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## Evaluation of dry eye syndrome after advanced technique of radiation therapy in head and neck cancers

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### Abstract

**Aim:** To assess structural and functional abnormalities of the ocular surface post radiation in head and neck cancers.

**Objective:** To assess the presence and severity of dry eye symptoms according to Ocular Surface Disorder Index (OSDI) questionnaire and Dry eye severity grading by DEWS 2007 classification in patients who underwent radiotherapy for head and neck cancers. To evaluate correlation between dose of radiation therapy and severity of Dry Eye Syndrome by various clinical methods of evaluation of dry eye.

**Design:** Observational case control study.

**Methods:** Participants considering 10% non-response a sample size of  $85+8.5=100$  subjects with head and neck cancer undergoing radiation. Data analysed using SPSS 22 version software. Chisquare used as test of significance. Independent t test will be used as test of significance to identify the mean difference. p value  $<0.05$  will be considered statistically significant.

**Results:** In the present study, majority of the study population belong to 41-50 years. It was observed that the incidence of dry eye disease was found to be more in patients receiving more radiation (60-70 Gy) in the immediate post radiation period. Many of them were put on medical management of DES and they improved symptomatically in the subsequent follow-ups. Variations in the dose, method of radiation and the usage of protective shields and early medical management of DES play an important role in the prevention of ocular complications especially dry eye syndrome post radiation therapy.

**Keywords:** Dry eyesyndrome, dry eye severity scheme by DEWS 2007, intensity modulated radiotherapy (IMRT), OSDI score

### Introduction

Dry eye syndrome (DES) is a disorder that results from deficiencies or defects in the components of lubrication that can lead to structural and functional abnormalities of the ocular surface<sup>[1]</sup>. Head and neck cancers (HNC) are the sixth most common malignancy worldwide. Radiation therapy (RT) for cancers of the head and neck plays a major role and is administered by linear accelerator machines which produce high-energy external radiation beams<sup>[2]</sup>, this plays a major role in development of dry eye. Radiation related complications of the eye and orbital structures have been recognized since the late 19<sup>th</sup> century. Which occur either as a direct result of irradiation for intraocular tumors or when the eye is within the entrance or exit beam<sup>[3]</sup>. Acute lesions usually occur in the eyelid, conjunctiva and corneal epithelium whereas delayed effects are related to development of cataracts, glaucoma, and retinopathy. One of the most frequent manifestations of radiation toxicity is a decreased visual acuity due to the effect on the cornea lens and retina.

Radiotherapy is one of the major causes of Dry Eye Syndrome (DES) and the incidence of DES is proportionate to the total dose of radiotherapy. It increases steeply at doses  $> 40$  Gy. And is due to cytostatic effects on the cells with high turnover and to specific alterations in cell type and function<sup>[4]</sup>. As a result of irradiation there is damage to the Meibomian glands, increase in the stratification of conjunctival epithelium and reduction in goblet cell numbers with reduction or, an absence of the lipid layer of the tear film with consequent increase in evaporation, there is damage to the acinar cells of the lacrimal glands<sup>[3]</sup>. Lacrimal puncta and Canaliculi undergo fibrosis hence a post-radiation obstruction resulting in epiphora. Radiotherapy also induced blepharitis, trichiasis, distichiasis, madarosis, entropion and

ectropion which also contribute to Dry Eye Syndrome. Advanced radiation therapy methods for head and neck carcinoma such as Intensity Modulated Radiation Therapy (IMRT) minimized these complications with resultant less morbidity [2]. The aim of the study is to assess the incidence of Dry Eye Syndrome following Radiation therapy in head and neck carcinoma this incidence is reported in literature as 6% to 90% [1]. However there is no agreement among the previous studies in relation to the exact incidence of Dry Eye syndrome. The objective of the present study is to find out the incidence after intensity modulated radiation therapy (IMRT) in head and neck cancer patients by OSDI questionnaire and grading Dry eye severity by DEWS 2007 classification. In previous studies there is a controversy in relation to dose dependence per fraction and duration of radiation therapy.

## Methodology

### Source of Data

**Study Area:** Department of Radiation Oncology, Department of Ophthalmology, Vydehi Institute of Medical Science and Research Centre, Bangalore.

