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The ocular surface status in individuals having long-term exposure to ionizing X-radiations

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ABSTRACT

Purpose: The present investigation was done to assess the status of tear film and corneal topography in individuals with long-term exposure to X-ray.

Method: This historical cohort study was carried out to compare the lacrimal and corneal findings between radiographers (n = 126) and non-radiographers (n = 172). Radiographers included individuals with at least 5 years of experience in radiography while subjects in the control group had no history of exposure to X-ray. The Ocular Surface Disease Index (OSDI) was filled out by all individuals. Besides, the Pentacam imaging of both eyes was done. Finally, the lacrimal tests including tear break-up time and Schirmer (with anesthesia) were performed for both eyes of the participants.

Results: The mean values of the Schirmer and Tear breakup time (TBUT) in the radiographer group (Schirmer: 11.1 ± 3.2 mm, TBUT: 11.3 ± 4.1 s) were significantly lower than the values in control group (14.6 ± 8.1 mm, TBUT: 12.8 ± 4.8 s) ($P < 0.0001$). The mean OSDI score of the radiographers was significantly higher compared to the control group (24.1 ± 17.6, and 12.3 ± 12.4 respectively ($P < 0.0001$)). The corneal thickness in the center, inferior, superior, temporal and nasal parts was significantly higher in radiographers versus the control group. In addition, the maximum thickness difference was observed in temporal part (34.00 µm thicker) ($P < 0.0001$). On the other hand, the corneal eccentricity factor was lower in radiographers compared to the control group ($P < 0.0001$).

Conclusion: Based on the findings of this study, it is concluded that the radiographers have thicker and flatter corneas are than the corneas of the subjects in the control group. However, their corneas had no irregularities. Regarding the tear point, a higher prevalence of dry eye symptoms was observed in the radiographers compared to the control group.

1. Introduction

Radiographers, as one of the most important imaging professions in medical and health sciences, are repeatedly exposed to X-radiation. Imaging procedures such as Computerized Tomography (CT) exposes both the patient and the examiner to such radiations. The effects of X-radiation on the human body depend on a number of factors, including the radiation intensity, wavelength, duration and frequency of exposure [1]. The effects may range from a series of minor changes in the physiologic performance of tissues to critical changes such as various types of cancers and carcinomas, infertility, and premature death [2,3].

Like many other tissues, X-ay can be detrimental to the eye. The most frequent ocular injuries reported to be caused by X-ray include the cataract and corneal opacities. Studies investigating the effect of direct exposure of the eyes to X-rays in mice and rabbits have shown that exposure to high dosages (higher than 200 r.) can cause cataracts. These

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studies have reported a small chance of cataract at low doses of radiation and in short-term exposures [4]. The cataract progresses even after the exposure according to a report by Rini. He described the cause of cataract to be the epithelium changes due to the radiation [5].

X-radiation can cause different changes in the cornea. Laboratory studies of the effects of x-ray exposure on animals have shown changes in the corneal transparency, cornea cells mitosis, corneal thickness, etc. [6,7]. In addition to animal studies, some studies have examined the effects of X-radiation on the human cornea.

In 1966, Emilit reported corneal nerves changes due to exposure to X-radiation [8]. Based on this study, X-radiation can alter corneal nerves and affect the corneal sensation. In 1958, Blodi investigated the effects of X-rays on the corneal tissue in patients undergoing radiotherapy [7]. In this study, eye injuries were observed in patients undergoing different radiotherapy treatments for head region malignancies, including eyelid and epibulbar tumors, nasopharyngeal carcinomas, etc. According to this study, injuries such as cornea epithelium keratinization, epithelial proliferation, bullous keratopathy, interstitial keratitis, pannus, vascularization of the corneal stroma, corneal perforation, and corneal ulcers and scars were observed in these patients [7]. The results also indicated that corneal changes were not similar in different individuals and one or more of the aforementioned injuries may be observed in the patients.

Considering the above studies, long-term X-ray exposure may affect the lacrimal system and cornea. Since previous studies have shown some changes in the corneal tissue, complete topographic and tomographic assessments are necessary in exposed subjects. On the other hand, the lacrimal system is important because there is a mutual relationship between this system and the corneal surface [9–11] and therefore corneal surface problems may disturb tear distribution and cause dry eye. On the other hand, it is possible that long-term exposure to X-radiation may affect lacrimal glands and cause dry eye through changing their structure or function.

