1 2	Original Research Article Assessment of pupil diameters in Pseudoexfoliation syndrome under scotopic, mesopic,
3	photopic and dynamic conditions using infrared pupillometer
4	(Assessment of pupil diameters in Pseudoexfoliation syndrome)
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7	Abstract
8	Aim: Our study aims to assess the mean pupil size under scotopic, mesopic, photopic and
9	dynamic conditions in patients with PXS.
10	Methodology: This study was performed in Ophthalmology Clinic at İstanbul Bakırköy
11	Dr.Sadi Konuk Training and Research Hospital. Fourty-six patients with PXS and 46 age and
12	sex matched controls were included in the prospective study. The subjects were allowed at
13	least 3 minute to adapt to the lighting condition in the room. Pupil diameters were measured
14	with infrared (IR) pupillometer integrated within CSO Sirius Corneal Topographer
15	(Costruzione Strumenti Oftalmici S.r.l,Italy) by the same examiner. The measurements were
16	taken in scotopic, mesopic, photopic and dynamic conditions. Statistical analyses were
17	evaluated.
18	Results: Mean pupil diameter were significantly lower in the PXS group than control group
19	for all measurements. Scotopic and mesopic pupil size were significantly lower in the PXS
20	group than control group (p=0.0001). Also photopic and dinamic pupil size were significantly
21	lower in the PXS group than control group ($p=0.014$, $p=0.013$).
22	Conclusion: The results suggest that pupillary light response in patients with PXS

22 Conclusion: The results suggest that pupillary light response in patients with PXS 23 significantly was affected not only in scotopic and mesopic conditions but also in photopic 24 and dynamic conditions.

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26 Key Words: dynamic; mesopic; photopic; pseudoexfoliation syndrome; pupil size; scotopic.

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29 INTRODUCTION

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31 Pseudoexfoliation syndrome (PXS) is a genetically determined, age-dependent 32 generalized disorder of the elastic fiber system, characterized by excessive production and 33 accumulation of an elastotic material within a multitude of intra- and extraocular tissues [1]. 34 PXS is diagnosed by visualising the pseudoexfoliative material on the pupillary ruff and/or on 35 the anterior lens capsule. In ultrastructural studies, pseudoexfoliative material has been shown 36 to be accumulated within conjunctiva, iris, ciliary epithelium, and the dilator muscle of fellow 37 eyes in unilateral or asymmetric PXS [2,3]. Early stage of the disease, it may be recognized 38 on the basis of the lens surface in addition to poor pupillary dilation and pigment-related signs 39 including pigment dispersion and peripupillary atrophy [4]. PXS is known to be associated 40 with pupil abnormalities. This is particularly important in situations that require cataract 41 surgery as well pupil dilation [3,4].

Pupil size has influenced by various factors, such as the light stimulus and the
stimulated eye, retinal illumination, accommodative state of the eye, sensory and emotional
state, various neuro-psychiatric diseases, drugs, as well as the age and diabetes [<u>5-8</u>].
However, studies as regards dynamic muscle functions and pupil function with PXS are rare
[<u>9,10</u>].

- From this perspective, our study aims to assess the pupil size under scotopic,
 mesopic, photopic and dinamic conditions in patients with PXS.
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50 MATERIAL AND METHODS

52 This prospective study was performed in Ophthalmology Clinic at İstanbul Bakırköy 53 Dr.Sadi Konuk Training and Research Hospital. Fourty-six patients with PXS and 46 age and 54 sex matched controls were included in the study. The research followed the tenets of the 55 Declaration of Helsinki, with local ethical committee approval and the full informed consent 56 of patients. A complete routine ophthalmological examination was applied to all subjects. Retinal or optic pathologies and other ocular pathologies such as glaucoma, ocular surgeries 57 58 and neuro-psychiatric diseases, the subjects with anterior segment and angle anomalies, 59 diseases affecting the autoimmune system like diabetes, uveitis, pupil anomalies like posterior 60 synechia, sleeplessness (including those with a history of partial sleeplessness) or with 61 previous medical treatment like pilocarpin or other topical and oral medications that may 62 affect autonomic function were excluded. The diagnosis of PXS were made by visualising the 63 pseudoexfoliative material on the pupillary ruff and/or on the anterior lens capsule. 64 Furthermore, the eyes with PXS were examined with Optical Coherence Tomography measurements in addition to the intraocular pressure to exclude glaucoma. In the study, it was 65 66 included same eyes of patients with unilateral PXS, right eyes of patients with bilateral PXS 67 and right eyes of control groups. In control group, unaffected eyes of patients with unilateral 68 PXS were not included due to reasons such as pseudophakia, cataract, possible physiological 69 anisocoria.

