

# What is New in the Treatment of Eyelid Tumors with Radiation Therapy?

Kiran Turaka, Aruna Turaka\* and Bobby N Koneru

Paramount Oncology Group, Cedar Rapids, USA

\*Corresponding author: For inquiries, contact Dr. Aruna Turaka, M.D., Medical Director, Radiation Oncology, Paramount Oncology Group, Cedar Rapids, Albert G. and Helen Nassif Radiation Center, Unity Point Health – St. Luke's Hospital, 202 10<sup>th</sup> Street SE, Suite 195, Cedar Rapids, IA 52403, USA, Tel: 319-861-6944; Fax: 319-861-6945; E-mail: [arunaturaka@gopog.com](mailto:arunaturaka@gopog.com)

Received date: July 26, 2016; Accepted date: July 27, 2016; Published date: August 01, 2016

Copyright: © 2016 Turaka K, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Keywords:** Basal cell carcinoma; Eyelid tumors; Electronic brachytherapy; Radiotherapy; Squamous cell carcinoma

## Abbreviations:

Gy: Gray; RT: Radiotherapy; EBRT: External beam radiotherapy; ESB: Electronic surface brachytherapy; HDR: High dose rate; I: Iodine; Ir: Iridium; BCC: Basal cell carcinoma

## Editorial

Malignant tumors of the eyelids can cause considerable functional and aesthetic complications. Most common eyelid tumor is basal cell carcinoma (BCC) followed by squamous cell carcinoma, sebaceous gland carcinoma, Merkel cell carcinoma and malignant melanoma (rare) [1]. They can be located at lower eyelid (most common site) or upper eyelid, outer canthus and inner canthus. Surgical excision is the standard primary treatment option for the eyelid tumors. However, in cases with incompletely excised primary tumors, recurrent tumors, or inoperable large primary tumors and elderly patients who cannot tolerate general anesthesia with significant co-morbidities, radiation therapy (RT) is considered as an effective alternative/adjuvant treatment modality [2-7]. Different radiation therapeutic methods such as external beam radiotherapy (EBRT) with x-rays [superficial (45-100 Kv), orthovoltage (100-250 Kv)] or megavoltage photons & electrons and radionuclide plaque brachytherapy has been used to treat various eyelid tumors with good success [2-9]. However, acute and chronic radiation side-effects (skin reactions, eyelid telangiectasia, eyelid atrophy, eyelash loss (madarosis), epiphora (tearing), ocular surface disorders (dry eyes), cataract, radiation papillopathy, retinopathy & maculopathy and second malignant neoplasms) can lead to significant functional and visual disabilities. Recently new techniques to precisely deliver the radiation to the target tumor has been developed that prevent damage to the surrounding healthy tissues and cause minimal radiation toxicities. Currently, interstitial high-dose-rate (HDR) brachytherapy and electronic surface brachytherapy (ESB) are the new techniques being used to treat various non-melanoma skin malignancies including the eyelid carcinomas [10-15].

Contact X-ray radiotherapy (50 kV) was used in the past to treat the small (<2 cm) eyelid tumors. At a dose of 42 Gray (Gy)/7 fractions/ 4 weeks, there was excellent regression of the tumors with long-term tumor control in 98%. However, loss of eye lashes, punctal stenosis, skin depigmentation was noticed even at doses of 1 or 2 fractions of 6 Gy per week. Also local tumor relapse was seen in few cases around the irradiated area. The cosmetic results were good with x-ray RT [2]. Following orthovoltage radiotherapy of medial canthal BCC, 10-year tumor control rate was 94% with no recurrence rates. However, patients developed significant complications within the radiation field such as madarosis, epiphora, ocular surface disorders and conjunctival

scarring [3]. When eyelid tumors (1-4 cm size) were treated by electron beam therapy at a dose of 45-70 Gy in daily fractions of 2-4 Gy, though there was reasonable local tumor regression, few cases had recurrences (11%) and few had local radiation side effects such as skin atrophy and mild deformities [4].

