

# A retrospective study to analyze acute & chronic side effects of radiotherapy in patients of head and neck cancer

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## Abstract-

**Background and purpose:** Use of Radiotherapy in head and neck cancer is widely accepted and it is becoming standard treatment for head and neck cancer. In addition to some advantages of radiotherapy, patients experience various side effects. The aim of the study was to analyze acute and chronic side effects of radiotherapy in cancer of head and neck. Learning of these side effects will help doctors to plan treatment for patients and may help better ways to treat cancer.

**Materials and method:** 1010 patients were studied retrospectively. Patients' data recorded between year 2006 and 2013 were evaluated. Study was presented before the members of ethics committee. Ethics committee members reviewed the study carefully. After valuable feedback and careful consideration the ethics committee cleared the study. Records were kept in the departmental patient registry and were retrieved from computer database. Sr no. name of patient, age, gender, type of cancer, type of radiation therapy given to the patient, dose of radiation, acute and chronic side effects seen after radiotherapy were recorded in CRF. From the collected data percentage of different side effects observed with different radiotherapy was calculated. Side effects with different radiotherapy took place in different weeks. Percentages of acute and chronic side effects were calculated on basis of week.

**Results:** Out of the 1010 patients included in the study, 93% were males and 7% were females. The mean age of patients was 55.9 years. Most number of patients had tumor in the buccal mucosa (n=200). Other locations where tumors were found were tongue, vocal cord, hypopharynx, base of tongue, nasopharynx, hard and soft palate, tonsils, parotid and maxilla. Four types of radiotherapy were given to patients namely 2D (8.9%), 3D CRT (10.8%), IGRT (39.6%) and IMRT (40.5%). The patients undergoing 2D therapy had more number of side effects, acute as well as chronic, as compared to patients undergoing the other therapies with the most common acute side effects being mucositis, skin darkening, loss of taste, pain and localized hair loss. In 2D and 3D therapies, most acute side effects appeared in the 4th week whereas in IGRT and IMRT, most acute side effects appeared in the 5th week. Regarding the chronic toxicities, the most commonly occurring were dryness of mouth, cough and subcutaneous fibrosis. Other toxicities occurring in a minority of the patients were hoarseness of voice, dental problems and ear problems. Again, these toxicities were more prominent in patients undergoing 2D therapy and 3D therapy. Very small

number of patients taking IGRT or IMRT were affected by any of these problems, ultimately proving that IGRT and IMRT are the safest options to opt for during radiotherapy for cancer, not only because of the lesser number of people suffering from the side effects but also because of the later onset of these effects.

**Conclusion:** The results of this study point to the fact that intensity of side effects of radiotherapy depend not only on the dosage of the therapy but also on the type of radiotherapy being given to the patients. Also, it can be seen that the onset of the side effects also depends on the type of radiotherapy. All the side effects were observed in all therapies with different onset of action and in varying proportions.

**Index Terms-** Head & Neck Cancer, IMRT, 3D-CRT, IGRT, Radiotherapy, Chemotherapy, Cancer.

## I. INTRODUCTION

Cancer is a disease of cells, the basic unit of our body. The term cancer is not used for a single disease but for group of disease. There is a close connection between cell cycle and cancer. Cell cycle is the process through which cells keep dividing into daughter cells and perform their function in orderly way and then they die. But sometimes if in cell cycle control mechanism if any problems take place number of unnecessary cells are produced by cell division cycle. Cell cycle is disrupted in cancer. Normally old cells die and new cells take their place. Cells divide and proliferate in regular fashion but in cancer, body's own cells become out of control and they proliferate and spread in abnormal way. It has been found that there is a decrease in sensitivity towards signals that balance proliferation, adherence and dying process. The proliferation increases in tremendous way as well, these cells do not die instead they produce cell mass called tumor. Cell tumors are of two types. First is benign tumor and another is malignant tumor. Benign tumors are generally harmless; they slowly grow at the site of origin and do not spread to the other part of the body. They grow more slowly compared to malignant tumor. Even benign tumors are not totally harmless. They are dangerous if they start originating near vital organ and push on the vital organ of the body like brain. Unlike benign tumor malignant tumors are not steady. They are cancerous and dangerous. They spread very rapidly to the other part of the body. Malignant tumors are responsible for the metastasis.