Due to the fact that radiographers are continually and repeatedly exposed to X-radiation, the question that previous studies have failed to respond is whether the usual dose of X-radiation in the workplace has any effects on the cornea or tear film. The aim of this study was to examine the state of ocular surface, including the tear film and cornea, in radiographers and compare it with that of the control group.

2. Methods

In this historical cohort study that was conducted in 2017, two groups, including radiographers and a control group, were analyzed. The radiographer group included people with at least 5 years of experience in radiography. The control group, on the other hand, lacked any long-term history of exposure to X-radiation. Subjects who were away from radiography for more than three months were excluded from the study. In addition, individuals with a history of ocular surgery, including cataract, strabismus, and all corneal surgical procedures were excluded from the study. To select the radiographers, a list of all subjects working in this field was obtained from the respective association and 150 individuals were randomly selected from radiographers practicing in Tehran. These individuals were invited to participate in the study via phone calls. Of 150 invited radiographers, 24 were unresponsive to phone calls or could not attend in person and 126 participated in the study. The control group was selected in the same areas as the radiographers. It was tried to select the same proportions of subjects from different districts of Tehran. Two hundred and seven subjects comprised the control group.

The tenets of the Helsinki Declaration were observed throughout the study. The Ethics Committee of Mashhad University of Medical Sciences approved the protocol of the study. Prior to the study, the participants received a detailed clear explanation of the examination methods and the objectives of the study. Then, written consent was obtained from each participant. They were well assured that they could withdraw from the study without any problems, and that their information would be used confidentially and anonymously. In the beginning of the study, the demographic characteristics of the participants as well as a full description of their work history were taken. Physical examination was done after completing the questionnaire.

2.1. Examinations

Examinations included visual acuity, refraction, slit lamp biomicroscopy, tear film tests, and Pentacam imaging. Visual acuity was measured using a distance Snellen chart. Then, refraction was measured with an auto refractometer for both eyes of the subjects and the results were recorded. In the next stage, Pentacam imaging was done prior to any ocular manipulation including slit lamp biomicroscopy and tear test.

After Pentacam imaging, slit lamp biomicroscopy and tear tests were done. Initially, the Tear breakup time (TBUT) was measured for both eyes. The subject was requested to sit at the slit lamp biomicroscope (TOPCON SL-6E, Japan). A strip impregnated with fluorescein (HAAG-STREIT AG, Switzerland) was moisturized with a drop of normal saline (SAMEN Pharmaceutical Co., Iran), and the superior bulbar conjunctiva was gently touched with the strip tip while the subject was looking down. Then, the person was instructed to blink slowly two or three times to spread the fluorescein evenly. The cornea was examined under cobalt blue filter on the slit lamp. Under this filter, fluorescein appears as a green layer on the cornea and dry areas are indicated by the presence of a black spot. The time between the last blink and the appearance of a dry spot measured with a stopwatch in seconds was recorded as the tear breakup time. This test was conducted 3 times for each eye and the mean time was recorded in the patient's sheet. It took 30 min for the patients to return to their normal tear status. Next, the Schirmer test was carried out. For this test, a drop of tetracaine was instilled into both eyes. After corneal anesthesia was achieved, the patient was asked to look up, and then a Schirmer strip was placed in the conjunctival fornix for 5 min. Then, the strip was removed from the fornix and the wet portion was recorded in millimeters.

2.2. Compared parameters

In this study, the results of lacrimal tests including the Schirmer with anesthesia and TBUT were considered as objective indicators of dry eye. On the other hand, the results of the OSDI questionnaire were considered as the subjective criterion for evaluating the tear film status. These two sets of parameters were compared between the two groups. To compare the results of corneal topography between the two groups, different Pentacam parameters were extracted. A list of the corneal parameters evaluated in this study is presented in Table 1. Information on the corneal curvature and its thickness was compared as numerical indices. In addition, to investigate the corneal surface irregularity regarding topographic issues, the indices of surface irregularity were compared between the two groups.

2.3. Definitions and classifications

In this study, the Tear Film and Ocular Surface Society (**TFOS**) Dry Eye Workshop (**DEWS**) **II** reports were used for dry eye diagnosis. As for the TBUT test, values less than 10 seconds were considered dry eye [12,13]. Regarding the Schirmer's test, values more than 10 and less than 5 mm were considered normal and dry eye, respectively [13,14]. To analyze the results of the OSDI questionnaire, the total score of the questionnaire was multiplied by 25 and the result was divided by the number of questions [15]. Values above 23 indicated dry eye. For classification of the intensity of dry eye based on the OSDI, a value of 0–12, 13–22, 23–32, and more than 33 was considered as normal, mild dry eye, moderate dry eye, and severe dry eye, respectively.