EBRT can be considered another option for treating the eyelid tumors [5-7]. Primary eyelid tumors when treated with median radiation dose of 60 Gy in 30 fractions (range 50 to 66.6 Gy/ 22 to 37 fractions), the local-progression-free and disease-free-survival rate at 5 years was 93% and 80%, respectively. EBRT was considered effective more for the elderly patients with non-operable tumors who are poor surgical candidates. Few patients had acute radiation side effects with none having more than grade 3 reactions. Chronic radiation effects included cataract, corneal ulcer in some patients. There was local tumor recurrence after RT among those cases of BCC's located at the medial canthus. There was good tumor control with local irradiation (~50-60 Gy at 2-2.5 Gy per fraction), satisfactory functional and cosmetic results with preservation of the eyelids and prolonged survival more so among the elderly population [5-7].

To avoid wide excision, enucleation or exenterating of large eyelid tumors (malignant melanoma), plaque radiotherapy is used as an alternative therapeutic modality [8,9]. After careful shielding of cornea and the eye, Iodine (I)-125 plaque brachytherapy at a dose of 37 Gy (range 17.3-67.6) over 113 h (range 47-190) regressed the eyelid tumors in 90% with no local recurrence [8]. Large, ulcerative, nodular amelanotic eyelid melanoma when treated with I-125 plaque radiotherapy, regressed completely with no local recurrence [9]. Plaque radiotherapy controlled the local tumor growth, preserved the visual acuity, salvaged the globe thereby providing good functional and cosmetic outcomes. Specialized equipment is required to protect the eye from radiation with this technique. Plaque RT also caused marked ophthalmic complications such as cataract, radiation retinopathy and rubeosis iridis.

Interstitial HDR brachytherapy with Iridium (Ir)-192 is an alternative modality to treat small eyelid tumors, incompletely excised primary tumors, or recurrent tumors after prior RT [10-12]. Interstitial HDR brachytherapy using Ir-192 wires at a dose of 42.75 Gy (range 32-50) with 10 fractions (range 9-11) twice a day (6 h apart) controlled the local eyelid tumors by 94% and had good cosmetic effect in 70%. Local recurrence rate was less with this technique. It caused madarosis in 65% of cases only among those who received high prescribed volumes [10]. Another study utilizing interstitial HDR brachytherapy with Ir-192 wires (with linear activity of 1.2-1.7 mCi/cm) at a dose of 66 Gy (range 51-70) for the eyelid tumors resulted in local tumor control in 97% and provided good functional & cosmetic outcomes in 68%. Only 3% of patients had more than grade 2 radiation reactions [11]. The outcomes of interstitial brachytherapy are comparable to

surgical outcomes in the treatment of eyelid tumors especially the tarsal tumors and early stage cancers. Interstitial brachytherapy is a highly effective method to treat these tumors with minimal dose delivery to the surrounding healthy tissues. It provides good local tumor control with better functional & cosmetic results and less local radiation side-effects. It is useful in all types of histology without restriction of site of the eyelids (lower eyelid/medial canthus) and patient's general health status.

A novel non-invasive modality, ESB (low energy x-ray HDR, ~50 kV) is currently used to treat non-melanoma skin cancers [13-15]. ESB delivers high dose of radiation to the local tumor with rapid dose fall off to the surrounding healthy tissues. It does not require radioactive isotopes or megavoltage linear accelerator. Because it uses low kilo voltage energies, minimal shielding of the room or local tissues is required. So far, radium needles, iridium wires or sources made from caesium or iridium are being used either superficially, intracavitary or interstitially. When non-melanoma skin tumors were treated by ESB at a dose of 40 Gy in 8 fractions twice weekly (5 Gy per fraction at a depth of 3-7 mm), there was complete resolution of all the lesions with no local recurrence or acute toxicities at short-term follow-up [13,14]. Excellent cosmetic results (93%) were reported at 1-year follow-up after ESB. However, at long-term follow-up, local tumor recurrence and mild radiation adverse effects were noted among these lesions [15]. There is very limited data utilizing the electron brachytherapy for the eyelid tumors. So far in the published literature, there is only one case report of BCC of the eyelid treated by ESB. At 10 month of follow-up after this hypofractionated radiation, there was local recurrence of BCC and few periocular complications such as ectropion of lower eyelid [16]. Few authors used ESB to treat a small BCC of the upper eyelid (dose 40 Gy to 3 mm depth), which regressed the tumor completely with no recurrence at 3 year follow up. This technique excellently preserved the patient's cosmetic status [13,14]. Electronic brachytherapy using surface applicators is considered a good non-surgical treatment option to treat the non-melanoma skin tumors including the ones located on the eyelids. Future studies are required to report the safety, efficacy and long-term outcomes of ESB for treating the eyelid tumors.