Similarly head and neck is a broad terminology which involves epithelial malignancies arising in pharynx, larynx, oral cavity, nasal cavity and paranasal sinus. Large numbers of head and neck cancers are squamous cell carcinoma in nature. More than 40,000 people in US develop head and neck cancer each year and approximately 14,000 people die because of head and neck cancer each year. Head and neck cancer involves various sites in body with aggressive biological behavior. 3% to 7% and 50% 75% new cancer develop in lungs or upper aero digestive tract due to progression of the head and neck tumor. Often the patients with head and neck cancer develop a second primary tumor. Regional lymph node involvement in advance stage H&N cancer patient is about two third. Initially distant metastasis is absent but it develops in about 10% of patients afterwards. Tobacco and alcohol drinking are the two main factors involved in developing head and neck cancer. Their contribution in development of this disease is thought to be 80%. Other than tobacco and alcohol, there is number of factors responsible for this cancer. Treatment modality in head and neck cancer is slightly complicated. Medical experts like medical oncologist, radiation oncologist, radiologist, head and neck surgeon and sometimes dentists and plastic surgeons are also needed for management of the treatment. Patient factors like swallowing, aspiration, organ involvement, concomitant illness and stage of tumor, spread of disease, tumor location are helpful to plan the treatment of head and neck cancer. Radiotherapy and surgery are the standard treatment for early stage cancer of H&N with cure rate achievement of 60-90%. For locoregionally advance disease and patients with metastases, traditional approach for treatment is radiotherapy after surgery and chemotherapy plus radiation. This has cure rate in 35-40% patients. [1]

## II. AIMS & OBJECTIVE

To analyze acute and chronic side effects of radiotherapy in cancer of head and neck & to compare and contrast acute and chronic side effects of different radiotherapy given in patients of head and neck cancer.

## III. Methodology

Data from Hospital's database were captured between 1<sup>st</sup> Jul 2014 to 1<sup>st</sup> Jan 2015 for period of six months.

The criteria for inclusion were as follows. 1) Patient should be 18 years or older 2) Patient should have head and neck cancer confirmed histologically 3) Patient should have undergone radiotherapy 4) Patients of both genders. There were no exclusion criteria because decision of radiotherapy was already taken by the clinician.

Demographic data collected were patient name, age and gender. Patients who received radiotherapy had different types of head and neck cancer like cancer of buccal mucosa, base of tongue, larynx, hypopharynx, vocal cord, pharynx, Supraglottis, nasopharynx, hard and soft palate, parotid gland and tonsils. Most of the patients were having squamous cell carcinoma of head and neck. Staging of cancer was done as per TNM classification. Patients with varying degree of cancer were included. External beam radiotherapy was given to all the

patients. Patients received different type of radiotherapy. 2D, 3D-CRT, IGRT and IMRT was given to the patients.

Conception stage involved defining the research question. In this study the research question was 'Is the side effects of different types of radiotherapy used in head and neck cancer patients same or different and when they occur during the treatment?' clinical scan of research question was done by discussing the research question with expertise in radio oncology field.

A literature search and review is a primary requirement for any work/study to start. Extensive literature search was carried out to find out technical, historical and economic background to the work. Articles were searched from various accessible sites and databases to obtain the data related to study's area of focus. Various sites like Science Direct, Cochrane database and various books were also used for literature review. In addition to original articles, some review articles, correspondence and editorials were also included.

Sample size selected for retrospective analysis was 1010 patient files. In retrospective review sampling means method by which cases/ records were selected from available database. There are three methods of collecting data in retrospective review: Convenience, quota and systematic sampling. In convenience method suitable cases are taken over a specified period of time.

In this study convenience method was used to collect the data. In patients having head and neck cancer and undergone radiotherapy were taken for the analysis. Patients' data recorded between years 2006 to 2013 were evaluated.

Before starting data collection, some useful documents were prepared like study synopsis, protocol outline and case report form to get clear understanding of the study. These documents were discussed with seniors to validate and approve them.

