



Dermatofibrosarcoma protuberans of the upper eyelid treated with surface mould high-dose-rate brachytherapy

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ABSTRACT

Dermatofibrosarcoma protuberans (DFSP) is a rare spindle cell tumor, comprising less than 0.1% of all malignant neoplasms. The trunk is the most commonly affected area, followed by the extremities and the head and neck. Of the latter cases, involvement of the periorbital area has been infrequently reported. Surgery is the cornerstone of treatment but is associated with a high rate of recurrence if margins remain close or positive. This rate has been shown to be considerably decreased by the use of adjuvant radiotherapy. However, most reported cases utilize external beam radiation therapy (EBRT) in the treatment of DFSP, including those with primary periorbital locations. We report a case of a 40-year-old male, presenting with a small nodule on the right upper eyelid, diagnosed as DFSP with positive margins post-surgery and treated with adjuvant customized surface mould high-dose-rate (HDR) brachytherapy in a low-resource setting.

Key words: brachytherapy; soft tissue sarcoma

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Introduction

Dermatofibrosarcoma protuberans (DFSP) accounts for less than 0.1% of all malignancies and only 1% of soft tissue sarcomas [1]. Its location in the periorbital region is even rarer. Head and neck involvement comprises 13% of cases, and periorbital tumors account for only 3.5% of these [2]. DFSP is known for its locally aggressive behavior but low metastatic potential [3]. Wide radical excision is the standard of care, and radiotherapy is indicated for positive margins, incomplete resection or, when used solely, for inoperable gross disease. In most cases, it is administered through external beam radiotherapy (EBRT). The National Comprehensive Cancer Network (NCCN) recommends doses of 50-66 Gy for positive margins, amounting to 25-33 daily fractions of EBRT [4]. We report a case

of periorbital DFSP treated with a cost-effective, five-fraction surface mould brachytherapy, while still attaining the recommended dose and producing acceptable outcomes. The following information is reported with the patient's consent.

Case presentation

A 40-year-old male presented last July 2017 with a small, painless nodule measuring around 1 cm in size over the right upper eyelid, initially managed with oral methylprednisolone. The lesion was unresponsive. Slow but progressive enlargement of the said nodule prompted another consult. In July 2018, cranial and orbital CT scan were done revealing a 1.8 × 1.8 × 1.0 cm (CC × W × AP) ovoid, well-defined, homogeneously enhancing nodule in the medial and inner aspect of the superior palpebra (Fig. 1).

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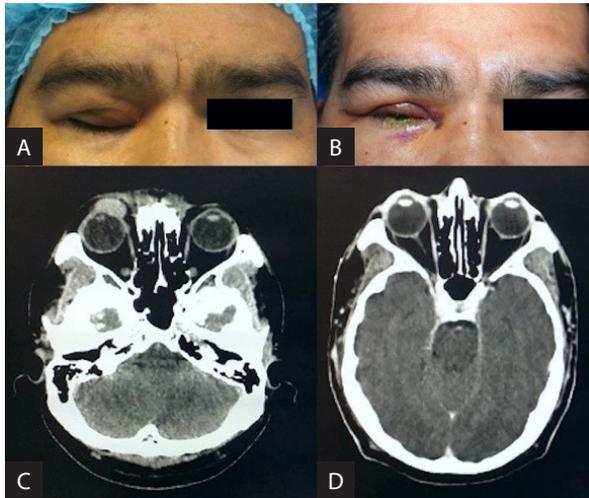


Figure 1. Pre-operative and post-operative images of the patient. **A.** Pre-operative image of the patient showing a $2.2 \times 1.6 \times 1.2$ cm nodule in the right upper lid with resultant mechanical ptosis. **B.** Post-operative image of the patient shows no gross apparent lesion in the right upper lid. **C.** Pre-operative CT of the head shows a $2.7 \times 1.2 \times 1.7$ cm enhancing nodule in the medial and inner aspect of the right superior palpebrae. **D.** Post-operative CT of the head shows no demonstrable lesion in the right orbit

On physical exam, there was a $2.2 \times 1.6 \times 1.2$ cm soft non-tender mass in the right upper lid. The primary consideration was a conjunctival cyst. The patient's baseline best-corrected visual acuity was 20/20 for both eyes, and extraocular muscle functions were likewise intact. He underwent excision of the nodule in January 2019. Histopathology showed a low-grade spindle cell lesion with positive margins of resection. Immunohistochemistry study with positive expression of CD34 confirmed the diagnosis of DFSP (Fig. 2). Given the positive tumor margin and inability to perform further ex-

