IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 21, Issue 4 Ser.5 (April. 2022), PP 20-25
www.iosrjournals.org

Vision Saving Radiotherapy Plan in Sebaceous Gland Carcinoma of Eyelid: A Dosimetric Analysis

G.S. Gautam, V.B. Rathore , R.R.Jain, P. Kushwaha, V.Choudhary, V. K. Mishra, M.Beck and R.S.Singh
(Department of Radiotherapy, Pt.J.N.M.Medical College and Regional Cancer Centre, Raipur, India)

Abstract:
Background*: It is tedious job to protect eye and eye-lens in case of Sebaceous Gland Carcinoma (SGC) of eyelid tumour whether any technique of radiation delivery like IMRT, IGRT or Volumetric Modulated Arc (VMAT) is adopted. So, keeping this view on context the authors of this paper herewith suggest a new technique may be called as Quadrant Segmentation of target PTV (dividing PTV in four quadrants) for achieving the goal of making safe eye and eye- lens in this type of cases.*
Materials and Methods*: In the present study 10 patients aged 45 to 75 years with histopathologically confirmed SGC of eyelid were taken for radiation therapy. Prescribed dose to tumour was 60Gy and fractionation scheme chosen 2Gy daily for 5 fraction per week, up to 6 week (42 days). CT images of 1 mm least slice thickness was acquired with immobilized patient from 124 slice CT scan machine. Critical structure and tumour target was delineated. Planning Target Volume (PTV) is divided in 4 quadrants. VMAT plan was created and each quadrant target was optimized iteratively. Sharp dose fall was selected in optimization process to achieve safeness of eye-lens and other critical structure. Plan was calculated for radiation dose with 2.5mm minimum grid and results were obtained.*
Results and Discussion*: Dose Homogeneity in PTV target was around 1.09 to 1.18 and Dose Conformity Index was around 0.74 to 0.86. Considerable variation in mean dose of critical structure was found from patient to patient. Ipsi-lateral and contra-lateral eye-lens was restricted to mean dose 8Gy to 10Gy, Ipsi-lateral and Contra-lateral eye was restricted to mean dose 24Gy. The maximum dose for other critical structure such as optic nerve, optic chiasm, Pituitary gland and temporal lobe was found around 26Gy, 10Gy, 8Gy and 6Gy respectively.*
Conclusion: *In case of SGC whenever radiation therapy was chosen where critical organ safeness has same importance as that of radiation dose to target, VMAT techniques with segmented quadrant approach gives better results with low mean dose to eye and eye-lens which leads to minimal normal tissue complication in such type of cases.*
Key Words*: Sebaceous Gland Carcinoma;Basal cell carcinoma;Surgery;Chemotherapy;Radiation therapy.*

Date of Submission: 02-04-2022 Date of Acceptance: 15-04-2022

I. Introduction

Sebaceous Gland Carcinoma, an uncommon malignancy usually occurs in periocular zone. It accounts for 1-5.5% of malignancies of all eyelid malignancies and it is considered to be the third most common malignancy of the eyelid after basal cell and squamous cell carcinomas. It typically affects the elderly and is characterized by a high incidence of local, regional and distant metastasis. A delay in diagnosis, which can be largely attributed to the tumor's tendency to masquerade as more benign conditions, frequently leads to poor treatment with higher rates of morbidity and mortality. Loss of vision is very common in these settings.

Sebaceous gland consists of three main gland Meibomian gland, Zeis glands or caruncle-associated gland in eyelids [1]. These malignancies are multifocal in nature. Its pagetoid diffusion gives it a special position among malignancy of eyelid. Sebaceous gland is found in skin follicles of periocular skin, carunkle and eyebrow. Unlike basal cell carcinoma or squamous cell carcinoma there are 2-3 times more common in eyelids. Surgery, Chemotherapy and Radiotherapy all accompanied to treatment of SGC.

