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Cross-sectional Study

Design of a novel smartphone-based photostress recovery time test for detecting abnormalities in the macula. A cross-sectional study

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ABSTRACT

Background: The study aims to present a new smartphone-based photostress recovery time test (K-PSRT test) that measures the stimulus-specific loss of visual sensitivity, as well as the differentiation between normal from abnormal macular function. This novel test defines a new standardized photostress application as an alternative tool for incorporation into clinical practice.

Materials and methods: A total of 48 visually impaired eyes and 47 normal sighted age-matched controls eyes were enrolled in the study. The median age in subjects with impairment was 71.0 years, while the median age in normal subjects was 70.0 years. A light produced by the smartphone camera at approximately 5 cm distance, perpendicular to the eye up 10 s filled the pupil. The photostress recovery time was assessed immediately after the exposure by asking the subjects to read correctly at least three successive letters of size corresponding to the previous line of the BCVA line at a distance of 40 cm. The digital photostress testing was performed with the best-corrected visual acuity (BCVA). The patients were examined twice within 2 weeks. Correlations among the recovery times, the visual acuity, and the contrast sensitivity function as well as correlations concerning each specific ocular disease were also performed. Furthermore, correlations among technology, usability, and ease of performance in both groups were analyzed.

Results: The initial median photostress recovery time in patients with impaired eyes was 83.5 (68.5, 126.0), while in the normal individuals was 39.0 (14.0, 43.0). The median visual acuity in individuals with impairment was 0.59 logMAR (0.40, 0.90), whereas in the normal individuals was −0,06 logMAR. Test-retest reliability study was performed on 26 eyes (16 males, 10 females) for visually impaired eyes as well as on 35 normal eyes (19 males, 16 females). Concerning the reliability, the average Intraclass Correlation Coefficients (with 95% confidence intervals) ICC (95% CI) = 0,99 (0,98–1,00), indicating significant correlation between them ($p < 0.01$). The coefficient of repeatability for eye measurements reaches clinically acceptable levels, which is demonstrated with increased repeatability and consistency. The recovery time in patients with diabetic retinopathy was statistically significantly lower than in those with dry age-related macular degeneration ($p = 0.027$) and those with wet age-related macular degeneration ($p = 0.032$). The patient group has lower scores concerning technology, usability, and ease of performance compared to the normal.

Conclusions: This new testing modality (K-Photostress Recovery time test), is designed to be an easily implemented measurement in ophthalmic practice, and it can expand our understanding of macular function. The above findings support the usefulness of a novel reproducible photostress application as an indicator of macular pathology.

1. Introduction

Photostress recovery time (PSRT) is an objective quantitative measure of macular function. Several studies have involved age [1,2] and different genetic factors [3] that affected recovery time in normal individuals. Various diseases are influencing central vision, including age-related macular degeneration (AMD) [4], central serous retinopathy (CSR) [5], retinal detachments (RD) [6], and retinitis pigmentosa (RP) [7] that may affect the recovery time.

The ability to recognize stimuli such as optotypes following a bleaching light depends upon the metabolic functioning of macular tissue, especially the retinal pigment epithelium (RPE) and the sensory

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retina [8–10]. Additionally, an alteration in the photoreceptors and the pigment epithelial compound, as well as, a change in the photochemical pathways, especially when occurring intra - or subretinal fluid may prolong photo recovery time [11–13].

The recovery time from normal individuals ranged from 10 to 50s [14]. Various instruments and techniques have been used to conduct photostress testing. Light sources have included the ophthalmoscope, penlight, and computer monitor. However, the lack of standardization for the intensityand duration of the bleaching light is the major limitation of the technique.

The simplicity of the PSRT test and the ability to detect worsening in underlying disease even before manifestations [15] could be an awesome advantage of the test. In real situations individuals could not experience these symptomatologies until essential photoreceptor damage has occurred. Thus, the evaluation of recovery may assist in detecting compromised photoreceptor function.

The new smartphone-based photostress test (K-PSRT test) is designed to measure the stimulus-specific loss of visual sensitivity by determining the relationship between controlled visual stimuli and a subject's response and can be a useful indicator of the functional status of the macula.

The main scope of the study is to present a new smartphone-based photostress recovery application evaluating the macular functionality.

This new test is designed as a measurement that can define a new standardized photostress application providing a better understanding of macular function. It also serves as a self-evaluation tool for early identification of changes that may indicate a deterioration in the underlying disease.