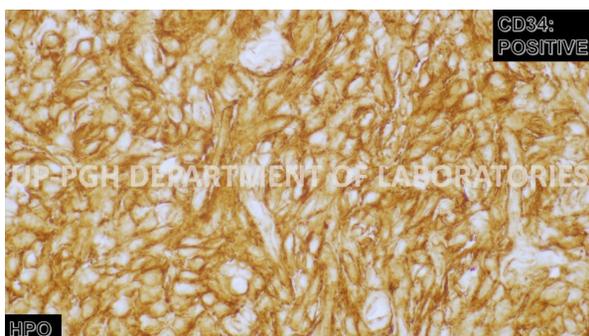


Figure 2. The tumor shows strong diffuse membranous staining in CD34. CD34 is a marker for dermatofibrosarcoma protuberans (DFSP)

cision without inducing significant cosmetic and functional deficits, the patient was referred to the Division of Radiation Oncology to explore options for adjuvant radiotherapy. His metastatic workup was negative. A multidisciplinary team decided to pursue brachytherapy. The patient was planned for surface mould high-dose-rate (HDR) brachytherapy in May 2019. The total prescribed dose was 35.3 Gy to the 90% isodose with an equivalent dose in 2 Gy (EQD2) of 65.51 Gy assuming an $\alpha/\beta = 45$, delivered in five fractions, one fraction per day, two fractions per week.

Treatment setup

A surface mould composed of a mixture of paraffin wax and mineral oil was prepared. The said mould is stiff at room temperature but becomes easily malleable when exposed to minimal heat and hardens once left to dry or cool.

The clinical target volume (CTV) was based upon the subjective evaluation of the patient by the radiation oncologist and the pre-operative imaging. Its borders were defined as follows: superiorly, at the skin just beneath the eyebrow; inferiorly, at the lower end of the upper eyelid; laterally, along the plane of the outer canthus; and medially, along the plane of the medial canthus including a region of fat stranding noted on pre-operative imaging (Fig. 3). The paraffin mould was then scaled to the CTV measurements. This was prepared before each fraction.

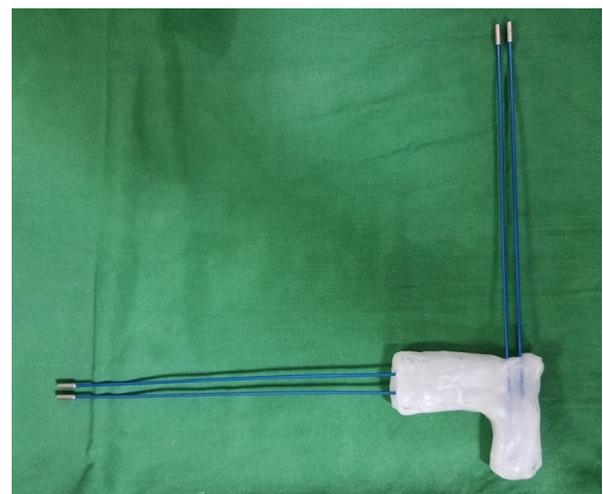


Figure 3. A surface mould composed of paraffin wax and mineral oil was scaled to the measurements of the clinical target volume. The orientation of the flexible catheters is also shown. This was the setup for the first fraction

Table 1. Techniques employed with each fraction of brachytherapy

Fraction	Techniques employed to increase the distance of the lid from the globe	Number and orientation of catheters
1 30 April 2019	Lid retractor to separate the upper lid from the globe	Two catheters horizontal Two catheters vertical
2 2 May 2019	Lid retractor to separate the upper lid from the globe	Two catheters horizontal Three catheters vertical
3 7 May 2019	Lid retractor to separate the upper lid from the globe	Two catheters horizontal Three catheters vertical
4 10 May 2019	Nine cotton buds placed in between the lid and the globe	Five catheters vertical
5 17 May 2019	Plastic internal eye shield with twelve cotton buds placed in between the lid and the globe	Six catheters vertical

The patient was placed in a supine position and topical anesthetic drops were placed in his right eye. A standardized treatment setup over five fractions was initially intended. However, because of a lack of an internal shielding device, it was difficult to meet dose constraints for the lens and eyeball. Dose distributions from previous fractions identified opportunities to improve the technique and optimize succeeding plans. Techniques included the use of readily available materials to improve dose distribution. The number and orientation of catheters were likewise modified. Table 1 shows the various techniques employed with each fraction.