The subjects were allowed at least 3 minute to adapt to the lighting condition in the room. Pupil diameters were measured with infrared (IR) pupillometer integrated within CSO Sirius Corneal Topographer (Costruzione Strumenti Oftalmici S.r.l,Italy) by the same examiner. The CSO Sirius Corneal Topographer consists of a placido disc topographer, a 3 D rotating Scheimpflug camera, aberometer and integrated IR pupillometer. It was used binocular photomotor stimulus that both eyes perceive the same illumination. Also IR 76 pupillometer had characteristics of dinamic pupillometry. The measurements were applied in 77 scotopic, mesopic, photopic and dynamic conditions. Scotopic, in which the only visible light 78 source is the LED source (0.4 lux). Mesopic, in which the disk is illuminated in such a 79 manner as to bring ambient light intensity to about 4 lux. *Photopic*, in which disk is 80 illuminated in such a manner as to bring ambient light intensity to about 40 lux. Another type 81 of lighting condition, called *Dynamic*, capture has begun with the rings disk fully illuminated 82 (500 lux ca.); it was switched off at the moment capture begins. In this manner, it is possible 83 to monitor pupil dilation. in conditions from photopic to absence of light (scotopic conditions) 84 and analyze pupil size and pupil offset instant by instant.

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86 Statistical Analysis

Statistical calculations were performed with (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) program for Windows. Besides, standard descriptive statistical calculations (mean and standard deviation), unpaired t test was used in the comparison of groups and Chi square test was performed during the evaluation qualitative data. *Pearson Correlation test used* to study the relationship between the variables. Statistical significance level was established at p<0,05.

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94 **RESULTS**

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In this study, it was included fourty-six patients with PXS and 46 sex, age-matched control subjects. There were no statistically significant differences in age and sex. The demographic data are listed in Table 1.

Pupil diameter in scotopic condition was measured between 2.65mm and 5.56 mm in
PXS group, 3.65mm and 6.52mm in control group. It was mesured in mesopic condition

101 between 2.43mm and 5.35mm; 2.93mm and 6.44mm, in photopic condition between 2.09mm 102 and 4.99mm; 2.47mm and 5.74mm and dynamic pupil diameter between 2.3mm and 4.67; 103 2.49mm and 5.07mm respectively. Mean pupil diameters were significantly lower in the PXS 104 group than control group for all measurements. Scotopic and mesopic pupil size were 105 significantly lower in the PXS group when we compared with control groups (p=0.0001). 106 Also photopic and dinamic pupil size were significantly lower in the PXS group when 107 comparing with control groups (p=0.014, p=0.013). Pupil size under scotopic, mesopic, 108 photopic and dynamic conditions are listed in Table 2.

Correlation analysis revealed strong correlation of pupil diameters in scotopic,
 mesopic, photopic and dynamic conditions of both PXS and control groups (Table 3).

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112 **DISCUSSION**

In our study, we aim to assess the pupil size under scotopic, mesopic, photopic and dinamic conditions in patients with PXS. To our knowledge, this will be the first study that evaluates the pupil measurements of patients with PXS using IR pupillometer integrated within CSO Sirius Corneal Topographer, since the Pub-Med search and other literature

117 researches did not reveal any other similar papers.

Pupil size has affected by many factors such as illumination conditions, age, microvascular diseases like as diabetes mellitus, accomodation, fatigue, sensory and emotional status, and various drugs. Traditionally, pupil size has been evaluated with static pupillometers [11]. The recent technological developments in pupillometers, particularly incorporation of IR systems provide standardized intensity and duration of test light exposed, non-invazive, easy applicable, low inter-observer and intraobserver changes [12-14]. In our study, pupil size was measured with IR pupillometer integrated within CSO Sirius Corneal 125 Topographer. Characteristics of this pupillometer include binocularity, objectivity,126 standardized illumination and dynamic pupil function.

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128 The majority of articles compared various pupillometers using different techniques 129 and devices [12,14-25]. The digital pupillometers allow examination of the dynamic pupil 130 function in addition to scotopic, mesopic and photopic measurements of pupil size and 131 provide objective data using a computer software. In these devices, intensities of test 132 illumination are well-defined. IR pupillometers are able to take monocular or binocular 133 mesurements. The fellow eyes taken with monocular pupillometer are affected due to 134 fluctuations in room illumination. In contrary, measurements taken with binocular 135 pupillometer can be more advantageous because of most likely real-life conditions simulated 136 [19,26].

137 All types of devices have been proved to give objective, standardized, reliable and 138 repeatable data [14-16,19,22-25,27-31]. Schallenberg et al. compared Colvard, Procyon, and 139 Neuroptics pupillometers for measuring pupil diameter under low ambient illumination. They 140 indicate that monocular pupillometry either with the Neuroptics or Colvard pupillometer is at 141 least as accurate as using the Procyon [14]. This result agrees with the studies of Kohnen et al. 142 and Michel et al. [16,32]. Kohnen et al. stated that hand-held IR pupillometers with their 143 simpler designs and portable features can also track the dynamic pupil process in an 144 experienced hand. Furthermore, they concluded that the digital IR device shows less variation 145 in scotopic pupil diameter and has better interrater repeatability than the hand-held IR devices 146 [16]. Bootsma et al. noticed that digital binocular IR pupillometry is superior for obtaining standardized measurements of pupil size, because it is much more closer to real-life 147 148 conditions [19]. Some features of Procyon and Sirius IR pupillometer are similar in terms of 149 binocularity, objectivity, standardization of illumination and dynamic measuring [21]. Altan

