average Improvement According to Amblyopia Type

		Sum of Squares	df	Mean Square	F	Sig.
1.5 Improve Vs. Amblyopia Type	Between Groups	15368.72	3	5122.91	3.090	.0378
	Within Groups	66322.07	40	1658.05		
	Total	81690.80	43			
3 Improve Vs. Amblyopia Type	Between Groups	9546.18	3	3182.06	1.364	.2676
	Within Groups	93326.45	40	2333.16		
	Total	102872.6	43			
6 Improve Vs. Amblyopia Type	Between Groups	7919.20	3	2639.73	.881	.4591
	Within Groups	119839.8	40	2995.99		
	Total	127759.0	43			
12 Improve Vs. Amblyopia Type	Between Groups	6490.35	3	2163.45	1.766	.1692
	Within Groups	49002.09	40	1225.05		
	Total	55492.43	43			
18 Improve Vs. Amblyopia Type	Between Groups	92.21	3	30.74	.502	.6832
	Within Groups	2450.33	40	61.26		
	Total	2542.55	43			

According to the presented data, there is a significant difference ($p<0.05$) in 1.5 VA improvement between the Amblyopia type groups. Graph 5 presents comparing figure of the average performance before and after the treatment in contrast sensitivity.

Graph 5: Comparing of Average Contrast Sensitivity Before and After Treatment



The graph demonstrates that in all VA contrast sensitivity levels, the average performance was improved due to the treatment.

6.12 BINOCULAR EXAMINATIONS

Two Binocular examinations, in order to evaluate the ability of the patient to use both eyes together for visual perception, were performed in most of the study group patients. The improvement was measured by comparing both the Worth4dot and Titmus values before and after the treatment.

The scale of both examinations was 0 to 4 (where 0 presents poor results)

The summary of the basic characteristics of the performances compared before and after the treatments is presented in Table 25.

Table 25: Summarized Data of Average Performance

		Mean	Std. Deviation	Std. Error Mean
Pair 1	Worth4dot - After	2.62	1.577	.243
	Worht4dot - Before	1.43	1.625	.251
Pair 2	Titmus - After	1.88	1.418	.216
	Titmus - Before	1.26	1.329	.203

According to the presented data, in both pairs, the patients improved their average abilities.

The correlation between the performances before and after treatment is presented in the following table.

Table 26: Correlation Between Performance (before Vs. after)

		N	Correlation	Sig.
Pair 1	Worth4dot - After Vs. Before	42	.427	.00480
Pair 2	Titmus - After Vs. Before	43	.610	.00001

Both pairs show high and significant correlation ($p<0.05$) comparing their performances before and after the treatment.

A Paired Sample T-Test was performed in order to determine whether there are significant improvements in performances. The data is shown in Table 27.

Table 27: Paired Sample T-Test for Significant Improvement in Performances

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Worth4dot - After Vs. Before	1.19	1.714	.2645	.66	1.72	4.501	41	.0001
Pair 2	Titmus - After Vs. Before	.63	1.215	.1854	.25	1.00	3.388	42	.0015

The presented T-Test shows that all the abilities improvements are statistically significant ($p<0.05$).

The average visual perception improvement according to the Amblyopia type is presented in Table 28.

Table 28: Summarizes data of Average Improvement According to Amblyopia Type

Amblyopia Type		Worth4dot Improvement	Titmus Improvement
Strabismic	N	8	8
	Mean	.1250	.2500
	Std. Deviation	1.7269	1.0351
Anisometropic	N	16	16
	Mean	1.5625	.8125
	Std. Deviation	1.7877	1.6419
Strabismic & Anisometropic	N	15	15
	Mean	1.4667	.6000
	Std. Deviation	1.5523	.8281
MonoFixation	N	3	4
	Mean	.6667	.7500
	Std. Deviation	1.5275	.9574
Total	N	42	43
	Mean	1.1905	.6279
	Std. Deviation	1.7142	1.2154

According to the presented data, on both examinations, the Anisometropic group had the best achievements, while the Strabismic group was the worst to improve. In order to determine whether the difference between groups is significant, an ANOVA test was performed. The results presented in the table below:

Table 29: ANOVA of Differences in Average Improvement of Worth4dot and Titmus According to Amblyopia Type

		Sum of Squares	df	Mean Square	F	Sig.
Worth4dot Improve Vs. Amblyopia Type	Between Groups	13.26	3	4.42	1.57	.2132
	Within Groups	107.21	38	2.82		
	Total	120.48	41			
Titmus Improve Vs. Amblyopia Type	Between Groups	1.76	3	.59	.38	.7684
	Within Groups	60.29	39	1.55		
	Total	62.05	42			

It can be seen that according to the calculated data no significant difference was found in the average improvement of Worth4dot and Titmus tests, between the Amblyopia type groups.

