Recurrent Bowen's disease of scalp treated with high dose rate surface mold brachytherapy: a case report and review of the literature

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Abstract

Our case is a 46-year-old female presenting to us with Bowen's disease of scalp since 5 years. Patient had failed topical therapy with 5% 5-florouracil, 0.1% tacrolimus and was intolerant to topical imiquimod. At presentation, she had 15 cm × 10 cm erythematous, hyperpigmented, crusted plaque with irregular border in the superior and lateral aspect of left side of scalp with extension in to forehead. Patient was treated with computed tomography based customized surface mold high dose rate brachytherapy with Iridium-192 to a dose of 35 Gy in 10 fractions (twice daily, 6 hours apart) over 5 days. Patient tolerated the treatment well and showed regression of the lesion with mild dermatitis at the end of treatment. Though dermatitis increased at 2 weeks, at 4 weeks post treatment there was near complete resolution of the lesion with adjacent alopecia. At 8 weeks after completion of the treatment, there was complete resolution of the lesion and patient was asymptomatic. Alopecia in the adjacent area has resolved and the skin pigmentation has begun. Patient is satisfied with both the disease control and the cosmetic outcome of the procedure. Our case report demonstrates successful application of surface mold high dose rate brachytherapy in the treatment of recurrent Bowen's disease of the scalp. Brachytherapy can play an important role in the management of recurrent malignant and premalignant diseases of the complex treatment sites like scalp and it's non-hesitant use should be encouraged in appropriately selected patients at the earliest.

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Purpose

Bowen's disease is synonymous with squamous cell carcinoma *in situ* and was originally described by James T. Bowen in 1912 [1]. It is a disease of old age (median age of presentation is 6th/7th decade of life) with slight female predilection [2,3]. The most common sites of affliction are head and neck (29-54%) and scalp (with a predilection towards male) is involved in around 20% of the cases [4].

Diagnosis is made clinically based on typical findings of an erythematous, ill-defined, hyperkeratotic plaque like lesion, and additional help of dermoscopy is often sought. A punch biopsy is done, if a confirmation is required in doubtful or recurrent/refractory cases [4]. The risk of progression to invasive squamous cell carcinoma has been reported to be 3-5% based on retrospective reviews, but it has been reported to be as high as 20% in some studies [5,6]. This mandates the treatment to be instituted as soon as possible after the diagnosis. No standard treatment exists and the treatment of Bowen's disease is widely variable [4]. The usual treatment approach is to use non-invasive topical therapies and reserve other treatments for recurrent/refractory cases. However, treatment options for recurrent/refractory lesion particularly large sized lesions and lesions at difficult sites like lower extremity or scalp are very limited. Surgical excision in these cases not only has poor wound healing rates [7], but also is cosmetically unacceptable. Radiation therapy has been used in these cases with excellent local control and cosmetic outcome [8-10]. Varying radiation treatment techniques has been used, but the reports of computed tomography (CT) based high dose rate (HDR) brachytherapy for the treatment of Bowen's disease of scalp is limited.

We report treatment of a large recurrent Bowen's disease of scalp refractory to topical therapy and not

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amenable to surgical excision with CT based customized HDR (remote after-loaded Iridium-192) surface mold brachytherapy.

Case report

A 46-year-old female presented with a non-healing, erythematous ulcer on the left side of her scalp for one year to the department of dermatology in our institute. She complained of purulent discharge from the lesion off and on, but there was no history of pain, itching or photosensitivity. No history of trauma to the local site, chronic sun exposure or any chemical exposure could be elicited. There was no history of any co-morbidities or immunosupression (history of recurrent infections, organ transplant etc.). At the time of presentation to dermatology department in 2008, a 1 cm × 1 cm erythematous lesion with erosion and purulent crust was noted on the antero-lateral aspect of the left scalp. No similar lesion or other lesion was noted in any other muco-cutaneous sites and systemic examination did not reveal any abnormality. Patient was started on fluticasone (steroid) and mupirocin (antibiotic) and the lesion resolved, but re-appeared after 3 months. At this time, she complained of itching, purulent discharge from the lesion and also burning sensation on sun exposure. Lesion size was 2.5 cm × 2.5 cm (erythematous with purulent crusting) and a skin biopsy was ordered at this point (June 2009). Skin biopsy (Fig. 1A-D) showed features consistent with diagnosis of Bowen's disease. She received topical 5% 5-florouracil (in August 2009) and had non-complete resolution of the lesion. Subsequently, the lesion progressed to a size of 5 cm × 5 cm and 0.1% topical tacrolimus was tried with minimal response. In view of recurrent nature, a repeat biopsy was done in January 2012, which again revealed same histology. She was started on 5% imiquimod, to which she developed dermatitis and could not tolerate it well. She also intermittently received steroids, antibiotics, sun protectants etc. throughout this course of treatment. In view of intolerance to therapy/non-responsiveness and progression of the lesion, she was referred to our department in July 2013.