Table 1
The corneal parapmeters evaluated in this study.

Parameter abbreviation	Full name	Definition
Ecc	Eccentricity	Index of measuring the rate of corneal flattening from the apex to the periphery
K_1	Keratometry 1	Flat meridian keratometry
K_2	Keratometry 2	Steep meridian keratometry
Mean K	Mean Keratometry	Mean value of steep and flat keratometries
Astig.	Corneal astigmatism	Toricity of the anterior cornea
Pachy-Apex	Pachymetry apex	Corneal thickness at apex
Pachy-Pupil	Pachymetry pupil	Corneal thickness at pupil area
Pachy-Sup	Pachymetry superior	Corneal thickness at superior region of cornea
Pachy-Inf	Pachymetry inferior	Corneal thickness at inferior region of cornea
Pachy-Nas	Pachymetry nasal	Corneal thickness at nasal region of cornea
Pachy-temp	Pachymetry temporal	Corneal thickness at temporal region of cornea
ISV	Index of Surface Variance	Index of measuring the irregularity of curvature of the anterior cornea
IVA	Index of Vertical Asymmetry	Index of measuring the curvature asymmetry between the superior and inferior cornea
IHA	Index of Height Asymmetry	Index of measuring the difference between the mean elevation of the superior and inferior cornea
KI	Keratoconus Index	Index of predicting of keratoconus
CKI	Central Keratoconus Index	Index of measuring the central protrusion of the cornea
IHD	Index of Height Decentration	Index of measuring the vertical decentration of corneal elevation data

2.4. Statistical analyses

SPSS (Version 17) was applied to analyze the data in this study. Independent sample *t*-test was used to compare the results between the two groups. P values less than 0.05 were considered significant.

2.5. Ethical issues

The Ethics Committee of Mashhad University of Medical Sciences approved the study protocol. Every stage of the study was conducted in accordance with the tenets of the Helsinki Declaration. Written informed consent was obtained from all participants.

3. Results

In this study, data obtained from 126 radiographers (mean age: 45.9 ± 12.8 years) and 172 control subjects (mean age: 45.5 ± 12.6 years) was analyzed. Since the correlation coefficient of all study variables was above 0.689, the data of one eye (the eye with poorer tear test values) were selected for the analysis. The mean duration of exposure in radiographers (was 11.2 ± 3.5 ranging from 6 to 26 Which was considered as long-term exposure).

3.1. Tear findings

The mean and standard deviation of tear tests and OSDI questionnaire in both study groups along with their respective *p*-values and comparative results are presented in Table 2.

According to Table 2, independent sample *t*-test showed that the TBUT and Schirmer values were significantly lower and the OSDI values were significantly higher in radiographers compared to control subjects.

To investigate dry eye in both groups, the data obtained from the OSDI questionnaire were assessed based on subjective complaints. The percentages related to severity of dry eye in both groups are presented in Fig. 1.

Table 2
The means and standard deviations of tear tests and OSDI questionnaire in two groups of study.

	Control n = 172	radiologist n = 126	p-value
TBUT (sec.)	12.8 ± 4.8	11.3 ± 4.1	= 0.0044
Schirmer (mm)	14.7 ± 8.2	11.1 ± 3.2	< 0.0001
OSDI	12.3 ± 12.4	24.1 ± 17.6	< 0.0001

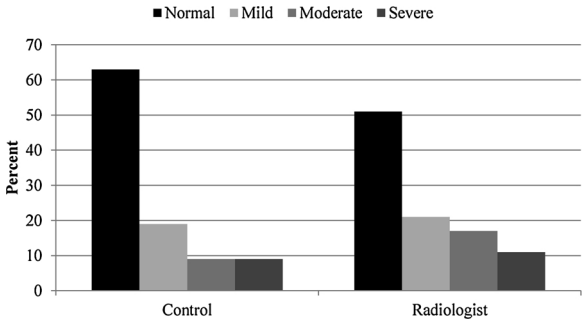

Fig. 1. The percentages of different OSDI categories obtainded from both studied groups.

According to Fig. 1, the prevalence of moderate and severe dry eye was higher in radiographers compared to control group.

3.2. Corneal findings

In addition to tear film findings, the corneal data were also compared between the two groups. The results of this comparison are presented in Table 3.