6.13 VA FOR READING EXAMINATIONS

The improvement was defined by comparing the reading visual acuity and the accommodation amplitude for the lazy eye measurements before and after the treatment.

The summary of the basic characteristics of the performances compared before and after the treatments is presented in Table 30.

Table 30: Summarized Data of Average Performance

		Mean	Std. Deviation	Std. Error Mean
Reading Visual Acuity	Base-Line	.78	.453	6.829E-02
	End-Point	.58	.205	3.084E-02
Accommodation Amplitude (lazy eye)	Base-Line	4.53	2.053	.309
	End-Point	5.05	2.608	.393

The analyzed data shows decrease in the reading visual acuity (i.e., improvement) and increase in the accommodation amplitude in the lazy eye (i.e., also improvement).

The correlation between the performances before and after treatment is presented in the following table.

Table 31: Correlation Between Performance (before Vs. after)

		N	Correlation	Sig.
Reading Visual Acuity	**Base-Line & End-Point**	44	.751	.00000
Accommodation Amplitude (lazy eye)	**Base-Line & End-Point**	44	.845	.00000

All pairs show high and significant correlation ($p<0.05$) comparing their performances before and after the treatment.

A Paired Sample T-Test was performed in order to determine whether there are significant improvements in performances. The data is shown in Table 32.

Table 32: Paired Sample T-Test for Significant Improvement in Performances

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Reading Visual Acuity	**Base-Line Vs. End-Point**	.20	.328	4.950E-02	.10	.30	4.05	43	.0002
Accommodation Amplitude (lazy eye)	**Base-Line Vs. End-Point**	-.52	1.403	.212	-.94	-9.E-02	-2.44	43	.0187

The presented T-Test shows statistically significant improvements ($p<0.05$) at abilities of the reading visual acuity and the accommodation amplitude for the lazy eye.

The average reading visual acuity improvement according to the Age group is presented in Table 33.

Table 33: Summarizes data of Average Improvement According to Age Group

Age Group		Reading Visual Acuity Improvement	Accommodation Amplitude Improvement (lazy eye)
9-20	N	10	10
	Mean	.18	1.43
	Std. Deviation	.334	2.230
21-30	N	10	10
	Mean	.16	.90
	Std. Deviation	.311	1.259
31-40	N	8	8
	Mean	.40	-.19
	Std. Deviation	.532	.741
41-55	N	16	16
	Mean	.13	6.25E-02
	Std. Deviation	.156	.566
Total	N	44	44
	Mean	.20	.52
	Std. Deviation	.328	1.403

The table shows that there are some differences at the lazy eye accommodation amplitude (improvement means negative values of averages). In order to determine statistically significant improvement, F-test was performed for all categories. The table below presents the results of this test:

Table 34: ANOVA for Differences in Reading and Accommodation Average Improvement According to Age Group

		Sum of Squares	df	Mean Square	F	Sig.
Reading Visual Acuity Improvement Vs. Age Group	Between Groups	.42	3	.14	1.31	.2839
	Within Groups	4.22	40	.11		
	Total	4.64	43			
Accommodation Amplitude Improvement (lazy eye) Vs. Age Group	Between Groups	16.99	3	5.66	3.35	.0284
	Within Groups	67.69	40	1.69		
	Total	84.67	43			

As suspected, the improvement at accommodation amplitude in the lazy eye has significant differences between the age groups, where young patients perform higher improvements.

6.14 VISUAL ACUITY PERSISTENCE

The Visual Acuity Persistence was measured for all the study group patients 3 months after completion of the treatment sessions.

The average of patients' Visual Acuity improvement as measured 3 months after completion of the treatment sessions is 0.1 lines, bringing the total VA improvement of the group to 2.6 lines, at this point of time.