During the first fraction, a lid retractor was applied in order to increase the distance between the eyelid and the globe. A 0.5 cm-thick paraffin mould was then heated using a blow dryer, and once pliable, it was moulded to the patient's upper lid which corresponded to the CTV. Four flexible HDR catheters of adequate length, spaced at 1 cm intervals were then fixed to the mould. Two of these were oriented vertically (on the medial side) while the other two, horizontally (on the lateral side). An additional 0.5-cm layer of paraffin was then applied to cover the catheters and to make the mould more stable. These techniques were later modified in the fourth and fifth fractions to further improve dose distribution.

Treatment planning

Simulation CT scan was performed using slice thickness of 1mm from the vertex to the maxilla. The previously defined CTV was delineated, as well as the eyeball and the lens. Dose points were subse-

quently created around the catheters and the dose was prescribed.

For each fraction, 90% of the CTV was planned to receive the prescribed dose. However, to make the treatment acceptable, compromise was made between target volume coverage and normal tissue sparing. The aim was to limit cumulative dose to the organs-at-risk (OARs) while still giving full therapeutic dose. This resulted in the adjustment of prescribed doses, as deemed appropriate by the radiation oncologist, depending on the dose distribution generated by the treatment setup at the time of fraction. Table 2 shows the prescribed doses to the CTV along with the doses received by the OARs. The total prescribed dose was 35.3 Gy to the 90% isodose with an EQD2 of 65.51 Gy4 delivered in five fractions, one fraction per day, two fractions

Table 2. Doses received by the clinical target volume (CTV) and organs at risk (eyeball and lens) for each fraction

Fraction	CTV $\alpha/\beta = 4$		Eyeball	Lens
	D90	EQD2	D0.2 cc	D0.2 cc
1 30 April 2019	5.8	9.47	5.8	3.2
2 2 May 2019	8	16.00	6.4	3.1
3 7 May 2019	7	12.83	5	2.9
4 10 May 2019	7	12.83	4.4	3.2
5 17 May 2019	7.5	14.38	4.2	2.6
Total	35.3	65.51	25.8	15

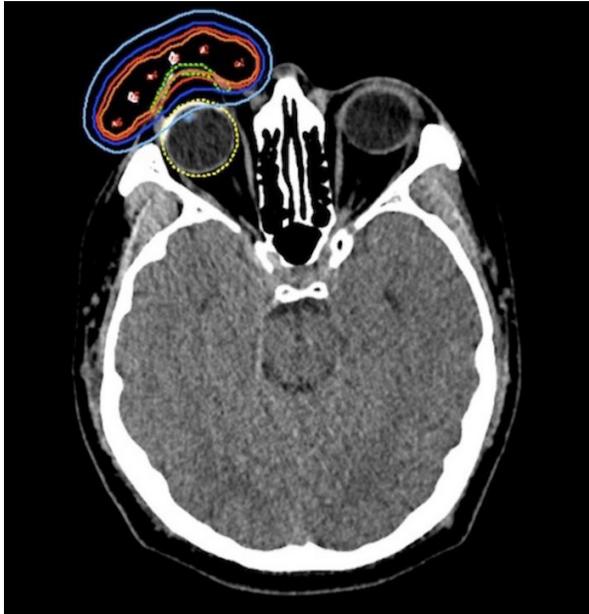


Figure 4. The clinical target volume (CTV) (green), eyeball (yellow) and lens (blue) in relation to the six flexible catheters, with corresponding isodose levels. Orange = 125%, red 100%, blue = 75%, cyan = 50%. This is the dose distribution of the fifth fraction

per week (Fig. 4). OAR dose limits were extrapolated from five-fraction stereotactic body radiation therapy constraints, as recommended by the American Brachytherapy Society (ABS) guidelines for sarcoma.^{6,7} A maximum threshold of 25 Gy was set. Treatment was delivered using Cobalt 60-HDR. The patient was then followed three weeks after completion of treatment, monthly for the first three months, and yearly thereafter.