Protocol included information about the Title of the study, rationale behind the study, study type, methodology, study duration, study center, aim and objectives, main inclusion criteria and statistical test if applied any. Data were collected in CRF. Sr no. name of patient, age, gender, type of cancer, type of radiation therapy given to the patient, dose of radiation, acute and chronic side effects seen after radiotherapy were recorded in CRF.

Study was presented before the members of ethics committee. Ethics committee members reviewed the study carefully. After valuable feedback and careful consideration the ethics committee cleared the study. All the patients' data were kept confidential and were not shared with any third party without prior approval from the hospital

From the collected data percentage of different side effects observed with different radiotherapy was calculated. Side effects with different radiotherapy took place in different weeks. Percentages of acute and chronic side effects were calculated on basis of week.

#### IV. Results

##### PATIENT CHARACTERISTICS

Table 1 describes total 1010 patients' data were taken for evaluation. Out of these there were 940 (93%) males and 70 (7%) females. Average age was found to be 55.9 year (range 30-85 years).

[Table 1: Gender Distribution]

Gender	N	%	Total (n)
Male	940	93	1010
Female	70	7	

Table 2 summarizes no. of patients with different types of head and neck cancer. The largest group of patient data had tumor location in region of buccal mucosa (n = 200). Followed by tumors tongue (n = 150), base of tongue (n = 120), vocal cord (n = 100), hypopharynx (n = 70), nasopharynx (n = 70), hard palate and soft palate (n = 60), tonsil (n = 60), parotid (n = 50) and maxilla (n = 20). Other tumors location found were pharynx (n = 20), larynx (n = 10), lip (n = 10), and Supraglottis (n = 10), olfactory neuroblastoma (n = 10), floor of mouth (n = 10), vallecula with left neck node (n = 10) and MUO with secondaries in neck (n = 10).

[Table 2: primary tumor location and no. of patients]

Primary tumor location	Total (n)	%
Oral cavity Cancer		
• Tongue	150	14.8
• Buccal Mucosa	200	19.8
• Floor of Mouth	10	0.9
• Alveolus	10	0.9
• Lip	10	0.9
Oropharyngeal Cancer		
• Larynx	10	0.9
• Glottis	10	0.9
• Tonsils	60	5.9
• Vocal cord	100	9.9
• Base of tongue	120	11.8
• Soft palate	40	3.9
• Hard palate	10	0.9
• Soft+hard palate	10	0.9
• Pharynx	20	1.9
• hypopharynx	70	6.9
Nasopharynx	70	6.9
Salivary gland		
• parotid	50	4.9
Maxilla	20	1.9
MUO with secondaries in neck	10	0.9
Nasal cavity	10	0.9
Olfactory neuroblastoma	10	0.9
Vellicula with left neck node	10	0.9

##### TREATMENT CHARACTERISTICS

All the patients had been given radiotherapy. Four type of RT was given to patients of H&D cancer. The treatment being given was 2D, 3D CRT, IGRT and IMRT. 8.9% patients received 2D therapy (n = 90), 10.8% received 3D CRT (n = 110), 39.6% received IGRT (n = 400) and 40.5% received IMRT (n = 410). The mean dose to tumor was 64.5 Gy. Mean dose for 2D plan of the treatment to tumor was 64.1 gy, for 3D CRT it was 63.3 Gy, for IGRT it was 64.3 and in IMRT it was found to be 64.4 Gy. The range of treatment duration was 2-4 months.

Table 4 and 5 summarize the total number of patients affected with acute and chronic side effects during radiotherapy. Results from the data indicate those patients received 2D plans were highly affected with different acute and chronic side effects than with the 3D CRT, IGRT and IMRT planning.

[Table 3: Treatment characteristics]

Type of radiation	No. of patients	%	TOTAL (n)
2D	90	8.9	1010
3D CRT	110	10.8	
IGRT	400	39.6	
IMRT	410	40.5	

[Table 4: Total number of patients suffered from acute toxicities.]