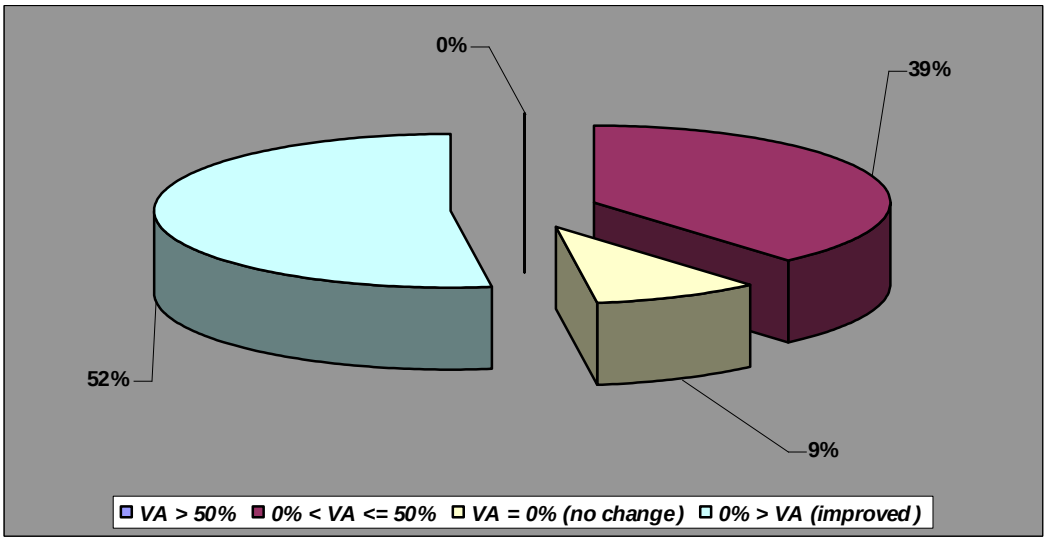
A table that details the VA persistence of all the treatment group patients is provided in attachment A.

6.15 SUCCESS CRITERIA

The success criterion for VA retention check, 3 months after completion of the treatment sessions was defined as loosing less then 50% of the VA improvement reached during the treatment.

According to this data, none of the patients lost more than 50% of their improvement. Furthermore, the average recorded change was 17% improvement (with 3% standard deviation), meaning the patients continued to improved. The summarized performances is presented in Graph 6:

Graph 6: Summarized Data of Retention Performance



As it may seen from the graph, no case was reported retention decrease of over 50%, 17 cases (39%) lost some of the Visual Acuity improvement achieved during treatment, and most cases (61%) did not lose their improvement, Among that group 23 patients (52%) even continued to improved their Visual Acuity after 3 months.

The following graph demonstrates the treatment group average Visual Acuity improvement and the Visual Acuity persistence 3 months after the treatment sessions end:

Graph 7: Average Retention of Visual Acuity Improvement Over Time

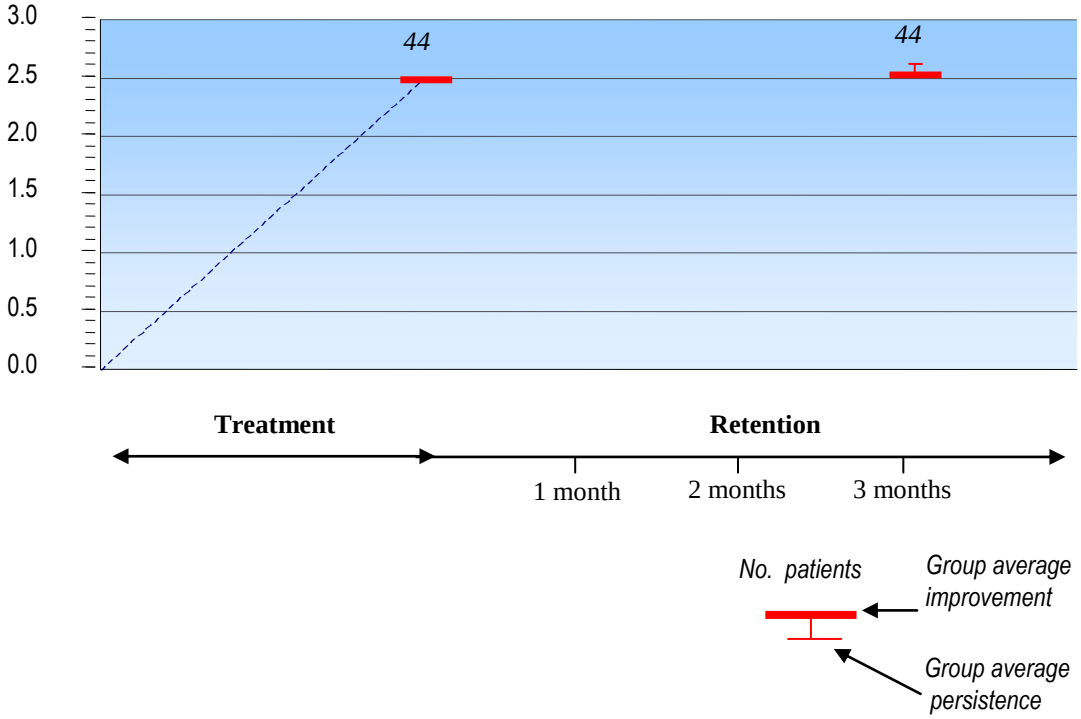


Table 35: VA Endpoint According to Baseline Group After 3 Months

VA Baseline group	No. of patients	Patients reaching 20/40 and better	Patients reaching 20/32 and better	Patients reaching 20/25 and better	Patients reaching 20/20 and better
Base < 20/40	8	N/A	N/A	8 (100%)	2 (25%)
20/40<=Base<20/50	16	N/A	13 (81%)	6 (37.5%)	2 (12.5%)
20/50<=Base<20/100	20	13 (65%)	8 (40%)	5 (25%)	2 (10%)

6.16 RAW DATA

The basic characteristics of the study patients are summarized in Table 1.

Table 36: Basic Characteristics of Study Patients

Pt. #	Initials	Age	Gender	Lazy Eye	Amblyopia Type	Study/ Control
2	RGU	21.3	Female	Right	Anisometropic	Study
4	DDM	47	Female	Right	Strabismic & Anisometropic	Study
5	ESH	43.7	Male	Left	Strabismic & Anisometropic	Study
6	BME	51.3	Male	Right	MonoFixation	Study
8	SSH	13.1	Female	Right	Anisometropic	Study
9	SHA	51.3	Male	Right	Strabismic & Anisometropic	Study
10	UAV	35.3	Male	Right	Anisometropic	Study
11	IZA	26.9	Female	Right	Strabismic & Anisometropic	Study
12	HMS	31.8	Female	Right	Anisometropic	Study
14	TGR	15.1	Male	Left	Anisometropic	Study
15	YLE	52.9	Male	Left	Strabismic	Study
16	DKA	49.8	Male	Left	Anisometropic	Study
17	DPA	37.8	Male	Left	Anisometropic	Study
18	ULU	45.9	Male	Right	Strabismic & Anisometropic	Study
19	GDE	30.7	Male	Right	Anisometropic	Study
20	EGO	14.4	Male	Right	Anisometropic	Study
21	GRO	27	Male	Left	Strabismic & Anisometropic	Study
22	TBA	30.3	Male	Left	Strabismic	Study
23	AGR	13.3	Female	Left	Strabismic	Study
24	NPO	47.8	Female	Right	MonoFixation	Study
25/c	AMA	34.3	Male	Right	Strabismic & Anisometropic	Control
26	AZI	11.3	Male	Left	Anisometropic	Study
27	YAT	39	Male	Left	Anisometropic	Study
32	TBA	43.4	Male	Left	MonoFixation	Study
33	YHE	44.9	Male	Left	Anisometropic	Study
35	LHU	37.2	Female	Right	Strabismic & Anisometropic	Study
38	IHA	38.7	Male	Right	Strabismic & Anisometropic	Study