The eyelid consists of two segments, the epithelial or epidermis and the cutaneous or dermis. It is the thinnest skin in the body. In two ways, SGC is different from other periocular malignancies. Firstly, Sebaceous carcinoma tends to originate from multifocal sources, unlike the single origin of other tumors. Second, SGC appears to spread superficially in a pattern known as pagetoid spread [4,5], unlike the radial spread of basal cells and SCCs. An erroneous histological diagnosis of epithelial dysplasia or carcinoma in situ may result from this spread. Histopathological cells occur in irregular lobular masses with distinctive invasiveness.SGC has a tendency to invade the periocular region [6].

For two main factors, diagnosis of SGC is always difficult: (1) the external symptoms are very subtle in the early stages, resembling a benign lesion such as chalazion or persistent blepharoconjunctivitis and (2) the appearance of yellowish material within the tumor gives it similarity to SCC.Therefore, it is mandatory to include SGC in the differential diagnosis of most eyelid masses and recurrent, non-responding eyelid inflammatory conditions because of the high index of suspicion. A delay in SGC's clinical diagnosis can be primarily attributed to its ability to masquerade as more prevalent benign eyelid conditions. This often leads to delayed management with increased morbidity and mortality rates [7]. The actual reported mortality associated with sebaceous carcinoma is around 6% [4]. Sebaceous adenoma on the eyebrows and eyelids is prevalent. The SGC list includes: hyperplasia of the congenital sebaceous gland, which is common on the face or scalp and tuberous sclerosis in the areas of the nasolabial fold and cheek.

SGC are often treated with surgery, chemotherapy and radiation therapy depending upon the stage of the tumor at the time of presentation. For early-stage tumor surgery is important. Prior to surgery, it is important to examine the patient carefully for signs of pagetoid spread or multicentric origin by double eversion of the eyelids and any conjunctival modification such as telangiectasia, papillary adjustment or a mass. In such a case, in addition to surgical resection of the lid lesion, conjunctival punch biopsies should be taken [8]. From a local excision to orbital exenteration, surgery can be performed. Roughly 30% of SGCs recur after surgery [9,10]. Chemotherapy in epibulbar and pagetoid SGC extension, sparing exenteration, is a useful adjunct to surgery.

Old Conventional Radiotherapy Treatment Plan may lead to adverse side effects such as subsequent conjunctival keratinization leading to dry eye, lid atrophy, skin necrosis, lash loss, lid telangiectasia, ectropion, epiphora, keratopathy, cataract [11]. Compared to surgery, higher recurrence rates do not allow histological confirmation of tumor classification and eradication and eventually, recurrences after radiotherapy are difficult to treat surgically due to inadequate irradiated tissue healing. The majority of severe complications associated with radiation arise in lower lid tumors. The reported outcomes of SGC proton electron irradiation are not excellent [10,12]. There are variable outcomes in radiation therapy as a primary form of therapy in eyelid SGC [4,12,13]. Radiation is generally reserved for patients who are not candidates for surgical procedures due to advanced stage or illness, for palliation in widespread disease and for patients who decline advanced local disease exenteration. Wide-field irradiation has, in some cases, either healed the tumor or created sufficient shrinkage to enable the residual mass to be surgically removed. Surgery for SGC restricted to the lid and to restrict the use of radiation to diffuse tumors with orbital or bone involvement, has been suggested as a prejudice.

Radiation is widely used for treatment of cancer since the invention of x-ray and radioactivity [14]. With the advancement of time, many new radiotherapy techniques have been developed e.g., IMRT, IGRT and Rapid Arc for superior target coverage and improving the sparing of critical structure. The conventional plans were not able to dictate the accurate uniformity of dose distribution in target as well as were not able to protect the critical structures with more accuracy which leads the invention of Intensity Modulated radiotherapy (IMRT) [15]. But it was realized accuracy of treatment setup need to be more accurate which led the invention of IGRT technique. Later on, it was realized that speedy delivery of radiation is also a part of treatment setup, which made a path for invention of Rapid Arc technology, which has the better clinical and technical aspects for delivery of radiation [16].