Acute effect	Side	2D	3D CRT	IGRT	IMRT
Mucositis		90	110	400	390
Dysphagia		30	60	190	200
Skin darkening		90	110	400	190
Loss of taste		90	100	310	300
Decreased salivation		30	20	70	50
Localised hair loss		90	110	400	410
Pain		90	110	400	410

[Table 5: Total number of patients suffered from chronic toxicities]

Chronic effect	side	2D	3D CRT	IGRT	IMRT
Dryness of mouth		90	100	20	40
Cough		20	30	-	-
Hoarseness of voice		10	-	40	10
Subcutaneous fibrosis		40	30	10	20
Dental problems		10	10	-	10
Ear problems		-	-	10	-
hypothyroidism		-	-	-	10

**PROPORTION OF SIDE EFFECTS SEEN WITH DIFFERENT RT**

Table 6, 7, 8 and 9 shows week wise proportion of side effects seen with four different kinds of radiotherapy.

Table 6 indicates that with 2D treatment mucositis appeared in 3rd, 4th and 5th week of the therapy. Cases of mucositis were seen in 90 patient data (100%) with 2D therapy. In third week incidence of mucositis was 11.2%. It increased in 4th and 5th week which was found to be 44.4%. Dysphagia was seen in 30 patients (33.3%). Dysphagia was observed in 3rd week of the therapy. Incidence of skin darkening, loss of taste was 100% in 4th week. Pain was observed during 3rd and 4th week in 66.6 (n=60) and 33.3 % (n=30) patients respectively.

[Table 6: week wise proportion of side effect with 2D therapy.]

Radiot herapy	Side effect	week							
		1 <sup>st</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>	4 <sup>th</sup>	5 <sup>th</sup>	6 <sup>th</sup>	7 <sup>th</sup>	8 <sup>th</sup>
2D	Mucositis	-	-	11.2 %	44.4 %	44.4 %	-	-	-
	Dysphagia	-	-	33.3 %	-	-	-	-	-
	Skin Darkening	-	-	-	100 %	-	-	-	-
	Loss of taste	-	-	-	100 %	-	-	-	-
	Decreased salivation	-	-	-	33.3 %	-	-	-	-
	Localized Hair loss	-	-	-	-	100 %	-	-	-
	Pain	-	-	66.6 %	33.3 %	-	-	-	-

Table 7 indicates that with 3D CRT treatment mucositis appeared in 4th and 5th week of the therapy. Cases of mucositis were seen in 100 patient data (90.9%) with 3D CRT therapy. In fourth week incidence of mucositis was 72.7% (n = 80). It decreased in 5th week which was found to be 18.1% (n = 20). Dysphagia was seen in 60 patients (54.5%). Dysphagia was observed in 3rd week of the therapy. Incidence of skin darkening, loss of taste was 100% (n = 110) and 90% (n = 100) respectively in 4th week. Localized hair loss was also observed in all the patients in 5th week of the therapy. Pain was observed during 3rd and 4th week in 63.6 (n=70) and 36.3 % (n=40) patients respectively.

**Table 8** summarizes the incidence of side effects seen with IGRT therapy. Mucositis was seen in third, fourth and fifth week of the therapy. Overall incidence of mucositis was 100% (n = 400) with IGRT therapy also. In third, fourth and fifth week it was seen 2.5% (n = 10), 60% (n = 240) and 37.5% (n = 150) respectively. Occurrence of dysphagia was 47.5% (n = 190) in fourth week. Skin darkening, loss of taste and pain was observed in all the patients. Skin darkening was observed 95% (n = 380) in 5<sup>th</sup> week and 5% (n = 20) in 6<sup>th</sup> week. In the same week 77.5% (n = 310) experienced loss of taste and 10% (n = 40) experienced localized

hair loss during the treatment. Salivation was decreased in 17.5% (n = 70) of patient in 5<sup>th</sup> week. With IGRT 90% (n = 360). Pain was observed in 53.5% (n = 210) and 47.5% (n = 190) in 3<sup>rd</sup> and 4<sup>th</sup> week respectively.