Pt. #	Initials	Age	Gender	Lazy Eye	Amblyopia Type	Study/ Control
39	AAL	28.8	Male	Right	Anisometropic	Study
40	HKO	52.7	Female	Left	Anisometropic	Study
41/c	EHA	40.8	Male	Right	Anisometropic	Control
43	DNA	41.7	Male	Left	Strabismic	Study
44	UBA	14.3	Male	Left	Anisometropic	Study
45	DGA	9.5	Male	Left	Strabismic	Study
46	IMA	25.3	Male	Right	Strabismic & Anisometropic	Study
47/c	MHA	27.8	Male	Left	Strabismic & Anisometropic	Control
49	AGU	27.7	Male	Left	Strabismic & Anisometropic	Study
50	NRO	33.8	Female	Left	MonoFixation	Study
51	RSH	54.8	Female	Left	Strabismic & Anisometropic	Study
52/c	DSA	39.2	Male	Left	Anisometropic	Control
53	TPE	26.1	Male	Left	Anisometropic	Study
54	SAL	16	Male	Right	Strabismic	Study
55	NBA	48.5	Male	Right	Strabismic	Study
56/c	ZBA	27.7	Male	Left	Anisometropic	Control
58/c	IBI	39.8	Male	Left	Strabismic & Anisometropic	Control
61/c	RTA	24.9	Male	Right	Strabismic & Anisometropic	Control
62/c	IYE	31.2	Female	Right	Anisometropic	Control
63	SMA	28.6	Female	Right	Strabismic & Anisometropic	Study
64	RBR	24	Male	Left	Strabismic & Anisometropic	Study
65	MAB	12.2	Female	Left	Strabismic	Study
66/c	RSH	49.6	Female	Left	Strabismic	Control
67	RCO	46.8	Female	Left	Strabismic & Anisometropic	Study
68/c	YFE	52	Male	Left	Anisometropic	Control
69	MFI	11.1	Female	Left	Strabismic & Anisometropic	Study
70	ACA	47.9	Male	Left	Anisometropic	Study

Table 37: Results (in VA) of the Visual Accuracy Tests

Patient #	Base-Line	Treat. 4	Treat. 8	Treat. 12	Treat. 16	Treat. 20	Treat. 24	Treat. 28	Treat. 32	Treat. 36	Treat. 40
2	0.30	0.25	0.24	0.20	0.10	0.06	0.04	0.10	0.02	0.04	
4	0.58	0.55	0.53	0.51	0.45	0.45	0.47	0.51	0.50	0.47	0.45
5	0.56	0.50	0.49	0.42	0.37	0.34	0.32	0.26	0.30	0.34	0.28
6	0.36	0.32	0.21	0.24	0.17	0.14	0.08	0.10	0.10	0.08	
8	0.37	0.30	0.34	0.21	0.15	0.04	0.02	-0.04	-0.06		
9	0.38	0.32	0.24	0.18	0.24	0.22	0.21				
10	0.53	0.37	0.25	0.16	0.16	0.13	0.14	0.10	0.10	0.02	0.00
11	0.51	0.34	0.28	0.29	0.26	0.26	0.24	0.19	0.18	0.24	0.19
12	0.33	0.19	0.14	0.13	0.09	0.12	0.06	0.12	0.08	0.12	0.10
14	0.19	0.11	0.11	0.11	0.12	0.12	0.06	0.04	0.00		
15	0.55	0.42	0.39	0.40	0.36	0.40	0.34	0.28	0.36	0.30	0.28
16	0.34	0.20	0.10	0.08	0.02	0.04	-0.02	-0.04	-0.02	-0.02	
17	0.18	0.14	0.14	0.09	0.16	0.14	0.12	0.12			
18	0.46	0.25	0.14	0.12	0.08	0.10	0.04	0.06			
19	0.31	0.23	0.23	0.16	0.13	0.16	0.19	0.24	0.18	0.20	0.23
20	0.55	0.46	0.44	0.41	0.31	0.26	0.30	0.26	0.18	0.26	0.24
21	0.28	0.25	0.23	0.22	0.16	0.16	0.14	0.16			
22	0.70	0.55	0.52	0.47	0.50	0.51	0.48	0.52	0.45		
23	0.40	0.25	0.17	0.16	0.15	0.14	0.13	0.24	0.20		
24	0.26	0.21	0.24	0.21	0.22	0.18	0.20	0.22	0.16	0.12	0.20
25/c	0.32	0.27	0.25	0.24							
26	0.63	0.43	0.44	0.48	0.42	0.39	0.44	0.40	0.38	0.38	0.34
27	0.34	0.28	0.23	0.25	0.25	0.27	0.26	0.26	0.23	0.26	0.22
32	0.51	0.39	0.39	0.32	0.26	0.41	0.32	0.34	0.32		
33	0.58	0.50	0.40	0.44	0.34	0.24	0.24	0.22	0.19	0.22	0.19
35	0.53	0.48	0.49	0.49	0.45	0.43	0.39	0.40	0.36	0.38	0.40
38	0.46	0.35	0.30	0.28	0.26	0.22	0.26	0.30	0.28	0.24	0.24
39	0.19	0.11	-0.06	-0.08	-0.06	-0.10					
40	0.21	0.15	0.14	0.13	0.12	0.16	0.06	0.12	0.12	0.09	
41/c	0.46	0.47	0.48	0.46							
43	0.52	0.48	0.54	0.46	0.48	0.52	0.50	0.52			
44	0.37	0.29	0.32	0.24	0.26	0.23	0.28	0.32	0.20	0.20	0.22
45	0.35	0.37	0.32	0.25	0.30	0.37	0.34	0.25			