Therefore, we propose this novel test for evaluating the response of the macula regarding recovery time after photostress using the K- Photostress Recovery Time test.

2. Materials and methods

This is a cross-sectional study. Approval for this study was granted by the bioethical committee (Ethical Approval code#1.60/21.11.2018) of the Aristotle University of Thessaloniki, School of Medicine, Medical Department, Aristotle University of Thessaloniki, and adhered to the principles embodied in the Declaration of Helsinki Code of Ethics of the World Medical Association. Consent forms for the research were acquired by all subjects before their participation. The General Data Protection Regulation GDPR in a research context, and the Greek Law of Data Protection were respected through the confidentiality and anonymity of the data.

All participants were recruited prospectively from our outpatient unit at Aristotle University of Thessaloniki, School of Medicine running the LIFE4LV project for patients with visual impairment, which was officially registered at ClinicalTrials.gov. The number of the study is NCT05184036 (https://www.clinicaltrials.gov/ct2/show/NCT05184036?cond=NCT05184036&draw=2&rank=1).The work has also been reported in line with the STROCSS criteria [16]

2.1. Participants

All subjects underwent a comprehensive eye examination including demographic variables and other information such as general health history, systemic conditions and medication along with the current spectacle correction. Measurement of BCVA was determined with the Early Treatment Diabetic Retinopathy Study (ETDRS) chart (Precision Vision, USA, chart 1) under standard clinical conditions. The ophthalmological examination was performed in our outpatient unit at Aristotle University including: slit-lamp examination, providing details of the anterior part of the eye,and fundoscopy. BCVA was converted to logarithm of the minimal angle of resolution (logMAR) visual acuity.

Each examinee has been studied individually and monocularly in the particular session. The patients completed the whole examination in a single visit. The order of testing has been changing systematically and adequate rest time was provided at intervals, if necessary. Only the eye with the BCVA was included from each subject, and in case of similar BCVAs, the right eye was chosen. Visually impaired patients were included if BCVA of the best eye was between 0,2 and 1,3 logMAR, whereas normal controls for BCVA up to 0,1 logMAR. Visual acuities, expressed in logMAR categories, were defined as normal ($\leq$0.1 in both eyes) and visual impairment ($\geq$0.2 in the better eye).

2.2. The exclusion criteria were as follows

The photostress testing requires a good level of communication, thus individuals with poor communication and mental disabilities did not participate in the study. Furthermore, among others pathologies cloudy cornea, keratitis, active uveitis, and glaucoma as well as patients with significant cataracts, (grade >1 LOCS II) that can also affect procedure as well as functional vision, were excluded.

2.3. Examination protocol

Subjects completed measurement of BCVA at 40 cm. At approximately 5 cm distance from the eye (self-fixation was confirmed), the light produced by the smartphone camera filled the pupil for up 10 s. The user turns back the smartphone to a horizontal position at a distance of 40 cm The photostress recovery time was assessed immediately after the exposure by asking the subjects to read correctly at least three successive letters of size corresponding to the previous line of the BCVA line on the screen, with the opposite eye shielded. Photorecovery testing was done with the pupils undilated. Recovery time (PSRT) was recorded in seconds. Two groups of individuals were studied. Group 1 consisted of 47 normal eyes. Group 2 included 48 eyes with pathology that were consisted of 4 subgroups: A) 11(22,9%) eyes with non-proliferative diabetic retinopathy, B) 10 (20.8%) eyes with dry age-related macular degeneration, C) 17 (35.4%) eyes with wet age-related macular degeneration, D) 10(20.8%) eyes with miscellaneous macular disorders.

The patients were examined twice within 2 weeks for test-retest reliability. Correlations among the recovery times, the visual acuity, and the contrast sensitivity function as well as correlations concerning each specific ocular disease were performed.

A multifactor questionnaire was formulated to record the responses of the users about 1) the level of familiarity to technology, 2) the usability, 3) how easy they coud perform the test. All the aforementioned metrics were measured on a 5-level Likert type scale, ranging from 1—strongly agree to 5—strongly disagree.

2.4. Apparatus

The application has been demonstrated with a Samsung A30S smartphone (display: Super Amoled, size 6.4 inches, resolution 720 × 1560 pixels, ratio 19.5:9, density ~268 ppi; GPU: Mali-G71 MP2) running Android OS 9.0. The device was switched on at least 5 min before each experimental session to allow its output to stabilize.