II. Materialsand Methods

In a present study 10 histopathology confirmed patient with eyelid cancer were taken for External Beam Radiotherapy. The patient`s age ranged from 45 year to 75 year. Maximum tumor size ranged from 20 cc to 67cc. 10 patients were selected among them 7 patients had T3 tumor, 3 patients had T4 tumor. Prescribed dose for radiation therapy treatment were 60Gy. Fractionation scheme for this treatment was scheduled for 2Gyper fraction and 5 fractions per week. Patients were immobilized with 3-point thermoplastic mould on CT Couch in supine position to achieve positional accuracy. Patient position and marking was done with fiducial marker in thermoplastic mould on CT indexed couch using all in one (AOI) base plate. Computed Tomography (CT) images were taken 5cm above and 5cm below eye region using Brilliance Big-Bore CT simulator (Philips Medical System, USA). Slice thickness for CT images is chosen 1mm to delineate target and critical structure more accurately.

GTV was delineated based on physical examination and through CT Scan images. CTV was drawn taking 5mm margin from GTV, then CTV was cropped for bone and muscle and eye. It was expanded by 5 mm to make Planning Target Volume (PTV-Eyelid). Critical structure Eye, lens, optic nerve, optic chiasm pituitaryand temporal lobe were delineated. Figure 1 (A, B, C, D) shows the delineated target and critical structure. The PTV-Eyelid structure was segmented in four Quadrant in each slice. Figure 2 shows the contour of PTV Tumor in 4 quadrant slice by slice,upper inner, upper outer, lower inner and lower outer quadrant.Eye and Eye-Lens are lying more closely to PTV of upper outer and lower outer quadrant. Figure 3 shows the segmentation of target in the image.

Volumetric Arc Plan was generated for all 10 patients using Eclipse Planning System (Varian Medical System, Palo Alto CA USA). Two arcs of radiation field were placed with 120 leaves millennium multi leaf collimator (MLC). Collimator of radiation field is closely fitted to PTV Eyelid with additional margin of 5mm. Each arc field was selected with beam energy 6 MV X-ray and dose rate 600 Monitor Units per minute. To avoid exposure posterior part of eye 2 half arc field is arranged to cover interior region of eye. Figure 4 shows the beam arrangement and iso-center placement of radiation treatment field.