[Table 7: week wise proportion of side effect with 3D CRT therapy]

Radiot herapy	Side effect	week							
		1 <sup>st</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>	4 <sup>th</sup>	5 <sup>th</sup>	6 <sup>th</sup>	7 <sup>th</sup>	8 <sup>th</sup>
3D C R T	Mucositis	-	-	-	72.7%	18.1%	-	-	-
	Dysphagia	-	-	54.5%	-	-	-	-	-
	Skin Darkening	-	-	-	100 %	-	-	-	-
	Loss of taste	-	-	-	90.0%	-	-	-	-
	Decreased salivation	-	-	-	18.1%	-	-	-	-
	Localized Hair loss	-	-	-	-	100 %	-	-	-
	Pain	-	-	63.6%	36.3%	-	-	-	-

[Table 8: week wise proportion of side effect with IGRT therapy]

Radiot herapy	Side effect	week							
		1 <sup>st</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>	4 <sup>th</sup>	5 <sup>th</sup>	6 <sup>th</sup>	7 <sup>th</sup>	8 <sup>th</sup>
I G R T	Mucositis	-	-	2.5 %	60%	37.5 %	-	-	-
	Dysphagia	-	-	-	47.5 %	-	-	-	-
	Skin Darkening	-	-	-	-	95%	5%	-	-
	Loss of taste	-	-	-	-	77.5 %	-	-	-
	Decreased salivation	-	-	-	-	17.5 %	-	-	-
	Localised Hair loss	-	-	-	-	10%	90 %	-	-
	Pain	-	-	52.5 %	47.5 %	-	-	-	-

**Table 9** summarizes the incidence of side effects seen with IMRT therapy. Mucositis was seen in third, fourth, fifth and 6<sup>th</sup> week of the therapy. Overall incidence of mucositis was 95% (n = 390) with IMRT therapy. In third, fourth, fifth and sixth week it was seen 17.07% (n = 70), 56.09% (n = 230) and 17.07% (n = 70) and 4.87% (n = 20) respectively. Occurrence of dysphagia was 48.78% (n = 200) in fourth week. Localised hair loss and pain was observed in all the patients. Skin darkening was observed 36.58% (n = 150) in 5<sup>th</sup> week and 9.75% (n = 40) in 6<sup>th</sup> week. Loss of taste was observed in 73.27% (n = 300) in 5<sup>th</sup> week. Incidence of decreased salivation was 12.19% (n = 50) in

5<sup>th</sup> week. Localised hair loss was observed in 7.31% (n = 30) and 92.68% (n = 380) of patients during 5<sup>th</sup> and 6<sup>th</sup> week. Pain was observed in 36.58% (n = 150) and 63.41% (n = 260) in 3<sup>rd</sup> and 4<sup>th</sup> week respectively.

[Table 9: week wise proportion of side effect with IMRT therapy]

Radiotherapy	Side effect	week							
		1 <sup>st</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>	4 <sup>th</sup>	5 <sup>th</sup>	6 <sup>th</sup>	7 <sup>th</sup>	8 <sup>th</sup>
IMRT	Mucositis	-	-	17.0 7%	56.0 9%	17.0 7%	4.87 %	-	-
	Dysphagia	-	-	-	48.7 8%	-	-	-	-
	Skin Darkening	-	-	-	-	36.5 8%	9.75 %	-	-
	Loss of taste	-	-	-	-	73.1 7%	-	-	-
	Decreased salivation	-	-	-	-	12.1 9%	-	-	-
	Localised Hair loss	-	-	-	-	7.31 %	92.6 8%	-	-
	Pain	-	-	36.5 8%	63.4 1%	-	-	-	-

Table 10 summarizes the overall incidence of chronic toxicities observed. With 2D and 3D CRT incidence of dry mouth was 100%. It was 5% and 9.75% with IGRT and IMRT respectively. 22.2% and 27% of patients had cough with 2D and 3D CRT respectively. 11.1%, 10% and 2.43% patients experienced hoarseness of voice. Ear problem was seen with 2.5% patient in IGRT. 11.1% patients in 2D and 2.43% patients in IMRT had dental problems. Incidence of subcutaneous fibrosis was observed with all therapy but in small proportion.