**Study Design:** A observational case control study.

**Study Duration:** January 2021 to December 2022(2 years).

**Study Population:** Patients attending ophthalmology and radiation oncology OPD of Vydehi institute of medical sciences and research center who having received radiation therapy, age group between of 20-70 year.

### The inclusion criteria

1. Patients who have been advised to undergo advanced technique of radiation therapy for head and neck carcinoma.
2. Patients whose age is between 20- 70 years
3. Normal Schirmer's score (>10 mm) before radiotherapy.
4. Patients willing to provide voluntary written informed consent for undergoing Ocular Examination and participation in the study.

### The exclusion criteria

1. Patients suffering from coexisting ocular conditions like dry eye, chronic conjunctivitis, scleritis, uveitis, glaucoma, stye, blepharitis, strabismus,cataracts, ptosis,proptosis and thyroid eye disorders.
2. Other causes of dry eye disease like sjogren's syndrome, vitamin A deficiency, trachoma, neuroparalytic keratitis, contact lens users, prolonged stay in air conditioned areas, lagophthalmos and congenital alacrimia.
3. Patients who have under gone ocular surgeries and LASIK.
4. Patients not willing to provide voluntary informed consent for ocular examination and participating in the study.
5. Patient unable to come back for follow up.

**Sample size calculation:** Sample size was estimated by using the proportion of dry eye (33%) after exposure to radiation among patients with head and neck carcinoma from the study by Sarita Maharia *et al.* [2] using the formula  $Sample\ Size = Z_{1-\alpha/2} p(1-p) / d^2$   $Z = 1.96$   $P = 33$   $q = 67$   $d = 10\%$  Using the above values at 95% Confidence level a sample size of 85subjects with ocular symptoms of dry eye, post advanced radiation therapy to head and neck cancer will be included in the study. Considering 10% Non-response a sample size of  $85 + 8.5 \approx 100$  subjects with head and neck cancer undergoing radiation will be included in the study.

### Method of collection of data

An informed consent form (Annexure I) and a pre-structured proforma which has following sections like demographic details, occupational details, personal history, chief complaints, local examination and evaluation of dry eye (Annexure 2) will be explained to all the study participants. General physical examination will be conducted to know the health status in the study group. All patients fulfilling inclusion and exclusion criteria will be taken up for the study. Ophthalmic examination: 1) Visual Acuity for distant vision (Snellen's chart) and near (Jagger's chart) 2) Automated Refractometry 3) Refraction using a streak retinoscope 4) Colour Vision using the Ishihara chart 5) Slit Lamp Examination of the anterior segment of the eye 6) Ocular Surface Disease Index(OSDI) Questionnaire 7) TBUT 8) Schirmer's Test- I & II 9) Posterior segment examination of the eye will be done following dilatation of the pupil with Tropicamide Eyedrops (1%) using 90 D lens /indirect ophthalmoscope using +20D lens. patients were referred to the department of Radiation oncology for radiation therapy and were reassessed immediately post radiotherapy, 3 months, 6months and after 12months of radiotherapy. After the collection of data a statistically evaluation done.

### Statistical analysis

**Statistical Methods:** Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square was used as test of significance. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference. p value <0.05 was considered statistically significant.

### Outcome Measure

The objective of the present study is to find out the incidence of Dry eye syndrome in patients with head and neck cancer after intensity modulated radiation therapy (IMRT), its dose dependence per fraction and duration of radiation therapy as there is controversy in previous studies. 1, 3, 5.

**Ocular surface disease index:** Ask your patients the following 12 questions, and circle the number in the box that best represents each answer. Then, fill in boxes A, B, C, D, and E according to the instructions beside each.

**Table 1:** Subtotal scores from 1 to 5 (a)

Have you ever experienced any of these in the last week?		All of the time	Most of the time	Half of the time	Some of the time	None of the time
1.	Eyes that are sensitive to light?	4	3	2	1	0
2.	Eyes that feel gritty?	4	3	2	1	0
3.	Painful or sore eyes?	4	3	2	1	0
4.	Blurred vision?	4	3	2	1	0
5.	Poor vision?	4	3	2	1	0