Patient #	Base-Line	Treat. 4	Treat. 8	Treat. 12	Treat. 16	Treat. 20	Treat. 24	Treat. 28	Treat. 32	Treat. 36	Treat. 40
46	0.35	0.18	0.14	0.18	0.18	0.20	0.24	0.20	0.16	0.14	0.12
47/c	0.28	0.28	0.25	0.22	0.25						
49	0.37	0.32	0.30	0.22	0.20	0.28	0.20	0.12	0.16	0.12	0.08
50	0.55	0.46	0.44	0.34	0.30	0.30	0.30	0.36	0.34		
51	0.33	0.40	0.26	0.26	0.28	0.26	0.20	0.22	0.20	0.20	0.24
52/c	0.44	0.47	0.48	0.43							
53	0.34	0.30	0.26	0.26	0.22	0.20	0.24	0.20	0.24	0.16	0.18
54	0.37	0.26	0.27	0.28	0.16	0.18	0.17	0.23	0.17	0.21	0.18
55	0.63	0.46	0.38	0.34	0.28	0.38	0.22	0.24	0.22	0.20	
56/c	0.28	0.26	0.24	0.28							
58/c	0.52	0.60	0.58	0.52	0.56						
61/c	0.46	0.44	0.44	0.44							
62/c	0.62	0.56	0.56	0.56							
63	0.32	0.26	0.30	0.28	0.26	0.30	0.28	0.26	0.22	0.26	0.22
64	0.60	0.48	0.36	0.28	0.30	0.30					
65	0.27	0.12	0.01	0.10	0.06	0.06	0.15	0.15	0.11	0.09	
66/c	0.48	0.54	0.52	0.54							
67	0.42	0.40	0.34	0.36	0.38	0.30	0.34	0.30			
68/c	0.26	0.30	0.28	0.36							
69	0.62	0.48	0.61	0.61	0.43	0.46	0.39	0.37	0.22		
70	0.28	0.28	0.16	0.16	0.20	0.20	0.17				

(Continue of Table 37)

Patient #	Treat. 44	Treat. 48	Treat. 52	Treat. 56	Treat. 60	Treat. 64	Treat. 68	Treat. 72	Treat. 76	Endpoint	Per. 1	Per. 2	Per. 3
2										0.00	0.02	0.08	0.09
4	0.47	0.45	0.48	0.47						0.46	0.46		0.47
5	0.30	0.32								0.30	0.38	0.43	0.39
6										0.08	0.08	0.10	0.03
8										-0.08		-0.08	-0.08
9										0.17	0.23	0.22	0.18
10	-0.02	-0.08	-0.06							-0.08	-0.06	-0.05	-0.10
11	0.20	0.10	0.10	0.24	0.16	0.16	0.16	0.14	0.12	0.09	0.09	0.10	0.10
12										0.09	0.11		0.13
14										-0.02	0.04	0.08	-0.02
15	0.36									0.26	0.28		0.32
16										-0.04	-0.03	-0.10	-0.12
17										0.14	0.12		0.08
18										0.06		0.06	-0.01
19	0.20	0.22	0.20	0.22	0.16	0.14	0.16	0.20	0.20	0.18	0.18	0.22	0.22
20	0.20	0.16	0.12	0.10	0.08	0.08	0.14			0.10	0.10	0.08	0.08
21										0.14	0.16	0.14	0.10
22										0.44			0.44
23										0.12	0.11	0.14	0.16
24	0.14	0.10	0.14	0.10	0.10	0.08	0.04	0.04		0.04	0.05	0.06	0.06
25/c										0.24			
26	0.40	0.40	0.32	0.38	0.34	0.30	0.26	0.26		0.26	0.26	0.27	0.25
27	0.26	0.28								0.26	0.26	0.26	0.30
32										0.25	0.30	0.26	0.28
33	0.16	0.11								0.12		0.09	0.07
35	0.34	0.34								0.31		0.37	0.36
38										0.24	0.24	0.24	0.22
39										-0.12		-0.02	-0.06
40										0.12	0.10	0.04	0.02
41/c										0.46			
43										0.42			0.45
44	0.24									0.22	0.21		0.18