[Table 10: Proportion of chronic side effects]

Toxicity	Therapy			
	2D	3D CRT	IGRT	IMRT
Dryness of mouth	100%	100%	5%	9.75%
Cough	22.2%	27%	-	-
Hoarseness of voice	11.1%	-	10%	2.43%
Subcutaneous fibrosis	44.4%	27%	2.5%	4.87%
Dental problems	11.1%	-	-	2.43%
Ear problems	-	-	2.5%	-
Hypothyroidism	-	-	-	0.9%

### Discussion

Radiation induced mucositis is one of the most common acute side effects. If we discuss about acute mucositis reaction in all types of RT it has been established that mucositis was seen in all

the patients (100%) with 2D, 3D CRT and IGRT. With IMRT (95%) incidence of mucositis was slightly less compared to all the other RT. It started in 4th week in case of 3D CRT and with remaining three RT it appeared in 3rd week after starting treatment. It confirms high incidence of mucositis after radiotherapy. Result of this study also supports one systematic review carried out to assess mucositis incidence in head and neck cancer patients. In that systematic review high incidence (100%) of mucositis has been observed. The overall incidence of mucositis was 98% in current study. Mean incidence of mucositis was found to be 80%, which is almost identical to present study, in one study carried out to evaluate the incidence and severity of mucositis after radiotherapy in head and neck cancer patient. Frequency of mucositis was higher in patients received altered fractionation affecting 100% patients. While with conventional radiotherapy incidence was found to be 90%. Result from these study and other published reports it reflects that mucositis is an unavoidable toxicity rather than preventable. Radiation causes death of basal keratinocytes. Death of the cells is thought to be due to mitotic arrest which may lead to loss of squamous epithelial cells (Sciubba and Berg 2006). Although not a part of this study recent investigation indicates that there is a statistical correlation between incidence of mucositis and weight loss and severity of mucositis and placement of feeding tube. Mucositis proves to be one of the causes of morbidity in head and neck cancer which greatly affect quality of life of the patient. [36, 41]

Another bothersome acute toxicity experienced by the patients in this retrospective study was dysphagia. Dysphagia could take place due to structural damage in pharyngeal and laryngeal muscles or muscles of base of tongue. Longitudinal and circular pharyngeal muscles, laryngeal adductor muscles of glottis and Supraglottis, suprahyoid muscle and muscle that pull backward the base of tongue may get damage due to radiation resulting in dysphagia (Eisbruch, Schwartz et al 2004). Number of patients showing dysphagia were nearly same in both IGRT and IMRT. The result obtained here is not supporting one literature in which most of the patient received IMRT experienced dysphagia during the second week of the treatment. Persistent dysphagia may lead to feeding tube dependence [26, 27]

Skin darkening is another side effect experienced by the patients undergoing radiation therapy. All the patients undergoing radiotherapy experienced skin darkening but the onset of the effect was different for different therapies. In 2D therapy and 3D CRT therapy, all patients showed this side effect in the 4th week. Onset was later in the IMRT and IGRT therapies as compared to the previous two therapies.

Loss of taste also occurred in a majority of patients in all therapies. Onset of the symptoms was different for different therapies. In 2D and 3D therapies, the symptoms were first seen in the 4th week whereas in IGRT and IMRT, they were seen first in the 5th week. All the patients in the 2D therapy group experienced loss of taste in the 4th week and 90% patients undergoing 3D CRT therapy showed this side-effect in the 4th week, suggesting that 3D CRT therapy is slightly safer as compared to 2D therapy. Only 77.5% of the patients in the IGRT group showed loss of taste in the 5th week whereas 73.17%

patients in the IMRT group showed this side effect in the 5th week, showing that IMRT is slightly safer than IGRT. Radiation therapy develops loss of taste by destroying cells of the taste receptors. [13, 19]

Decreased salivation was observed in very few patients in all therapies, onset of the effect being different for different therapies. The highest number of patients who experienced this side effect was present in the 2D therapy group. 33.3% patients of this group showed this side effect in the 4th week. In the 3D therapy group, only 18.1% patients showed decreased salivation during the 4th week, suggesting that for this side effect as well, 3D therapy is safer than 2D. 17.5% patients undergoing IGRT therapy were affected by this effect during the 5th week whereas only 12.19% patients in the IMRT group were symptomatic for decreased salivation showing that patients undergoing IMRT were the least affected by decreased salivation problems. [10, 36]

All patients undergoing any radiotherapy have suffered from localized hair loss. This is one of the major side effects of radiation therapy. For all therapies, this effect has been seen during the 5th week. All patients in the 2D and 3D therapy have shown localized hair loss during the 5th week whereas 10% and 7.31% patients in the IGRT and IMRT respectively, have shown hair loss during the 5th week. The other 90% in IGRT and 92.7% in IMRT experienced localized hair loss during the 6th week showing a later onset of this effect in the latter two therapies.