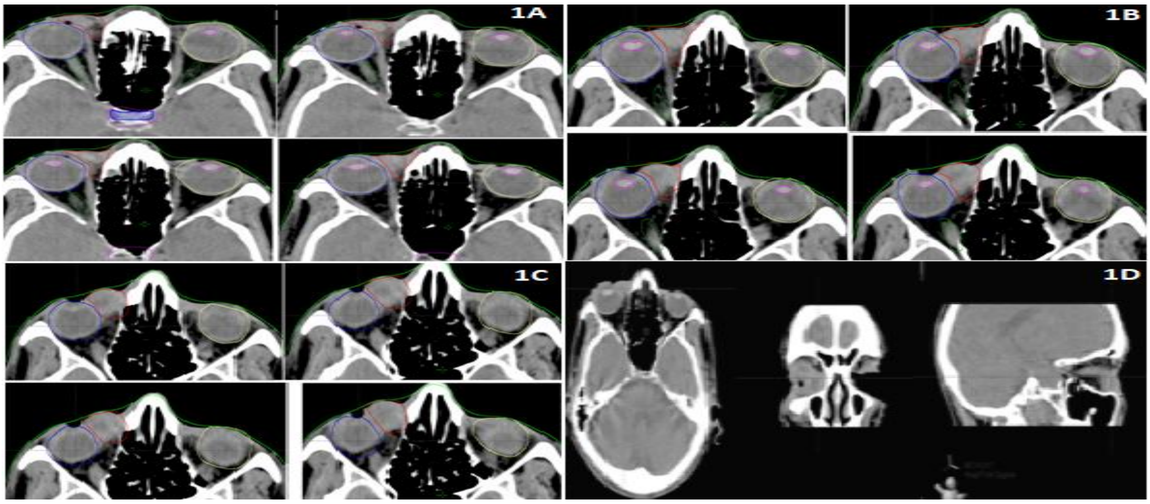

Figure-1 (A, B, C, D) showsthe delineate target and critical structure

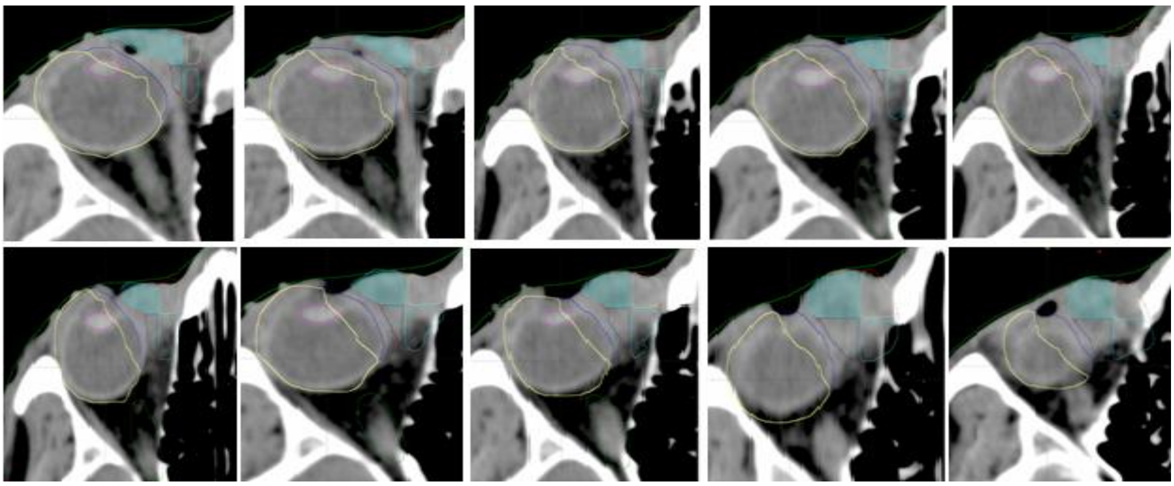

Figure-2 shows the contour of PTV Tumor in 4 quadrant slice by slice, upper inner, upper outer, lower inner and lower outer quadrant.

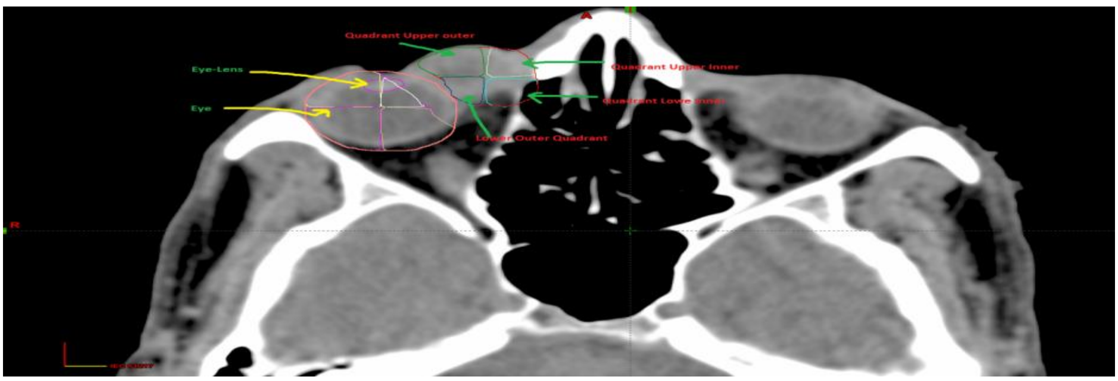

Figure-3shows the segmentation of target in image.