Follow-up and toxicity assessment

Three weeks post-treatment, the patient developed Grade 3 radiation dermatitis to the upper eyelid demonstrated by skin thinning and wet desquamation, with accompanying hemorrhagic and serous crusting. He was prescribed a course of oral antibiotics together with daily saline wash and topical ointment. These resolved after two weeks. Epilation of the eyebrow with surrounding hypopigmentation was also observed. The patient's visual acuity on the right is 20/25 from a baseline of 20/20.

At 19 months, there remains no gross evidence of recurrence and no significant change in visual acuity. There is, however, persistence of hypopigmentation and epilation of the eyebrow (Fig. 5). Continuous monitoring is being done to assess long-term



Figure 5. Follow-up status. **A.** After 3 weeks (presence of grade 3 radiation dermatitis demonstrated by skin thinning and wet desquamation, with accompanying hemorrhagic and serous crusting, epilation of the eyebrow and hypopigmentation); **B.** After 19 months (hypopigmentation and epilation)

local control, manage toxicities, and evaluate cosmetic outcomes.

Discussion

The standard of care for DFSP is surgical excision with a complete histologic margin examination.⁴ As with other sarcomas, this requires a substantial margin which may generally be acceptable for tumors involving the trunk and extremities but may induce significant cosmetic and functional morbidities in tumors involving the head and neck. In cases where attaining adequate margins is not possible, conservative excision with adjuvant radiotherapy is acceptable.⁸

However, adjuvant radiotherapy for most of DFSP cases reported in literature is delivered through external beam radiotherapy (EBRT). The literature search showed nine prior case reports of DFSP involving the orbit [2, 9–16]. Of these, four underwent adjuvant radiotherapy, in the form of EBRT, following unresectable residual tumor or positive margin status. To the best of our knowledge, this is the first report of periorbital DFSP treated with adjuvant brachytherapy.

In the ABS guidelines for skin cancer published in 2020, involvement of the orbital region is among the contraindications of performing brachytherapy [17]. However, in the ABS guidelines for sarcoma, the use of surface mould brachytherapy is justifiable in the eyelid and periorbital regions where radical surgery is not possible [6]. The decision to use brachytherapy in this patient was influenced primarily by tumor location. The upper eyelid is

a curved region with thin cutaneous layers close to the eyeball. Performing EBRT comes with disadvantages. Use of high energy photons is unsuitable for treating superficial tumors as the maximum dosage level is attained beneath the skin surface, requiring the use of bolus material [18]. An appreciable exit dose may also be received by underlying structures including the lens, retina, and optic nerves, especially in the absence of internal shielding devices [19]. This may be avoided by the use of electrons, but a more generous margin should be allotted for beam constriction. The curvature of the eyelid may also significantly affect dose distribution. The use of surface moulds in brachytherapy is valuable in treating these curved and irregular surfaces.

Brachytherapy as a sole modality in this patient is appropriate given the rare involvement of regional lymph nodes in DFSP [20] Furthermore, it utilizes the principle of inverse square law allowing for better sparing of OARs. The small number of fractions is also more convenient for the patient and reduces inter-fraction positional error.

Our dose and fractionation are also in line with the current recommendations. The ABS guidelines recommend that when treating soft tissue sarcomas solely with high-dose-rate brachytherapy, the dose is 30–50 Gy in 4–7 days with a 2–4 Gy twice daily fractionation [6]. In our patient, a once daily fractionation was chosen because it was more technically feasible and convenient. The cumulative equivalent dose is also adequate for DFSP with microscopic residual disease post-surgery.

A limitation of our study is the short follow-up of 19 months. Although DFSP has a good overall prognosis of 99.1% at 10 years, morbidity is more often due to local recurrence. This ranges from 10–60%, and the risk is the highest in the first three years after treatment [21]. The positive margin status and tumor location in the head and neck also predispose our patient to a higher risk of recurrence. It remains to be observed if this patient will develop local recurrence with continued follow-up, but so far, treatment-related toxicities and cosmesis are acceptable.

Conclusion

Surface mould brachytherapy is a feasible option for properly selected tumors of the upper eyelid when radical surgery is not feasible.

Conflict of interest

None declared.

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