According to Table 3, eccentricity and keratometry values were significantly lower in radiographers compared to the control group. The mean astigmatism and corneal thickness in all quadrants were significantly higher in radiographers versus the control group. The greatest difference in the corneal thickness was seen in the temporal and superior cornea. None of the corneal surface irregularity indices showed a significant difference between the two groups.

4. Discussion

The present study was the first comprehensive study of the ocular surface status in radiographers. To date, no study has investigated the tear film characteristics of these individuals. On the other hand, the studies related to corneal effects of X-ray are generally carried out in the distant past. In addition, no study has investigated the effects of long-term exposure to a routine dose of X-radiation in the radiographers' working environment on the corneal tissue. Thus, the results of this study could shed light on the lacrimal and corneal complications of radiographers and other individuals who have similar exposure to X-ray.

The most important finding of the present study was that the radiographers' corneas had a greater thickness (by about 26 μm in the center and up to 33 μm in the peripheral regions on average) compared

Table 3
The comparison of different corneal parameters between two groups.

	Control N = 172	Radiologists N = 126	Mean difference: (control) – (radiologist)	P-value
Ecc.	0.48 ± 0.23	0.47 ± 0.29	0.114	< 0.0001
K $_1$ (d)	43.48 ± 1.03	42.53 ± 1.13	0.948	< 0.0001
K $_2$ (d)	44.06 ± 1.07	43.36 ± 1.14	0.727	< 0.0001
Mean k	43.78 ± 1.04	42.95 ± 1.10	0.837	< 0.0001
Astig.	0.61 ± 0.34	0.83 ± 0.55	−0.221	= 0.003
Pachy-apex (μ)	538.02 ± 30.26	564.11 ± 21.51	−26.096	< 0.0001
Pachy-pupil (μ)	534.85 ± 31.09	561.36 ± 22.80	−26.517	< 0.0001
Pachy-sup (μ)	636.81 ± 45.15	667.17 ± 40.67	−30.356	< 0.0001
Pachy-inf (μ)	594.02 ± 44.88	622.14 ± 41.05	−28.116	< 0.0001
Pachy-nas (μ)	622.93 ± 43.66	651.24 ± 34.29	−28.313	< 0.0001
Pachy-temp (μ)	588.62 ± 66.78	622.62 ± 11.80	−33.999	< 0.0001
Isv	15.50 ± 4.63	16.70 ± 6.42	−1.198	= 0.569
Iva	0.12 ± 0.05	0.13 ± 0.06	−0.031	= 0.297
Iha	4.85 ± 3.80	5.12 ± 4.43	−0.274	= 0.867
Ki	1.01 ± 0.02	1.01 ± 0.02	0.000	= 0.997
Cki	1.00 ± 0.01	1.00 ± 0.01	−0.000	= 0.737
Ihd	0.01 ± 0.01	0.01 ± 0.01	−0.001	= 0.452

to the control group. Blodi studied the corneal effects of X-radiation during radiotherapy treatment of tumors in the head region and reported changes in the corneal thickness in many cases [7]. According to the Blodi's study, individuals receiving radiotherapy for tumors of the eyelid and other parts close to the eyes had an increased corneal thickness, especially in the epithelial region. A probable reason for these changes is the increased proliferation of the corneal epithelial cells. Additionally, changes in the number of corneal stromal cells were also seen in some cases in this study [7]. Several studies have reported that X-radiation can cause changes in the process of cell division and proliferation [16–18]. Therefore, the findings of this study regarding the corneal thickness can probably be attributed to the long-term effects of X-radiation. In fact, it is likely that frequent radiation in radiographers may lead to some changes in the corneal cells division and proliferation of corneal epithelial cells, eventually resulting in corneal thickening. Of course, in order to investigate corneal thickening, analyses should be done via instruments such as confocal microscopy to locate the thickened spot on the cornea accurately and determine the reason and mechanism of these changes.

According to this study, the radiographers' corneas were about 1 D flatter than the corneas of control individuals. This finding is clinically significant, as well. It may seem that the reason for the increased curvature radius in such people is increased corneal thickness. In fact, because of the increased corneal thickness, the corneal protrusion is lower and the central cornea shows a lower curvature. However, studies of the corneal thickness and its curvature indicate that these two variables do not have a significant correlation with one another and are independent [19]. It seems that the results of this study cannot provide a reason for corneal flattening. Therefore, further studies are needed to clarify the reason(s) behind the findings of this study via accurate analysis of the corneal tissue. It is worth mentioning that although the corneal thickness and curvature were different between radiographers and the control group, no particular irregularity was observed in their corneas. As mentioned previously, none of the surface irregularity indices showed a significant difference between the two groups. Hence, although the radiographers' corneas are generally flatter and thicker compared to the control group, no topographic irregularity exists on their corneal surface. This is indicative of the fact that the changes in the corneal thickness and curvature are global and not localized to a certain region.