**Table 2:** Subtotal scores from 6 TO 9 (B)

Have problems with your eyes limited you in performing any of the following activity during the last week?		All of the time	Most of the time	Half of the time	Some of the time	None of the time	N/A
6.	Reading?	4	3	2	1	0	N/A
7.	Driving at night?	4	3	2	1	0	N/A
8.	Working with a computer or bank machine (ATM)?	4	3	2	1	0	N/A
9.	Watching TV?	4	3	2	1	0	N/A

**Table 3:** Subtotal scores from 10 to 12 (c)

Have your eyes felt uncomfortable in any of the following situations during the last week?		All of the time	Most of the time	Half of the time	Some of the time	None of the time	N/A
10.	Windy conditions?	4	3	2	1	0	N/A
11.	Places or areas with low humidity (very dry)?	4	3	2	1	0	N/A
12.	Areas that are air conditioned?	4	3	2	1	0	N/A

Add subtotals a,b and c to obtain d.  
 (d=sum of scores for all questions answered).  
 Total number of questions answered e

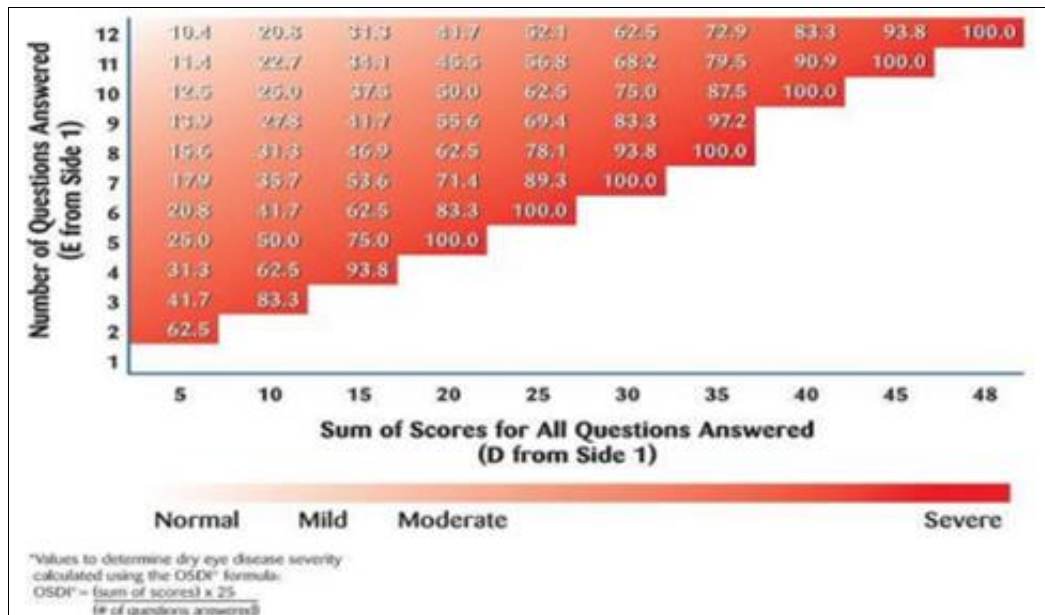
**Evaluating the OSDI Score**

The OSDI is assessed on a scale of 0 to 100, with higher scores representing greater disability. The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease. The OSDI is a valid and reliable instrument for measuring dry eye disease severity (normal, mild to moderate and

severe) and effect on vision- related function.

**Assessing your patient’s dry eye disease**

Use your answers D and E from side 1 to compare the sum of scores for all questions answered (D) and the number of questions answered (E) with the chart below. Find where your patient’s score would fall. Match the corresponding shade of red to the key below to determine whether your patient’s score indicates normal, mild, moderate or severe dry eye disease.



**Fig 1:** Assessment of dry eye disease of the individuals based on OSDI score

Head and neck cancers (HNC) are the sixth most common malignancy worldwide. Modern radiation therapy (RT) for cancers of the head and neck is administered by linear accelerator machines which produce high-energy external radiation beams. It has undergone many advancements and

refinements over time with improved shielding techniques to protect the neighboring tissues [2]. Radiation complications of the eye and orbital structures have been recognized since the late 19th century. Ocular and orbital injuries may occur either as a direct result of irradiation for

intraocular tumors or when the eye is within the entrance or exit beam [3]. Ionizing radiation is associated with side effects like treatment induced oral mucositis, xerostomia, xerophthalmia and dysphagia. Acute lesions may occur in the eyelid, conjunctiva, and corneal epithelium. Typical delayed effects include cataract, glaucoma and retinopathy. One of the most frequent manifestations of radiation toxicity is a decreased visual acuity. The incidence of DES is proportional to the total dose of radiotherapy increases steeply at doses > 40 Gy. Results from the cytostatic effects of radiation on the meibomian glands with reduction or absence of the lipid layer of the tear film and evaporation. Damage to the acinar cells of the lacrimal glands and increase in the stratification of conjunctival epithelium [19, 4].