Surgical extirpation is the first line therapy often with curative intent for the eyelid tumors. However, non-surgical, less invasive treatment modality is warranted in some cases. RT is safe and effective adjuvant or alternative treatment modality for the eyelid tumors. Local relapses and radiation toxicities may limit utility of traditional external beam or plaque brachytherapy. Advanced techniques such as interstitial HDR brachytherapy and ESB provide good local tumor control, cause fewer radiation toxicities and also prolong the survival, preserve the eyelid function and cosmesis.

## References

1. Asproudis I, Sotiropoulos G, Gartzios C, Raggos V, Papoudou-Bai A, et al. (2015) Tumors at the University Eye Clinic of Ioannina, Greece: A 30-year Retrospective Study. *Middle East Afr J Ophthalmol* 22: 230-232.
2. Buatois F, Coquard R, Pica A, Barbet N, Grange JD, et al. (1996) Treatment of eyelid carcinomas of 2 mm or less by contact radiotherapy. *J Fr Ophthalmol* 19: 405-409.
3. Krema H, Herrmann E, Albert-Green A, Payne D, Laperriere N, et al. (2013) Orthovoltage radiotherapy in the management of medial canthal basal cell carcinoma. *Br J Ophthalmol* 97: 730-734.
4. Sinesi C, McNeese MD, Peters LJ, Goepfert H, Kong J, et al. (1987) Electron beam therapy for eyelid carcinomas. *Head Neck Surg* 10: 31-37.
5. Schlienger P, Brunin F, Desjardins L, Laurent M, Haye C, et al. (1996) External radiotherapy for carcinoma of the eyelid: report of 850 cases treated. *Int J Radiat Oncol Biol Phys* 34: 277-287.
6. Hata M, Koike I, Maegawa J, Kaneko A, Odagiri K, et al. (2012) Radiation therapy for primary carcinoma of the eyelid: tumor control and visual function. *Strahlenther Onkol* 188: 1102-1107.
7. Inaba K, Ito Y, Suzuki S, Sekii S, Takahashi K, et al. (2013) Results of radical radiotherapy for squamous cell carcinoma of the eyelid. *J Radiat Res* 54: 1131-1137.
8. Stannard CE, Sealy GR, Hering ER, Pereira SB, Knowles R, et al. (2000) Malignant melanoma of the eyelid and palpebral conjunctiva treated with iodine-125 brachytherapy. *Ophthalmology* 107: 951-958.
9. Stanowsky A, Krey HF, Kopp J, Kanitz W, Wagner T (1990) Irradiation of malignant eyelid melanoma with iodine 125 plaque. *Am J Ophthalmol* 110: 44-48.
10. Mareco V, Bujor L, Abrunhosa-Branquinho AN, Ferreira MR, Ribeiro T, et al. (2015) Interstitial high-dose-rate brachytherapy in eyelid cancer. *Brachytherapy* 14: 554-564.
11. Krenkli M, Masini L, Comoli AM, Negri E, Deantonio L, et al. (2014) Interstitial brachytherapy for eyelid carcinoma. Outcome analysis in 60 patients. *Strahlenther Onkol* 190: 245-249.
12. Azad S, Choudhary V (2011) Treatment results of high dose rate interstitial brachytherapy in carcinoma of eye lid. *J Cancer Res Ther* 7: 157-161.
13. Bhatnagar A (2013) Nonmelanoma skin cancer treated with electronic brachytherapy: results at 1 year. *Brachytherapy* 12: 134-140.
14. Ouhib Z, Kasper M, Perez Calatayud J, Rodriguez S, Bhatnagar A, et al. (2015) Aspects of dosimetry and clinical practice of skin brachytherapy: The American Brachytherapy Society working group report. *Brachytherapy* 14: 840-858.
15. Cognetta AB, Howard BM, Heaton HP, Stoddard ER, Hong HG, et al. (2012) Superficial x-ray in the treatment of basal and squamous cell carcinomas: a viable option in select patients. *J Am Acad Dermatol* 67: 1235-1241.
16. Eftekhari K, Anderson RL, Suneja G, Bowen A, Oberg TJ, et al. (2015) Local Recurrence and Ocular Adnexal Complications Following Electronic Surface Brachytherapy for Basal Cell Carcinoma of the Lower Eyelid. *JAMA Dermatol* 151: 1002-1004.