2.5. Statistical analysis

The Shapiro- Wilks test was used for the normality assessment. Continuous variables were described using mean (sd) or median (IQR). Categorical variables were described using frequencies (percentages/ relative frequencies). The relationship between two independent samples was examined using the Mann-Whitney's *U* Test, while the Wilcoxon signed-rank test was used for the relationship between two dependent samples. The Kruskal-Wallis test was used for the evaluation of the relationship between more than two independent samples. Spearman's correlation coefficient was used to measure the association between continuous variables. The Pearson correlation coefficient and the intra-class correlation coefficient (ICC) were used as a measure of

test-retest reliability of the score of TEST and RETEST. P values less than 0.05 were considered statistically significant. IBM SPSS 27.0 (IBM Corp., Armonk, NY) was used for the statistical analysis, and R ver.4.0.0 (R Foundation of Statistical Computing, Vienna, Austria) was used for the calculation of ICC.

3. Results

3.1. The sample

A total of 95 eyes were examined.

The group of normal eyes consists of 47 eyes, 22 (46.8%) females and 25 (53.2%) males, with an average age of 70.00 ranging from 45.0 to 76.0 years. The recovery time was 39.0 (14.0, 43.0.) The average best-corrected visual acuity (logMAR) for normal eyes was −0.06. and the median contrast sensitivity was 1.9 log units (Table 1).

The group of pathological eyes consists of 48 eyes, 21 (43.8%) females and 27 (56.2%) males with an average age of 71.0 ranging from 63.0 to 78.0. The recovery time for visual impaired eyes was [median (IQR) = 83.5 s (68.5, 126.0)], while in the normal eyes the recovery time was [median (IQR) = 39.0 s (14.0, 43.0)], $p < 0.001$, Fig. 1. The average best-corrected visual acuity (logMAR) for pathological eyes was 0.59 and ranged from 0.90 to 0.40. The median contrast sensitivity was 0.85 log units(0.37, 1.2).

Regarding the characteristics of the study population, there is no statistically significant difference in age, sex, and the presence of intraocular lens between pathological and normal individuals($p > 0.05$). There is no difference between men and women in recovery times among normals. Normal individuals with intraocular lenses have a higher recovery time than normal without intraocular lenses ($p = 0.001$).

3.2. Test-retest results

Successive measurements were performed in the same patients and under the same conditions to assess the test-retest reliability of the application to prove the test as a valid and reliable tool for evaluating recovery time.

The patients were examined twice within 2 weeks and their scores were recorded. The test-retest reliability analysis was performed by Pearson correlation and showed a statistically significant correlation ($p < 0.001$) between test and retest in normal in 35 eyes as well as in 26 affected eyes.

Test-retest reliability analysis was also applied by estimating the Intraclass Correlation Coefficients (ICCs) and the corresponding 95% confidence intervals. The correlation was performed at two different sessions The ICCs were also statistically significant ($p < 0.001$) for both groups, suggesting the high repeatability and consistency of the smartphone-based photostress-test. The summaries are presented in Table 2. Both Pearson correlation and ICC indicate excellent reliability of the K-PSRT. Figs. 2 and 3.

Table 1
Demographic data of participants in study.

Characteristic	Normal (n = 47)	Pathological (n = 48)
	Median (IQR)	Median (IQR)
Number of eyes	47	48
Female/Male	22 (46.8%)/25 (53.2%)	21 (43.8%)/27 (56.2%)
Age	70.0(45.0, 76.0)	71.0(63, 78.0)
BCVA (logMAR)	−0.06(-0.06, −0.06)	0.59(0.40, 0.90)
CSLOG	1.9 (1.9, 1.9)	0.85 (0.37, 1.2)
IOL	16 (34.0%)	25 (52.1%)

Distribution of the clinical/demographic characteristics of the study population (age, sex, visual acuity, contrast sensitivity). BCVA: best-corrected visual acuity, logMAR: logarithm of the minimum angle of resolution (poor vision >0.50 logMAR and normal vision <0.50 logMAR, CSLOG: Contrast Sensitivity in log units, IOL: Intraocular lens).

3.3. Comparison among the ocular diseases regarding the recovery time

There is a statistically significant difference in recovery time among diseases ($p = 0.016$). More specifically, the recovery time in patients with diabetic retinopathy was statistically significantly lower than in those with dry age-related macular degeneration ($p = 0.027$) and those with wet age-related macular degeneration ($p = 0.032$). No statistically significant differences in recovery time were observed between the two comparisons (pairwise comparisons) of the other diseases ($p > 0.05$), Table 3, Fig. 4.