The major modalities of radiotherapy are external beam radiotherapy and brachytherapy (application of plaques). Both photons (X-rays and gamma-rays) and particles (e.g. protons) interact with matter and may lead to either direct damage to DNA or indirect injury through interactions with nearby molecules (such as water) and subsequent free radical formation. Radiation can also cause cell death through the induction of apoptosis. By giving radiation doses over a number of fractions, damage to normal tissues can be reduced due to the repair of sublethal damage between fractions and repopulation of cells. Radiotherapy has undergone many advancements and refinements over time with improved shielding techniques to protect the neighboring tissues.

**Table 4:** Tolerance doses of the optic nerve, retina, ocular surface and lens.

Ophthalmic structure	Manifestation of toxicity	TD 5/5 (Gy)	TD 50/5 (Gy)
Optic nerve	Optic neuropathy	> 55	> 65
Retina	Retinopathy	45-50	55
Ocular surface	Severe dry eye	35	50
Lens	Cataract	10	18

TD = tolerance dose.

## Results

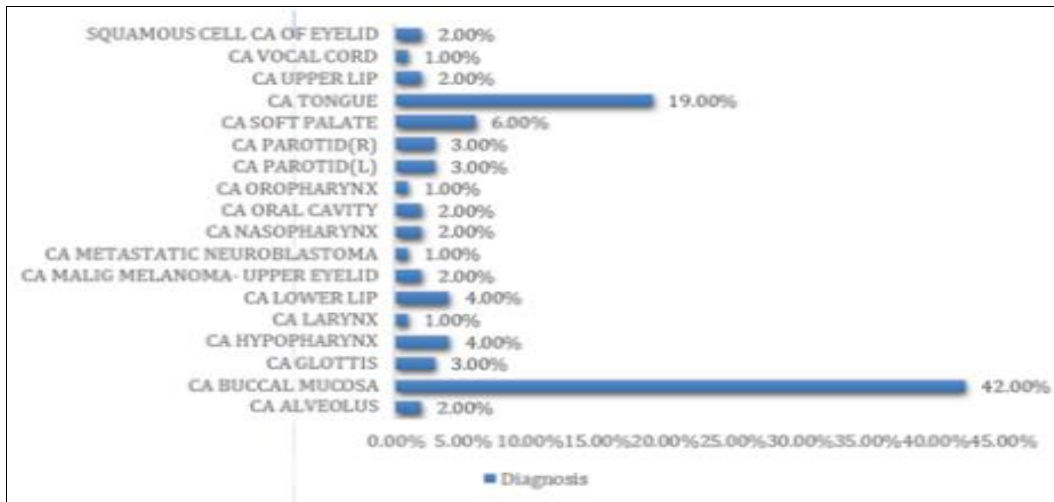
This prospective study was conducted in Department of ophthalmology and department of radiation oncology in Vydehi hospital for a period of 2 years comprising 100 subjects satisfying inclusion and exclusion criteria with informed consent. The study was done to identify the incidence of Dry eye syndrome in patients with head and neck cancer after intensity modulated radiation therapy (IMRT), its dose dependence per fraction of radiation therapy as there is controversy in previous studies. The presence and severity of dry eye symptoms were assessed according to ocular surface disorder (OSDI) questionnaire and graded by using dry eye severity scoring according to DEWS classification (2007) in patients who underwent radiotherapy for head and neck cancers. They were assessed immediately post radiotherapy, 3 months, 6 months and 12 months post radiation therapy. The second objective is to evaluate correlation between dose of radiation therapy and severity of dry eye syndrome. In the present study, mean