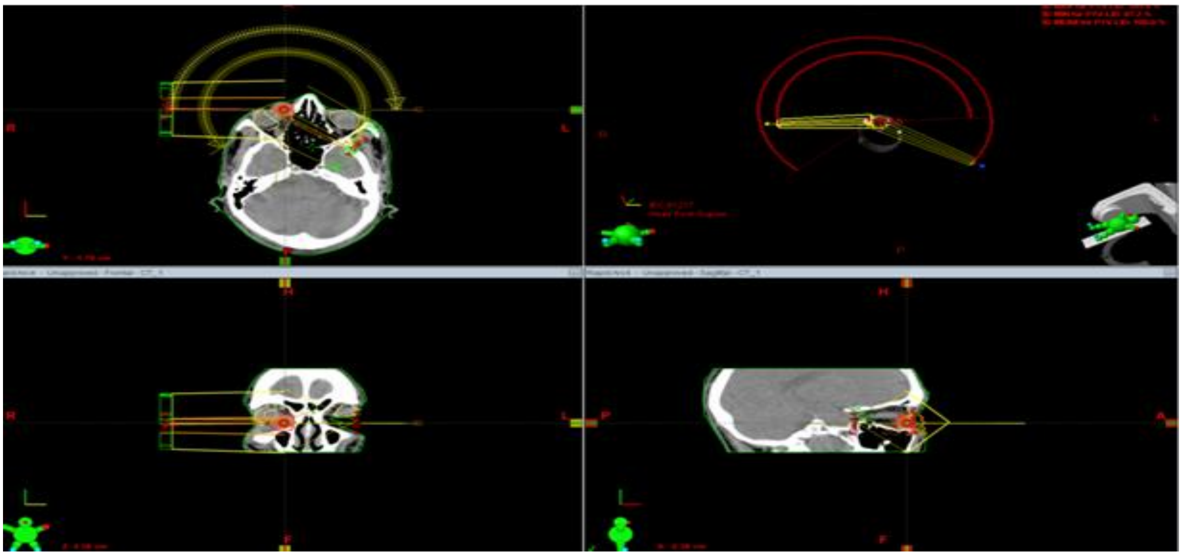

Figure-4Shows the beam arrangement and iso-Centre placement of radiation treatment field

Optimized Radiation Plan was generated with VMAT (Rapid Arc) technique. Sharp dose fall was selected in optimization process from PTV-Tumor (Eyelid) border. Optimization Process was performed through Progressive Resolution Optimization (PRO-3) from Multi Resolution (MR) Level 1 to Level 4 iteratively to achieve normal tissue objective as well as minimum 95 percent dose coverage to PTV-Eyelid. Optimized plan was calculated for volumetric dose using Anisotropic Analytical Algorithm (AAA). Least Grid Size 2.5 mm was chosen for volumetric dose calculation to achieve dose more accurately. Dose calculated plan was normalized to PTV-tumor (Eyelid) mean dose to cover entire volume of target. Dose to PTV-Eyelid and mean dose to critical structure was evaluated.

III. Results and Discussion

In SGC of eyelid, Eye and lens were lying very close to the tumor contour. The dose to this critical structure was main obstacle to decide for radiation therapy in such type of cases where safeness of eye and lens has same importance as to treat lethal (tumoricidal) dose to tumor. A new approach of Quadrant technique allows this type of cases to restrict mean dose below to limiting values and simultaneously deliver lethal (prescribed) dose to SGC tumor. Radiation plan was optimized iteratively to achieve the objective and we found that the tumor was fully covered with 95% of Prescribed dose. Figure 5 clearly shows with dose color wash coverage area of SGC Tumor.