Moreover, there is a high positive correlation between test recovery time and age in the normal group (test: rho = 0.763, $p < 0.001$). As age increases, so do test times. This is not observed in the pathological group.

3.4. Correlation between technology, usability, and performance in both groups

In this context, a multifactor questionnaire was formulated to record the responses of the users about the relation to technology, usability, and easy to perform.

The pathological eyes have lower scores in technology, usability, and ease of performance compared to the normal ones ($p < 0.001$ for all three comparisons), Table 4.

There is no significant correlation between technology, usability and ease of performance, vision, and contrast sensitivity ($p > 0.05$).

Furthermore, there is no significant correlation between usability technology and age ($p > 0.05$).

On the other hand, there is a marginally statistically significant correlation between ease of performance and age ($p = 0.048$).

There is no difference in technology, usability, and ease of performance between men and women in both pathological and normal groups ($p > 0.05$).

4. Discussion

In the study, we evaluated the status of the retinas of normal and visually impaired patients using the novel photostress test. A wide range of normal data has been detailed in the literature regarding photostress recovery time. Recovery testing has largely been used for investigation purposes, but not for the general clinical setting.

In this study, a simple, reproducible novel smartphone-based photostress recovery test was used. The novel test is simple, safe, and non-expensive. The hypothesis of the novel test involves: 1. The bleaching of the retina after an intensive light stimulus, 2. The scotomas after image production, 3. The visual pigment resynthesis in the R.P.E-photoreceptor complex.

The recovery time for pathological eyes was 83.5sec (68.5, 126.0), while in the normal eyes the recovery time was 39.0 s (14.0, 43.0.), which is in agreement with the study of Bindu et al. [17].

Moreover, there are no statistically significant differences in age, sex, and the presence of intraocular lens between pathological and normal individuals($p > 0.05$).

In the test-retest evaluation, subjects performed the test with serious intent and concentration. The correlation at two different sessions was evaluated over a two week period. The test-retest reliability analysis was performed by Pearson, as well as analysis, was also applied by estimating the Intraclass Correlation Coefficients (ICCs) and the corresponding 95% confidence intervals. Both the analysis by Pearson and ICCs were statistically significant for both groups, suggesting the high repeatability and consistency of the K-PSRT test for both trials. Thus, the new digital test is a reliable screening test with good reproducible results.

Prolonged PSRT was seen in patients irrespective of the type of AMD

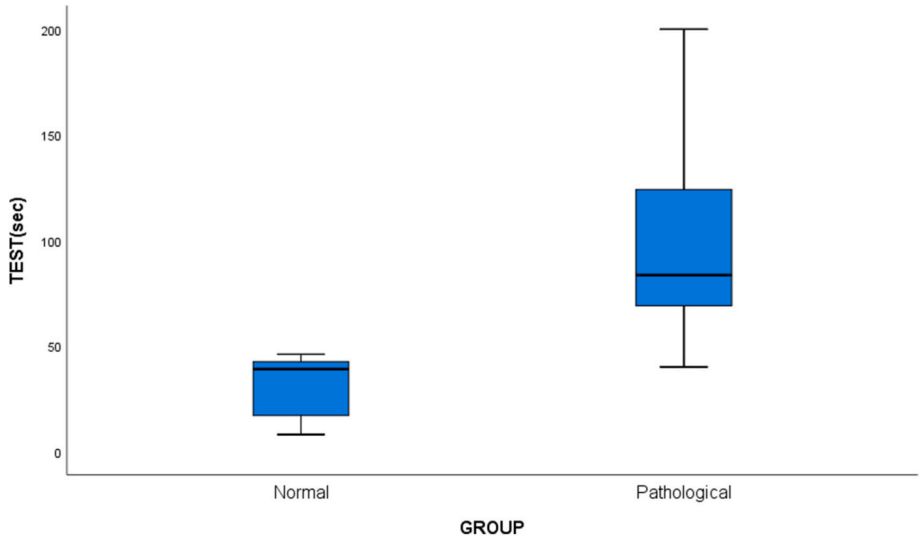

Fig. 1. *Boxplot* for the differences in the recovery time (test) between normal and pathological eyes.