age of the participants was  $49.97 \pm 11.80$  years. 2% were between 21-30 years, 17% of the participants belonged to 31-40 years, 39% belonged to 41-50 years, 22% of the participants belonged to 51-60 years and 20% were between 61-70 years of age. Males constituted 65% of the study population and females constituted 35% of the study population. In the present study conducted among 100 subjects satisfying the criteria mentioned we had a diagnosis distribution of carcinoma Buccal mucosa 42%, carcinoma tongue 19%, carcinoma soft palate 6%. Carcinoma of lower lip 4% and carcinoma hypopharynx 4%. Carcinoma parotid (L) 3%, carcinoma parotid (R) 3% and carcinoma glottis 3% in the study population. Squamous cell carcinoma eyelid 2%, carcinoma oral cavity 2%, nasopharyngeal carcinoma 2%, malignant melanoma eyelid 2%, carcinoma upper lip 2% and alveolar carcinoma 2% of the study population. Carcinoma of vocal cord 1%, oropharyngeal carcinoma 1%, carcinoma metastatic neuroblastoma 1% and carcinoma of larynx constitute 1% of the study population.

**Table 5:** Diagnosis Distribution

Diagnosis	Frequency	Percentage
CA Alveolus	2	2.00%
CA Buccal Mucosa	42	42.00%
CA Glottis	3	3.00%
CA Hypopharynx	4	4.00%
CA Larynx	1	1.00%
CA Lower Lip	4	4.00%
CA Malig Melanoma-Upper Eyelid	2	2.00%
CA Metastatic Neuroblastoma	1	1.00%
CA Nasopharynx	2	2.00%
CA Oral Cavity	2	2.00%
CA Oropharynx	1	1.00%
CA Parotid(J)	3	3.00%
CA Parotid(J)	3	3.00%
CA Soft Palate	1	1.00%
CA Tongue	19	19.00%
CA Upper Lip	2	2.00%
CA Vocal Cord	1	1.00%
Squamous Cell CA of Eyelid	2	2.00%
Total	100	100.00%





**Fig 2:** Diagnosis distribution

In the study population TBUT, Schirmer-I, Schirmer-II, DESS by DEWS 2007 and OSDI scoring were found to 100% normal.

**Table 6:** Pre-Radiotherapy

	Frequency	Percentage
TBUT	Normal 100	100%
	Abnormal (<10 sec) 0	0%
SCHIRMER-I Test	Normal 100	100%
	Abnormal (<10 mm) 0	0%
SCHIRMER-II Test	Normal 100	100%
	Abnormal (<10 mm) 0	0%
DES by DEWS 2007	Normal 100	100%
OSDI Scoring	Normal 100	100%

In the study population immediate post radiotherapy, 21% of the subjects had normal TBUT, Schirmer’s-I & II, DESS by DEWS 2007 classification and OSDI questionnaire scoring. 79% of them had abnormal TBUT, Schirmer’s -I &II. According to DESS by DEWS 2007 classification 38% of them had Grade-I DES, 32% had Grade-II DES and 9% had Grade-III DES. According to OSDI questionnaire scoring 23% were normal, 36% had mild dry eye, 31% had moderate dry eye and 10% had severe dry eye

**Table 7:** Immediate Post radiotherapy

	Frequency	Percentage
TBUT	Normal 21	21%
	Abnormal (<10 sec) 79	79%
SCHIRMER-I Test	Normal 21	21%
	Abnormal (<10 mm) 79	79%
SCHIRMER-II Test	Normal 21	21%
	Abnormal (<10 mm) 79	79%
DES by DEWS 2007 classification	Normal 21	21%
	Grade-I 38	38%
	Grade-II 32	32%
	Grade-III 9	9%
	Grade-IV 0	0%
OSDI questionnaire Scoring	Normal 23	23%
	Mild 36	36%
	Moderate 31	31%
	Severe 10	10%

3 months Post radiotherapy, 58% of the subjects had normal TBUT, Schirmer’s-I & II, DESS by DEWS 2007 classification and OSDI questionnaire scoring. 42% of them had abnormal TBUT, Schirmer’s -I &II. According to DESS by DEWS 2007 classification 22% of them had Grade-I

DES, 12% had Grade-II DES and 8% had Grade-III DES. According to OSDI questionnaire scoring 56% were normal, 24% had mild dry eye, 13% had moderate dry eye and 7% had severe dry eye.