150 et al. concluded that the tendency of smaller pupil size measurements with the Ocular 151 Wavefront Analyzer might be due to the slightly higher ambiance illumination or an effect of 152 accomodative miosis when subjects fixated on the a red light-emitting diode target in this 153 device. Also it emphasizes that the larger pupil diameter found with the Sirius than with the 154 Ocular Wavefront Analyzer and NeurOptics pupillometers may represent the different 155 illumination levels used with each instrument together with relaxation of accommodation due 156 to target fogging and software interpretation. It was reported that different measurements are 157 related not only with illumination and accommodation but also with measurement algoritms 158 or technique differences of instruments [25]. In our study, it was used binocular IR 159 pupillometry.

160 It is known that mydriasis in eyes with PXS is restricted [2-4]. While making literature 161 research, we did not find studies about investigating pupil measurements using IR 162 pupillometer. Yulek et al. were used videonystagmography in asymmetric pseudoexfoliation 163 patients. They were measured the percent of change in pupillary diameter in one second 164 during the change in pupillary diameter during fixation to an accomodative target at 30 cm 165 that is the accomodative response, during the light reaction, during the convergence-induced 166 miosis, and finally during the divergence-induced mydriasis, both at fixed speed. They were 167 declared that the difference between control group and pseudoexfoliative eyes of patient with 168 PXS; between unaffected eyes and pseudoexfoliative eyes of patient with PXS was significant 169 [10]. But they were unable to take measurements in different illumination conditions. 170 Moreover, lack of normative data for responses of pupil to different illumination conditions 171 can be interpreted as a limiting factor. Our study stands out with more numerous patients 172 enrolled and a device with nomogram. It has shown significant variations in patients with PXS for 3 different light intensities and dynamic response. However, it was influenced 173 174 dilation more than miosis.

175 In our study, it was determined that the eyes of PXS have smaller pupil diameters than 176 control groups. The results suggest that pupillary light response in patients with PXS 177 significantly deteriorate not only in scotopic and mesopic conditions but also in photopic and 178 dynamic conditions as well. According to our findings, pseudoexfoliation material seems that 179 dilator muscles affect more profound than the sphincter muscles. Recently, cataract surgery is 180 refractive surgery at the same time and visual expectations of individuals are extremely high. 181 Physicians should choose the multifocal IOL that best suits individual patients' desired 182 outcomes, increasing patients' visual outcomes and satisfaction. Therefore, we highlighted 183 that pupil size assessments under variable illumination conditions could be useful along with 184 careful preoperative evaluation, particularly for patients with PXS who need better 185 intermediate vision and refractive multifocal IOL.

As Schlötzer-Schrehardt et al. say: "The Puzzle Continues"[1]. Does the smaller pupil size provide a decrease in mean correction in patients with PXS? Are the abberations of eyes less in PXS patients? How much does PXS affect the pupil velocity? We will continue to look for answers to these questions.

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191 CONCLUSION

192The results suggest that pupillary light response in patients with PXS significantly was193affected not only in scotopic and mesopic conditions both also in photopic and dynamic

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194 conditions. We believe that our study will be useful for further researches.
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Scotopic

286 Table 1.Demographic data of pseudoexfoliation syndrome and control groups

Age		synar 73	ome group	<u> </u>	roup 3+6.92	P 0.963	
	Female	22	47.83%	20	43.48%	0.7 00	
Sex	Male	24	52.17%	26	56.52%	0.675	

4.16±0.65

4.77±0.66

0.0001

	Mesopic	3.85±0.67	4.56 ± 0.68	0.0001		
	Photopic	3.28±0.66	3.64±0.72	0.014		
	Dynamic	3.14±0.56	3.42±0.5	0.013		
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3 1	Table 3. Results o	t the correlation analys	as of pupil diame	eters in scoto	opic, mesopic, p	notopic
4 5	and dynamic cond	itions of both groups				
3						

Pseudoexfoliatio	n				
Group		Scotopic	Mesopic	Photopic	Dynamic
	r		0.882	0.837	0.76
Scotopic	р		0.0001	0.0001	0.0001
	r	0.882		0.85	0.812
Mesopic	р	0.0001		0.0001	0.0001
	r	0.837	0.85		0.905
Photopic	р	0.0001	0.0001		0.0001
	r	0.76	0.812	0.905	
Dynamic	р	0.0001	0.0001	0.0001	
Control Group		Scotopic	Mesopic	Photopic	Dynamic
	r		0.962	0.716	0.724
Scotopic	р		0.0001	0.0001	0.0001
	r	0.962		0.792	0.781
Mesopic	р	0.0001		0.0001	0.0001
	r	0.716	0.792		0.849
Photopic	р	0.0001	0.0001		0.0001
		0 724	0 781	0 849	
	r	0.724	0.701	0.042	