Table 2
Both Pearson and ICC correlation of the K-PSRT for the two trials.

GROUP	Pearson's r (p)	ICC (95%CI)
Pathological	0.985 (<0.001)	0.99 (0.98, 1.00)
Normal	0.983 (<0.001)	0.99 (0.98, 0.99

[18]. Photo stress recovery time can be prolonged in other diseases affecting the macula like diabetes and drug-induced maculopathy [19,20] Recovery time are more prolonged in cases of ARMD than in diabetic retinopathy as the pathology lies at the level of the RPE photoreceptor complex. In diabetic retinopathy, it is in the inner retinal layers. There is a statistically significant prolongation of photostress recovery in the presence of diabetic macular edema, but to a less pronounced degree than with AMD or subretinal fluid [21]. In our study, the results are in agreement. The recovery time in patients with diabetic retinopathy was statistically significantly lower than in those with dry age-related macular degeneration ($p = 0.027$) and those with wet age-related macular degeneration ($p = 0.032$). Similarly, in the study of Gloria et al., the group of patients with ARMD has prolonged meantime than patients with diabetic retinopathy [21].

Regarding the questionnaire recording the opinion of the users. The pathological eyes have lower scores in technology, usability, and ease of performance compared to the normal individuals ($p < 0.001$ for all comparisons). However, there is a marginally significant positive correlation between ease of performing and age ($p = 0.048$).

Furthermore, the new test is simple and fast (approximately 3 min for a single eye). The novel test is not examiner-dependent, which is a significant advantage. It is reproducible regardless of the examiner.

Most low-vision -causing diseases tend to have an evolutionary course and therefore, early detection of signs of their deterioration is of great importance for medical support. Home self-screening and self-monitoring have become significant in modern Ophthalmology, especially in the era of Social Distancing during COVID-19 pandemic [22,23] There's a clear requirement for domestic monitoring in conditions such as to identify, foveal sensitivity alterations.

Therefore, this study also proposes how ophthalmology may adapt to the new digital innovations. Especially in cases of patients, who are in remote areas, the performance of the novel smartphone-based photostress recovery test becomes even more important showing that innovations are not only reserved for the remote but can routinely serve the wider population. Limitations of the study include the initiation of the COVID-19 crisis discouraged a larger number of individuals to participate in our study. Further study is required to strengthen

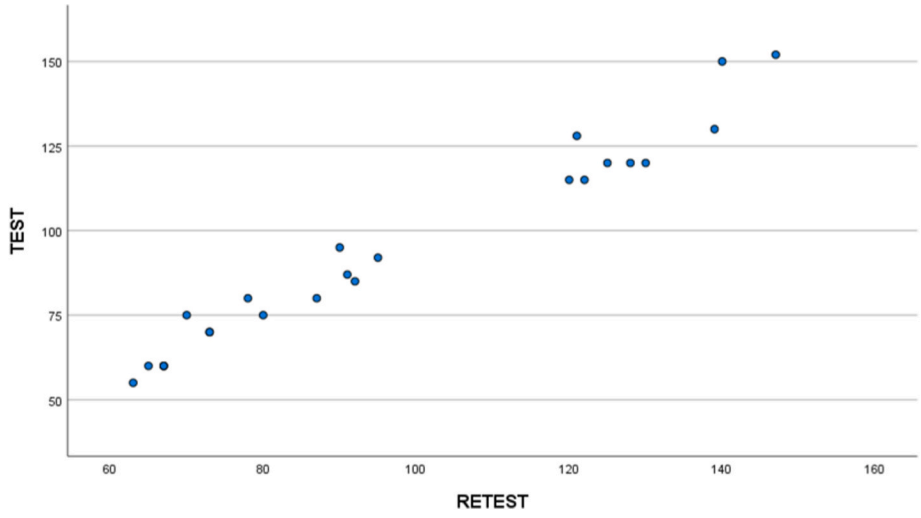

Fig. 2. Scatterplot between test and retest for the patient group.