**Table 8:** 3 Months Post radiotherapy

	Frequency	Percentage
TBUT	Normal 58	58%
	Abnormal (<10 sec) 42	42%
SCHIRMER-I Test	Normal 58	58%
	Abnormal (<10 mm) 42	42%
SCHIRMER-II Test	Normal 58	58%
	Abnormal (<10 mm) 42	42%
DES by DEWS 2007 classification	Normal 58	58%
	Grade-I 22	22%
	Grade-II 12	12%
	Grade-III 8	8%
	Grade-IV 0	0%
OSDI questionnaire Scoring	Normal 56	56%
	Mild 24	24%
	Moderate 13	13%
	Severe 7	7%

6months Post radiotherapy, 69% of the subjects had normal TBUT, Schirmer’s-I & II, DESS by DEWS 2007 classification and OSDI questionnaire scoring. 31% of them had abnormal TBUT, Schirmer’s -I &II. According to DESS by DEWS 2007 classification 16% of them had Grade-I DES, 9% had Grade-II DES and 6% had Grade-III DES. According to OSDI questionnaire scoring 68% were normal, 17% had mild dry eye, 11% had moderate dry eye and 4% had severe dry eye.

**Table 9:** 6 Months Post radiotherapy

	Frequency	Percentage
TBUT	Normal 69	69%
	Abnormal (<10 sec) 31	31%
SCHIRMER-I Test	Normal 69	69%
	Abnormal (<10 mm) 31	31%
SCHIRMER-II Test	Normal 69	69%
	Abnormal (<10 mm) 31	31%
DES by DEWS 2007 classification	Normal 69	69%
	Grade-I 16	16%
	Grade-II 9	9%
	Grade-III 6	6%
OSDI questionnaire Scoring	Normal 68	68%
	Mild 17	17%
	Moderate 11	11%
	Severe 4	4%

12 months Post radiotherapy, 72% of the subjects had normal TBUT, Schirmer's-I & II, DESS by DEWS 2007 classification and OSDI questionnaire scoring. 28% of them had abnormal TBUT, Schirmer's -I & II. According to DESS by DEWS 2007 classification 14% of them had Grade-I DES, 9% had Grade-II DES and 5% had Grade-III DES. According to OSDI questionnaire scoring 74% were normal, 13% had mild dry eye, 9% had moderate dry eye and 4% had severe dry eye.

**table 10:** 12 months post radiation

	Frequency	Percentage
TBUT	Normal 72	72%
	Abnormal (<10 sec) 28	28%
SCHIRMER-I Test	Normal 72	72%
	Abnormal (<10 mm) 28	28%
SCHIRMER-II Test	Normal 72	72%
	Abnormal (<10 mm) 28	28%
DES by DEWS 2007 classification	Normal 72	72%
	Grade-I 14	14%
	Grade-II 9	9%
	Grade-III 5	5%
OSDI questionnaire Scoring	Normal 74	74%
	Mild 13	13%
	Moderate 9	9%
	Severe 4	4%

## Discussion

Dry eye syndrome also known as keratoconjunctivitis sicca (KCS) is a disorder of the tear film which occurs due to tear deficiency or excessive tear evaporation and is characterized by inflammation of the ocular surface and lacrimal glands having a prevalence rate of 5-34%. This leads to increase risk of infections, medications toxicity, contact lens intolerance, progressive ocular surface disease, scarring, cornea morbidity (keratinisation, corneal thinning, vascularisation), microbial and sterile corneal ulcer leading to perforation and finally severe visual loss [5]. In 2007, the International Dry Eye Workshop (DEWS) defined DES as ‘‘a disease of tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to ocular surface along with increased osmolarity of tear film and inflammation of the ocular surface [1].’’

Compared with conventional radiotherapy IMRT for head and neck cancers allows better conformity to the target tissue, sparing the surrounding ones. Technical and non-

technical factors have been known to influence radiation induced ocular complications such as blindness, retinopathy and optic neuropathy. The technical factors are fraction size, type of radiation, fractionation, duration of treatment and the radio sensitivity of the treated area including the age of patient. Variations in technical factors and the use of protective measures, to the eye is making it increasingly difficult to study the incidence and grade the severity of ocular morbidity. Other factors influencing the treatment affect IMRT are histological type of tumour, latent period, location of the tumour in association with adjacent structure, volume, age, co-morbidities and chemotherapy as an adjunct treatment, influence the effect of IMRT on ocular morbidity. In spite of all the above limits we have found a considerable effect of dry eye symptoms in the immediate period of radiotherapy. Which improved on medical management.