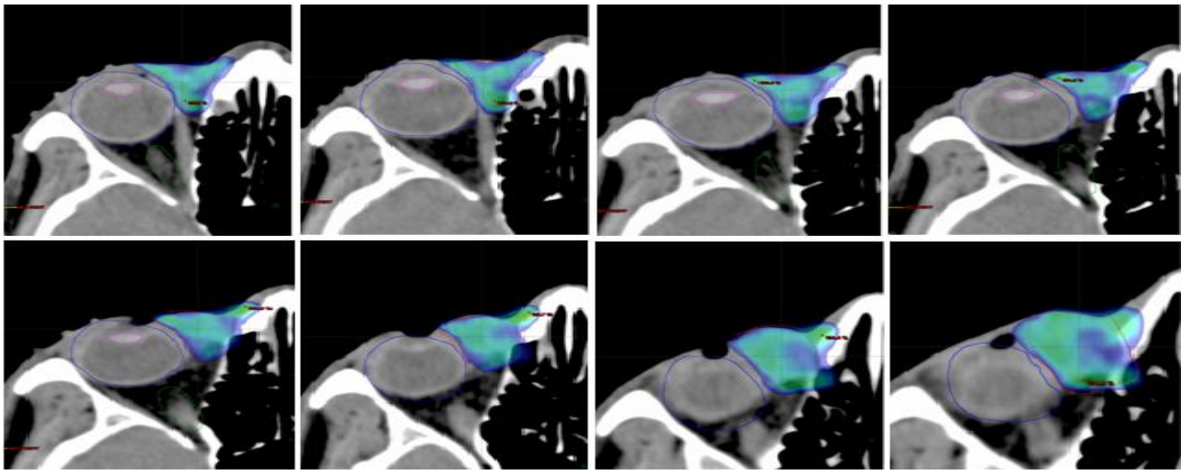

Figure-5 Shows with dose colour wash coverage area of SGC Tumour and sparing Eye-lens

Radiation Plan was evaluated for Dose Homogeneity and Dose Conformity in Tumour (PTV). Homogeneity Index (HI) and Conformity Index (CI) were calculated using RTOG guideline. Equation 1 shows the formula for evaluating the Homogeneity index (HI).

$$\mathrm{HI} = \frac{D_2 - D_{98}}{D_{50}} \qquad (1)$$

The conformity index (CI) was calculated using formula as shown in Equation 2.

$$\mathrm{CI} = \frac{(V_{95\%}\ \mathrm{DVH\ OF\ PTV})^2}{\mathrm{TV} * V_{95\%}\mathrm{isodose\ line}} \qquad (2)$$

Where - D_2- 2% dose cover to the target volume,
D_{98}- 98%doses cover to the target volume,
D_{50}–50%doses cover to the target volume,
$V_{95\%}$DVH of PTV - volume covered by 95% of DVH target volume
$V_{95\%}$ Isodose line - volume covered by 95% of isodose line.

The Dose Homogeneity Index was found from 1.09 to 1.18 in PTV volume (Tumour) and the Dose Conformity Index in PTV was achieved from 0.74 to 0.86. Case wise Evaluation of Dose Index with PTV Volume is tabulated in Table 1.

Table 1. Show Homogeneity Index and Conformity Index value.

S. No.	PTV Volume	Dose Conformity Index	Dose Homogeneity Index
1	48cc	0.76	1.09
2	50cc	0.82	1.16
3	53cc	0.74	1.14
4	55cc	0.66	1.17
5	57cc	0.83	1.13
6	59cc	0.78	1.18
7	60cc	0.85	1.15
8	61cc	0.75	1.16
9	63cc	0.86	1.19
10	67cc	0.74	1.11

In VMAT radiation planning rapid dose fall from the tumour target border was chosen and plan was iteratively optimized for result of mean dose to critical structure. Mean dose to ipsi-lateral eye restricted to 10Gy, while contra-lateral mean dose to eye was found below 8Gy. Mean dose to ipsi-lateral and contra-lateral eye-lens restricted to 2Gy to 7Gy which is great task in treating eyelid and sparing eye and lens in such cases. Optic nerve was comparable more tolerable radiation dose up to 54Gy however mean dose to both ipsi-lateral and contra-lateral optic nerve found 10Gy to 15Gy, which is too below acceptable value. Mean dose to all critical structure optic nerve, optic chiasm, pituitary gland and temporal lobe is tabulated in Table 2.

Table 2. Shows mean dose to critical structures

S.No.	Dose to OAR								
	Lens		Eye		Nerve		Optic Chaism	Pituitary	Temporal lobe
	(Dmean)		(Dmean)		(Dmax)		(Dmax)	(Dmean)	(Dmax)
	Ipsi-lateral	Contra-leteral	Ipsi-lateral	Contra-leteral	Ipsi-lateral	Contra-lateral			
1	8Gy	8Gy	30Gy	20Gy	28Gy	16Gy	12Gy	8Gy	5Gy
2	10Gy	9Gy	24Gy	15Gy	26Gy	14Gy	10Gy	9Gy	4Gy
3	8Gy	8Gy	26Gy	20Gy	27Gy	15Gy	11Gy	8Gy	3Gy
4	10Gy	9Gy	25Gy	18Gy	28Gy	14Gy	10Gy	8Gy	4Gy
5	9Gy	9Gy	24Gy	19Gy	25Gy	12Gy	10Gy	8Gy	4Gy
6	9Gy	9Gy	28Gy	22Gy	28Gy	13Gy	12Gy	7Gy	5Gy
7	10Gy	10Gy	29Gy	27Gy	26Gy	14Gy	11Gy	9Gy	4Gy

IV. Conclusion

SGC can be treated effectively with Radiotherapy but major task is to achieve safeness of eye and eye-lens while full eradication to PTV- Eye lid. Above task can be achieved better with Volumetric Modulated Arc Technique (VMAT), limiting dose to eye and eye lens without compromising dose to Eyelid tumour (PTV).