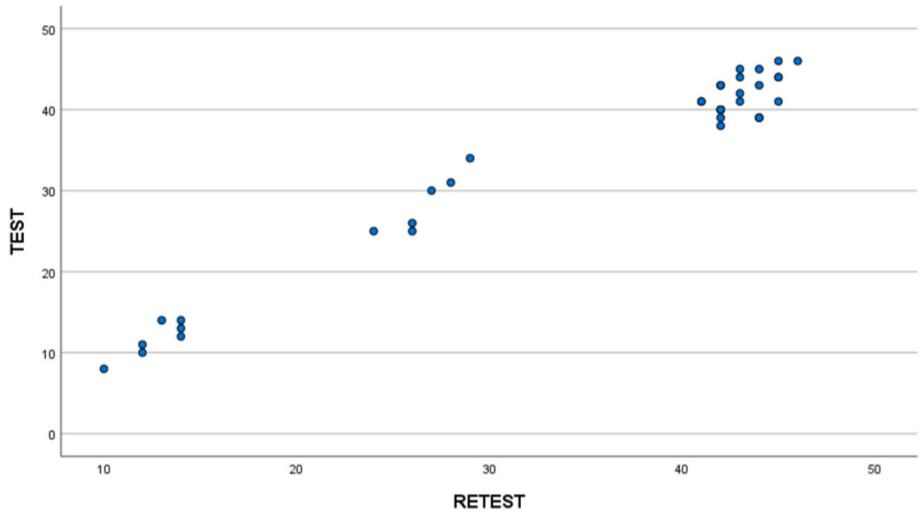

Fig. 3. Scatterplot between test and retest for the normal group.

Table 3
Differences in the recovery time (test) between the diseases.

Disease	Median (IQR)	p
Test		0.016
non-proliferative diabetic retinopathy	68.0 (54.0, 71.0)	
dry age - related macular degeneration	125.0 (82.0, 152.0)	
wet age-related macular degeneration	87.0 (75.0, 128.0)	
miscellaneous macular disorders	82.5 (60.0, 120.0)	

standardization and validation of the novel application.

5. Conclusions

This new testing modality, designed to be an easily implemented measurement in clinical ophthalmic practice, can expand our understanding of macular function. The above findings support the usefulness of a reproducible photostress application as an indicator of macular pathology. It may also serve as a self-monitoring tool for earlier detection of alterations indicating deterioration of the underlying disease.

Therefore, we propose a new method for evaluating the response of the macula to photostress using a smartphone-based application. This application may assist in detecting abnormalities earlier, aiming to reduce visual impairment.

Ethical Approval

Approval for this study has been obtained by the Bioethical Committee (Ethical Approval, code#1.60/21.11.2018), School of Medicine, Medical Department of the Aristotle University of Thessaloniki. Its conduction was following the rules and regulations of the Declaration of Helsinki.

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Author contribution

Karampatakis V.:Design innovation, scientific responsible, moderator, writing. Almaliotis D.: Data collection, draft preparation, writing, measurements. Papadopoulou E.P.: Bibliographic support, draft preparation. Almpanidou S.: writing, measurements.

Guarantor

Prof. Vasileios Karampatakis.

Table 4
Correlation between technology, usability, and ease of performance in both pathological – and normal individuals.

	Pathological	Normal	p
Technology, median (IQR)	2.0 (2.0, 4.0)	1.0 (1.0, 2.0)	<0.001
Usability, median (IQR)	2.0 (1.75, 4.0)	1.0 (1.0, 2.0)	<0.001
Easy to perform, median (IQR)	2.0 (1.0, 4.0)	1.0 (1.0, 2.0)	<0.001

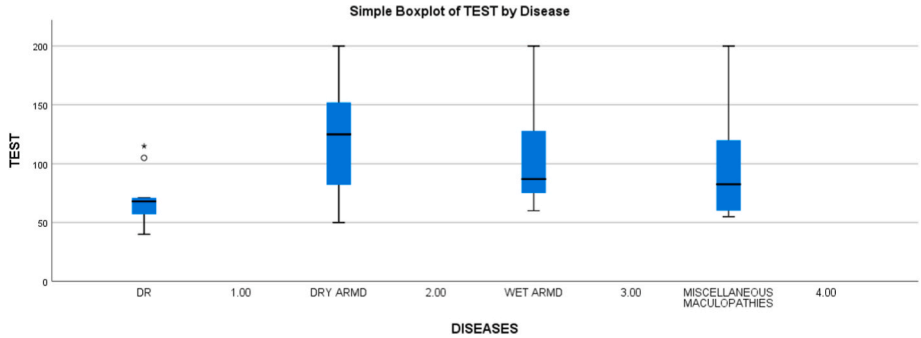

Fig. 4. Boxplot for the differences in the recovery time (test) between the diseases.

Consent

Informed consent was obtained from all participants included in this study.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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