Ocular reaction to IMRT can be graded as those occurring in first three weeks as the early reactions and those occurring after 3months as late reactions. Early reactions are very mild and include hyperaemia, chemosis and conjunctivitis along with mild corneal edema. There can also be corneal keratitis which responds well to treatment or in cases with co-morbidities it can result in corneal ulcerations. Where as late reactions are more permanent in the form of corneal opacification with or without vascularisation advancing to corneal necrosis A study by Chen *et al* found that the use of IMRT was more effective in protecting visual loss compared to conventional radiotherapy however some studies have reported late ocular complications severe dry eye, lacrimal canalicular stenosis, radiation induced retinopathy and cataract, the latter complications can develop complications, which are more severe and cause high degree of ocular morbidity such as cataract, glaucoma, retinopathy and stricture related complications with lacrimal drainage. These complications arise within a few months to several years later depending upon total radiation dose, radiation field and fractionation. Lastly eyelid related complications have also been several years after therapy. Similar reports were reported by Lana *et al*, where in 76.5% of patients receiving radiation therapy experience acute ocular effect varying from mild to severe of morbidity. Acute radiation dermatitis as a complication has been reported. The incidence of which has considerably decreased by the use of IMRT. Parson's *et al* observed 100% incidence of dry eye for doses >57Gy. Whereas in our study we found According to DESS by DEWS 2007 classification 38% of them had Grade-I DES, 32% had Grade-II DES and 9% had Grade-III DES. According to OSDI questionnaire scoring 23% were normal, 36% had mild dry eye, 31% had moderate dry eye and 10% had severe dry eye. Similarly Liang *et al* reported a 30% incidence of dry eye for doses >40Gy. Bessel *et al* noted incidence of dry eye increased as the dose of radiation increased.

The radiation effect on conjunctival epithelium goblet cells, Lacrimal gland, corneal surface altering the quality and quantity of tear production impairs the dynamic stability of tear film resulting in the corneal morbidity. Karp *et al* demonstrated in their study histological damage to meibomian gland causing a complete loss of both the glands and ducts as a result of squamous metaplasia, predisposing the patient to develop dry eye complications. Bhandare *et al*. (2012) [1] described the development of posterior sub capsular cataract following radiotherapy as a result of damage to mitotically active cells in germination zone

resulting in cell death, compensatory mitosis due to which there is defective lens fibre migration to the posterior pole. The cataract formation occurs 2-3years after the radiation therapy, severity of cataract depending on total dose of radiation. Henk *et al.* (1993) have reported that lens tolerate a total dose of 5Gy.

Takeda *et al* have reported the development of retinal complications, in patients receiving a range between 54-75Gy.

Jayachander, Kamath *et al* in their study reported that the severity was proportional to the exposure dose and inversely proportional to the orbital margins and field of radiation. The above study is the only study which evaluated risk during the course of the radiation treatment. In their report exposure to 30-45Gy can cause appearance of DES in 4-5yrs. While >50Gy causes corneal opacification and vascularisation within 1 yr following completion of the treatment. They also showed an impairment in corneal stability causing chronic dry eye as a result of damage of conjunctiva and corneal epithelium. This study suggested good shielding measures to anterior segment structure like conjunctiva, cornea and lacrimal glands to minimize the DES.

It is very important to be aware and study all the problems of potential radiation induced complications to eye in terms of risk benefit ratio. In this study we have studied only complications such as severe dry eye, lacrimal canalicular stenosis, radiation induced retinopathy and cataract. However there are several other ocular clinical methods of evaluation of dry eye. The present study included 100 patients who underwent advanced radiotherapy for head and neck carcinoma who have given reported in literature by Ganathan *et al.*

The incidence of post radiation DES increases significantly and its latency decreases with an increase in the total dose, dose fraction applied to the lacrimal glands. This study with a duration of 2 years has its limitations because we have not taken into count the late complications.