In the cases where the critical organs safeness has the same importance as that of the delivery lethal dose to target and the critical organ is very nearer to target then it is advocated here that in these types of cases the Rapid Arc treatment (VMAT) shows its superiority among all radiotherapy treatment.

Acknowledgement

We would like to thanks Dr Tripti Nagariya Dean Pt. J.N.M.Medical College, Raipur and Dr. Vishnu Dutt, Director Medical Education, Chhattisgarh for their continuous encouragement and support for the study. We are also thankful to all the staff of Department of Radiotherapy for their cooperation.

References

[1]. Joseph BW, A.K.,Sebaceous carcinoma: The great masquerader: Emgerging concepts in diagnosis and treatment. DermatolTher. 2008; 21: 459–66.
[2]. Ni C, KouPK,Meibomian gland carcinoma: A clinico-pathological study of 156 cases with long-period follow up of 100 cases. Jpn J Ophthalmol. 1979; 23: 388–401.
[3]. Rao NA,Hidayat AA, Mclean IW, Zimmerman LE. Sebaceous carcinomas of the ocular adnexa: A clinico-pathological study of 104 cases, with five year follow up data. Human Pathol. 1982; 13: 113–22.
[4]. Shields JA, Demirci H, Marr BP, Eagle RC, Jr Shields CL. Sebaceous carcinoma of the eyelids: Personal experience with 60 cases. Ophthalmology. 2004; 111: 2151–7.
[5]. Zurcher M, Hinstchich CR, Garner A, Bunce C, Collin JR, Sebaceous carcinoma of the eyelid: A clinicopathological study. Br J Ophthalmolo. 1998; 82:1049–55.
[6]. Shields JA, Demirci H, Marr BP, Eagle RC, Jr Shields CL, Sebaceous carcinoma of the ocular region: A review. SurvOphthalmol. 2005; 50: 103–22.
[7]. Cook BE, Bartley GB, Treatment options and future prospects for the management of eyelids malignancie. Opthalmolgy. 2001; 108: 2088–98.
[8]. Putterman AM,Conjunctival map biopsy to determine pagetoid spread. Am J Ophthalmol. 1986; 102: 87–90.
[9]. Ginsber J, Present status of Meibomian gland carcinoma. Arch Ophthalmol. 1965; 73: 271–7.
[10]. Epstein GA, Putterman AM, Sebaceous adenocarcinoma of the eyelid. Ophthalmic Surg. 1983; 14: 935–40.
[11]. Levitt SH, Bogardus CR, BrandtJr, JrEN, Complications and late changes following radiation therapy for carcinoma of the eyelid and canthi. Radiol. 1966; 87: 340–7.
[12]. Nunery WR, Welsh MG, McCord CD, Jr Recurrence of Sebaceous carcinoma of the eyelid after radiation therapy. Am J Ophthalmol. 1983; 96: 10–5.
[13]. Hendley RL, Reiser JC, Cavanagh HD, Primary radiation therapy for meibomian gland carcinoma. Am J Ophthalmol. 1979; 87: 206–9.
[14]. The physics of Radiation Therapy, F.M. Khan.
[15]. Practical Essential of Intensity Modulated Radiation Therapy K.S. Cliffor Chao, Smith Apisarnthanarax, GokhanOzyigit.
[16]. Otto K. Volumetric modulated Arc therapy, MedPhys. 2008.

G.S. Gautam, et. al. "Vision Saving Radiotherapy Plan in Sebaceous Gland Carcinoma of Eyelid: A Dosimetric Analysis." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(04), 2022, pp.20-25.