Patient #	Treat. 44	Treat. 48	Treat. 52	Treat. 56	Treat. 60	Treat. 64	Treat. 68	Treat. 72	Treat. 76	Endpoint	Per. 1	Per. 2	Per. 3
45										0.31	0.28	0.23	0.18
46	0.12									0.14	0.16	0.17	0.13
47/c										0.25			
49	0.06	0.04								0.04	0.08		0.08
50										0.30	0.34	0.34	0.22
51	0.22	0.22	0.18	0.20	0.24	0.24	0.17			0.16	0.20	0.16	0.14
52/c										0.43			
53	0.12	0.12								0.10	0.10		0.08
54										0.15	0.20	0.17	0.13
55										0.20	0.13	0.13	0.15
56/c										0.28			
58/c										0.56			
61/c										0.44			
62/c										0.56			
63	0.26									0.29			0.25
64										0.29		0.32	0.32
65										0.07	0.05	0.05	0.07
66/c										0.54			
67										0.32	0.34	0.34	0.30
68/c										0.36			
69										0.34	0.31	0.24	0.19
70										0.12	0.12	0.12	0.02

7.0 DISCUSSION

In the primary visual cortex the output of a large number of neurons, each tuned to a different orientation, spatial frequency and spatial location, is providing the input for further processing of the visual images. This process is an early and necessary stage for recognition (visual acuity for far and near) and binocular functions (binocular summation and stereopsis). Normal neuronal activity is considered to provide the ability to those normal visual functions. However, abnormal neuronal activity in the amblyopic visual cortex is preventing a considerable amount of neurons from contributing to this process, thus affecting normal visual functions of the amblyopic eye. Therefore, an effective treatment for the improvement of the visual functions in amblyopia will have to restore and improve the sensitivity of the neurons. The AA-1 treatment has proven to be effective and has achieved the goal of improving the visual functions in the amblyopic eye. It has been well proven that an improvement of VA, CSF and other visual functions can be achieved by the method of perceptual learning. After the course of the AA-1 treatment an impressive amount of improvement (of visual functions) was achieved, indicating that the AA-1 approach was successful.

Even though the AA-1 treatment is based on monocular training of the amblyopic eye, the binocular functions of the treatment group improved on both tests; Worth-4-Dot and the Stereo Titmus test. The AA-1 results are consistent with the idea that normal activity of both eyes is required for normal binocular functions. This idea is supported by earlier studies as detailed in the Scientific Background section, which is presented in Section 5 of the 510(k) submission).

The AA-1 results show that there was no significant difference of the improvement of the VA, binocular functions and CSF between the

categories of amblyopia. This result is consistent with the idea that a major consequence of amblyopia is abnormal lateral interactions which is found to be uniformly abnormal among anisometropic and strabismic amblyopia.

The improvement of the visual acuity was retained, and even slightly improved, 3 months after the termination of the treatment. These results are consistent with the prediction from perceptual learning techniques and from the improvement of the other visual functions such as CSF and the binocular functions. Improvement of the visual functions to within a close range of the normal vision leads to a diminishing if not preventing of the suppression on the amblyopic eye, caused by the good eye. Suppression of the amblyopic eye is considered to be one of the main causes for amblyopia, and reducing the amount of suppression is expected to diminish the likelihood for recurrent amblyopia, thus retaining the improved vision. Moreover, the common practice is that the indication for success of treatment can be seen at 3 months after cessation (of the treatment of patching in children). If the improvement has been retained it may be indicative for long-term persistence of the results. In cases of deterioration, repeating the patching is considered. In the AA-1 treatment, no such deterioration was found.

8.0 CONCLUSION

In conclusion, a normal output from the neurons in the early visual cortex is essential for normal visual functions. In amblyopia, deficiencies of some of the neurons, especially those that are sensitive for the high spatial frequencies, may prevent further visual processes from functioning normally.

Proper perceptual training, that improved neuronal sensitivity, has provided the basis for more efficient visual processing. This has enabled the restoration of visual functions that were otherwise dysfunctional.

Consequently, a significant and remarkable improvement in visual acuity as well other important visual functions such as contrast sensitivity and binocular functions were found in most of the AA-1 amblyopic patients, as a result of the perceptual training. This treatment has provided them with significant enhancements in the everyday functioning of their visual system with the resulting benefits in visual performance and thus improving the quality of vision.