12 months post radiotherapy by DEWS 2007 classification majority (72%) of the study population remained asymptomatic, 14patients had Grade-I DES, 9 patients had Grade- II DES and 5patients had Grade- III DES. According to OSDI questionnaire 74% were normal, 13% were mild DES, 9% were moderate DES and 4% were severe DES. It was concluded that the incidence of dry eye syndrome was significantly more common in patients immediately post radiotherapy which significantly decreased in subsequent follow-ups. It was also observed that the incidence of dry eye disease was found to be more in patients receiving more radiation (60-70G y) in the immediate post radiation period. Many of them were put on medical management of DES and they improved symptomatically in the subsequent follow-ups. In the observation it is seen that variations in the dose, method of radiation and the usage of protective shields and early medical management of DES play an important role in the prevention of ocular complications especially dry eye syndrome post radiation therapy.

### Summary

Radiotherapy is one of the causes of Dry Eye Syndrome. The mechanism of pathogenesis is due to damage to the Meibomian glands, decrease or absence of the tear film lipid layer due to evaporation, and damage to the acinar cells of the lacrimal glands. This prospective observational study was undertaken from Jan 2021-June 2022 in Radiation

oncology and Ophthalmology Department of VIMS and RC, Bangalore in 100 patients who were undergoing advanced radiation therapy for head and neck carcinoma with a regular follow-up at 3, 6 and 12<sup>th</sup> month. The incidence of DES is proportional to the total dose of radiotherapy and increased steeply at doses > 40 Gy. It results in the cytostatic effects of radiation on the meibomian glands with reduction or absence of the lipid layer of the tear film and its evaporation. It damages the acinar cells of the lacrimal glands and causes stratification of conjunctival epithelium [19, 4].

The objectives of the study are- to assess the presence and severity of dry eye symptoms according to Ocular Surface Disorder Index (OSDI) questionnaire and Dry eye severity grading scheme by DEWS 2007 classification in patients who underwent radiotherapy for head and neck cancers and to evaluate correlation between dose of radiation therapy and severity of Dry Eye Syndrome by various clinical methods of evaluation of dry eye. The present study included 100 patients who underwent advanced radiotherapy for head and neck carcinoma who have given informed consent satisfying the inclusion and exclusion criteria following the methodology of thorough ocular examination. The data was statistically analyzed. In the present study, majority of the study population belong to 41-50 years. Among the study population 65% of the study population were males and 35% of the study population were females.

In the study population all the patients were asymptomatic in the initial of assessment. When assessed by DEWS 2007 classification immediately post radiotherapy majority (38%) had Grade-I DES, 21% of the study population remained asymptomatic, 32% had Grade-II DES and 9% had Grade-III DES. According to OSDI questionnaire 23% of subjects were normal, 36% were mild DES, 31% were moderate DES and 10% were severe DES.

3months post radiotherapy by DEWS 2007 classification majority (58%) of the study population remained asymptomatic, 22 patients had Grade-I DES, 12 patients had Grade-II DES and 8% had Grade- III DES. According to OSDI questionnaire 56% were normal, 24% were mild DES, 13% were moderate DES and 7% were severe DES.

6 months post radiotherapy by DEWS 2007 classification majority (69%) of the study population remained asymptomatic, 16 patients had Grade-I DES, 9patients had Grade- II DES and 6 patients had Grade- III DES. According to OSDI questionnaire 68% were normal, 17% were mild DES, 11% were moderate DES and 4% were severe DES.

12 months post radiotherapy by DEWS 2007 classification majority (72%) of the study population remained asymptomatic, 14patients had Grade-I DES, 9 patients had Grade- II DES and 5patientshad Grade- III DES.

According to OSDI questionnaire 74% were normal, 13% were mild DES, 9% were moderate DES and 4% were severe DES. It was concluded that the incidence of dry eye syndrome was significantly more common in patients immediately post radiotherapy which significantly decreased in subsequent follow-ups. It was also observed that the incidence of dry eye disease was found to be more in patients receiving more radiation (60-70G y) in the immediate post radiation period. Many of them were put on medical management of DES and they improved symptomatically in the subsequent follow-ups.

In the observation it is seen that variations in the dose,

method of radiation and the usage of protective shields and early medical management of DES play an important role in the prevention of ocular complications especially dry eye syndrome post radiation therapy.

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#### Author's Contribution

Not available.

#### Conflict of Interest

Not available.

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