As mentioned in the Methods section, comprehensive objective and subjective investigations were done on the tear film in the present study. The results indicated significantly lower values of Schirmer and TBUT in radiographers. The low TBUT values actually indicate the lower tear film stability in this group [13]. In fact, the difference in the TBUT results is statistically significant yet not clinically important. Lower values of the Schirmer test are more remarkable and indicate less tear production in radiographers compared to controls. This disorder tends to be of greater importance than tear instability. However, the most important lacrimal finding in the study was the difference in the OSDI score between the two groups, indicating that the dry eye complaints were more frequent in radiographers compared to subjects in the control group. The mean OSDI score was 12 in the control group and 24 in radiographers. This difference is of great importance. Recent research on dry eye has shown that the best way to diagnose this disease is based on symptom questioning [20–22]. Therefore, greater attention should be paid to OSDI results versus objective findings, i.e. the Schirmer and TBUT tests. Earlier studies have shown no considerable overlap between findings of dry eye tests and the subjective findings related to the patients' complaints [22]. Consequently, a diagnosis of dry eye based on the OSDI results is becoming more and more important. According to these explanations, the prevalence of dry eye is markedly high in radiographers. Fig. 1 helps to understand that the greatest difference between the radiographers and the control group is in the moderate dry eye column. The data related to severe and mild dry eye have a little difference between the two groups.

The challenging question is that, "Why do radiographers have higher rates of dry eye?" Two possible causes can be considered. One possible reason could be the corneal sensation. A study by Emilit regarding the effects of X-radiation on the corneal nerves showed that X-ray exposure could reduce the corneal sensation [8]. Studies have shown that reduced corneal sensation is one of the most fundamental causes of decreased tear secretion and dry eye [9,10,23,24]. Considering the findings of the present study showing a low tear secretion in radiographers, this reduction can be attributed to long-term corneal exposure to X-radiation. In fact, a hypothesis is that long-time exposure to X-ray can lead to reduced corneal sensation and tear production, eventually resulting in aqueous deficiency dry eye.

Another for a low tear secretion and a higher rate of dry eye in radiographers could be the possible changes in the performance of lacrimal secretory glands. Since the lacrimal glands such as the accessory exocrine glands of Krause and Wolfring are located in the eyelid structure [25–28], they may undergo biological changes due to long-term X-ray exposure, disrupting their secretions. Several studies have shown changes in the exocrine glands following X-ray exposure. Based on these studies, X-radiation can cause dysfunction of various glands, including the thyroid, salivary, parotid, and pituitary glands [29–32]. Studies of salivary glands have shown that long-term exposure to X-

radiation can reduce salivary gland secretion, eventually resulting in xerostomia [29]. Since lacrimal glands are exocrine and have a similar function to that of salivary glands [33,34], this dysfunction may occur in lacrimal glands, as well. Therefore, the second hypothesis to explain dry eye in radiographers is that the continuous long-term exposure to X-radiation may cause dysfunction in the lacrimal glands responsible for aqueous tear production, leading to reduced secretion. This explanation, which is consistent with Schirmer test results, eventually leads to aqueous deficiency dry eye, which is in line with the OSDI results.

This study has several limitations and strengths. A strong point of this study is that the radiographers' lacrimal system and corneas were examined for the first time in the world. However, tear film osmolarity tests can provide a better quantitative assessment of the tear film compared to the Schirmer's test [13]. However, since this test was not available, Schirmer's test was done. Although the Schirmer's test may not be error-free, it was tried to do the test with utmost care to obtain valid results.

Generally, based on the results of the present study, it can be concluded that the prevalence of dry eye is higher in radiographers compared to non-radiographers. Regarding all tear analyses, it can be stated that the dry eye in radiographers is mostly caused by aqueous deficiency. In addition to the tear film, the corneal findings were also different between radiographers and control subjects. Based on the findings of the present investigation, radiographers have thicker and flatter corneas; however, no topographic irregularities were observed in their corneas.

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Conflict of interest

No conflicting relationship exists for any author.

Disclosure

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper

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