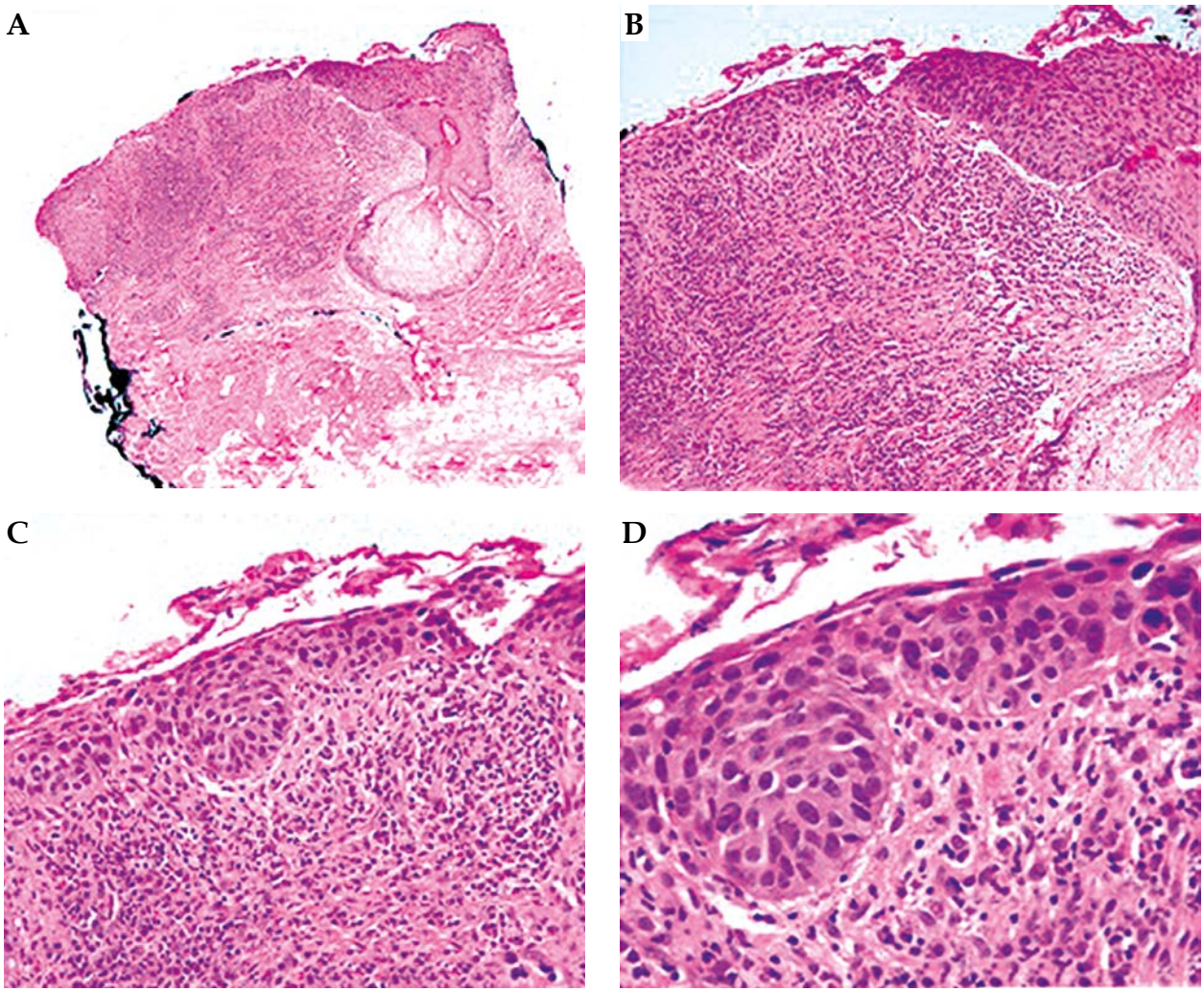

Fig. 1. A) The epidermis show irregular acanthosis with loss of normal maturation pattern (H&E ×4). B) Focally the epidermal abnormality also extending into the follicular infandibulam (H&E ×10). C) Marked cellular disarray in the epidermis with no evidence of invasion (H&E ×20). D) The neoplastic cells showing moderate degree of pleomorphism and high nucleo-cytoplasmic ratio. Frequent mitotic figures are seen (arrow) (H&E ×40)

She was evaluated jointly by a radiation oncologist and surgical oncologist. At presentation to us, she had complains of pain, itching, and purulent discharge from the lesion, with exacerbation of symptoms since the last 6 months. On examination, she had a 15 cm × 10 cm erythematous, hyperpigmented, crusted plaque in the superior and antero-lateral aspect of the left side of scalp with well defined irregular border and extension to forehead (Fig. 2A). No regional lymphadenopathy was noted and rest of the systemic examination was normal. Hematological parameters were normal and HIV (human immunodeficiency virus) was non-reactive. Contrast enhanced CT scan of head revealed no underlying bone erosion. Surgery was deferred in view of large lesion size, cosmetic and reconstructive issues, and patient's un-willingness. A decision was taken to treat the patient with radiotherapy after discussion with the patient and after an informed consent.