Pain was also experienced by all patients undergoing radiotherapy, some later than others. Onset of pain was either in the 3rd or 4th week for all patients in all therapies. 66% patients in the 2D therapy group experienced pain first during the 3rd week and the other 34% suffered during the 4th week. Similar results were seen in the 3D CRT group. 64% patients in the IGRT group suffered from pain in the 3rd week and the other 36% showed pain during the 4th week. 52.5% and 47.5% patients showed pain in the 3rd and 4th week respectively, whereas 63% and 37% patients showed pain in the 3rd and 4th week respectively, suggesting that IGRT and IMRT are safer than 2D and 3D with respect to pain as a side effect.

Dryness of mouth was seen in all the patients' data that were given 2D and 3D CRT. With IGRT it was observed 5% and with IMRT the result was 9.75% indicating that with IGRT and IMRT incidence of dryness of mouth was less. This finding is in line with the result obtained in one study in which only 14% patients experienced dryness of mouth after having been exposed to IMRT. In contrast dry mouth syndrome was reported in all the patients (100%) having nasopharyngeal, Oropharyngeal and laryngeal cancer. [35, 44]

Hypothyroidism may take place as a chronic side effect of radiotherapy due to altered function of thyroid gland. Irradiation to the larynx and neck region causes change in thyroid function. Past reports suggest that approximately 6 to 15% suffer from hypothyroidism after radiation therapy. While in this study it has been found that only 1% patient had hypothyroidism with cancer of larynx. In present investigation if we discuss about dental problems it was predominant with 2D therapy (11.1%). With

IMRT, only 2% patients experienced dental problems after radiation. Radiation induced dental problems are dental carries, periodontitis, soft tissue complications and even death of bone (osteonecrosis). The incidence of dental problems reported in other literature is in the range of 8.2 to 42% after radiotherapy. Subcutaneous fibrosis was observed in 8% patients in present evaluation with 44% incidence in 2D (conventional therapy) and 27% incidence in 3D CRT. Incidence of subcutaneous fibrosis was very less in IGRT (2.5%) and IMRT (4.8%), which do not support one literature showing 13% incidence of fibrosis with conventional radiotherapy. Hoarseness of voice was observed in high proportion with 2D therapy. It was less low with IMRT and IGRT. Another chronic effects Cough and Ear problems were also seen in fewer incidences. [9, 26, 31]

### Conclusion

The results of this study point to the fact that intensity of side effects of radiotherapy depend not only on the dosage of the therapy but also on the type of radiotherapy being given to the patients. Also, it can be seen that the onset of the side effects also depends on the type of radiotherapy. Mucositis is the unavoidable side effect of radiotherapy and occurs in all the patients undergoing any form of radiotherapy. Other acute toxic effects seen were dysphagia, skin darkening, loss of taste, localized hair loss, dryness of mouth and pain. Decreased salivation was a minor side effect also seen in all therapies. Though all these side effects were seen in all therapies, the onset of the effects and also the percentage of patients suffering was different and for almost all effects, IGRT and IMRT proved to be the better treatment options as almost all side-effects occurred relatively later than 2D and 3D therapy and the number of patients suffering was smaller as compared to 2D and 3D. The major chronic toxic effects seen were hypothyroidism, subcutaneous fibrosis and dental problems, which were all more prevalent in patients receiving 2D and 3D therapies, showing that these two therapies are less safe as compared to the more sophisticated IGRT and IMRT therapies.

### Limitation

In this study it was not possible to analyze degree of seriousness (measured in grade) of all side effects, but the relationship of RT and onset of acute toxicities and appearance of chronic toxicities were evaluated.

As this retrospective study was conducted in only one Centre, the result cannot be generalized.

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