A customized thermoplastic immobilization cast of the head was made. Flexible plastic brachytherapy catheters (12 catheters at a distance of 1 cm from each other) inserted between layers of wax was pasted in close contact with the thermoplastic cast (Fig. 3A). Computed tomography scan (3 mm thickness) was acquired and a lead wire was also placed around the circumference of the lesion (before the assembled cast was applied) for proper delineation of the treatment area. The planning CT scan was transferred to Oncentra treatment planning system (Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden). Clinical target volume (CTV) was delineated based on the markers and clinical findings. Organs at risk including brain parenchyma, bones of skull, eyes, lens, optic nerves, optic chiasm, and brainstem was also delineated on serial CT slices (Fig. 3B). Catheters were reconstructed with axial and multi-planar views. Dwell positions were created with spacing of 5 mm and normalization was done using catheter points. Graphical optimization was done to ensure 95% coverage of the CTV (Fig. 3C). A dose of 35 Gy was prescribed in 10 fractions (2 fractions per day, 6 hours apart). Lesion coverage factor [11] was 0.951 (TV_{RI} [volume of target covered by the reference isodose line]/TV [target volume]). Target volume measured 33.59 cm^3. Brain parenchyma received a mean

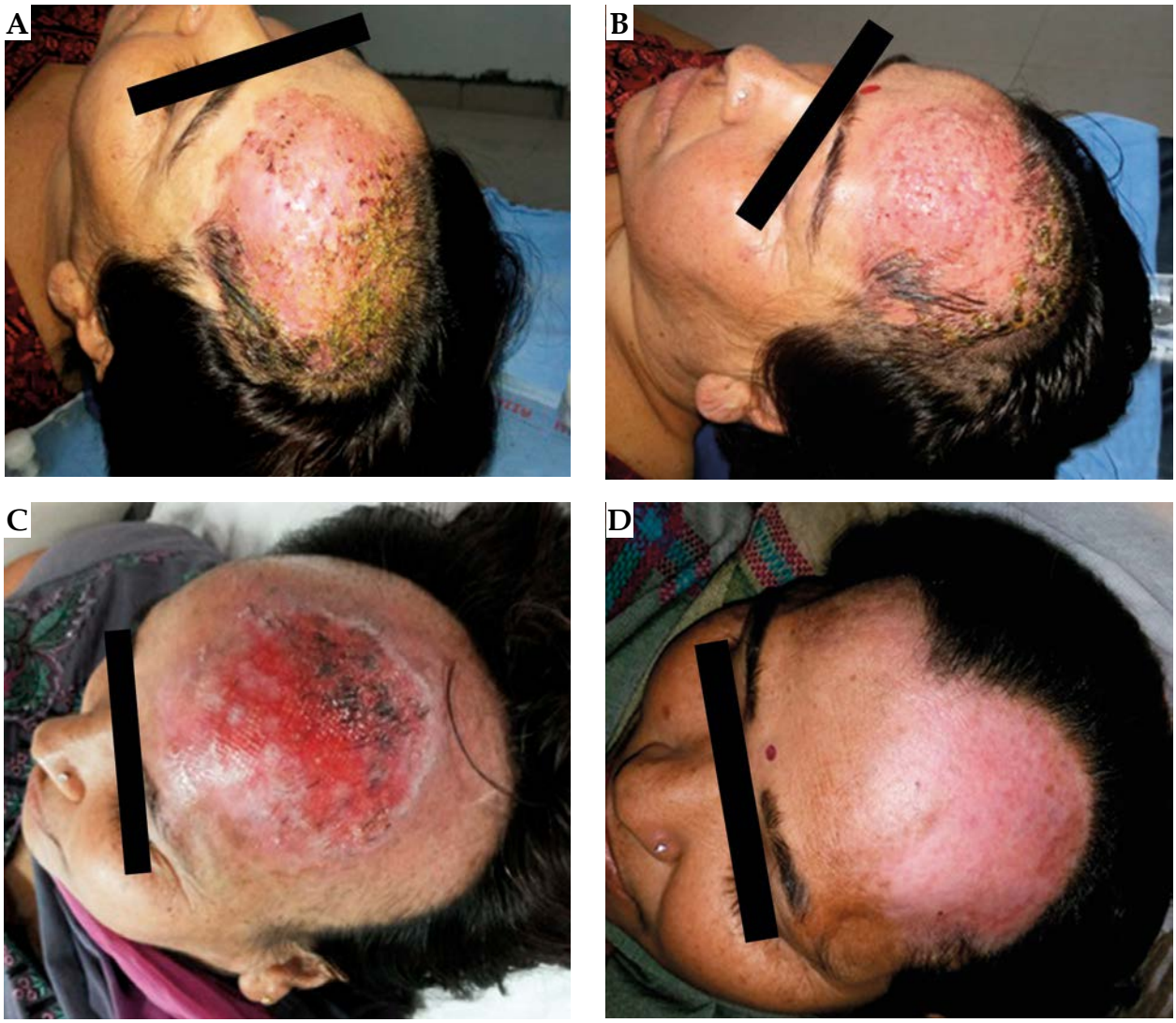

Fig. 2. A) Clinical picture of the patient before radiotherapy treatment. B) On the day of completion of treatment. C) Two weeks after completion of treatment. D) Eight weeks after completion of treatment

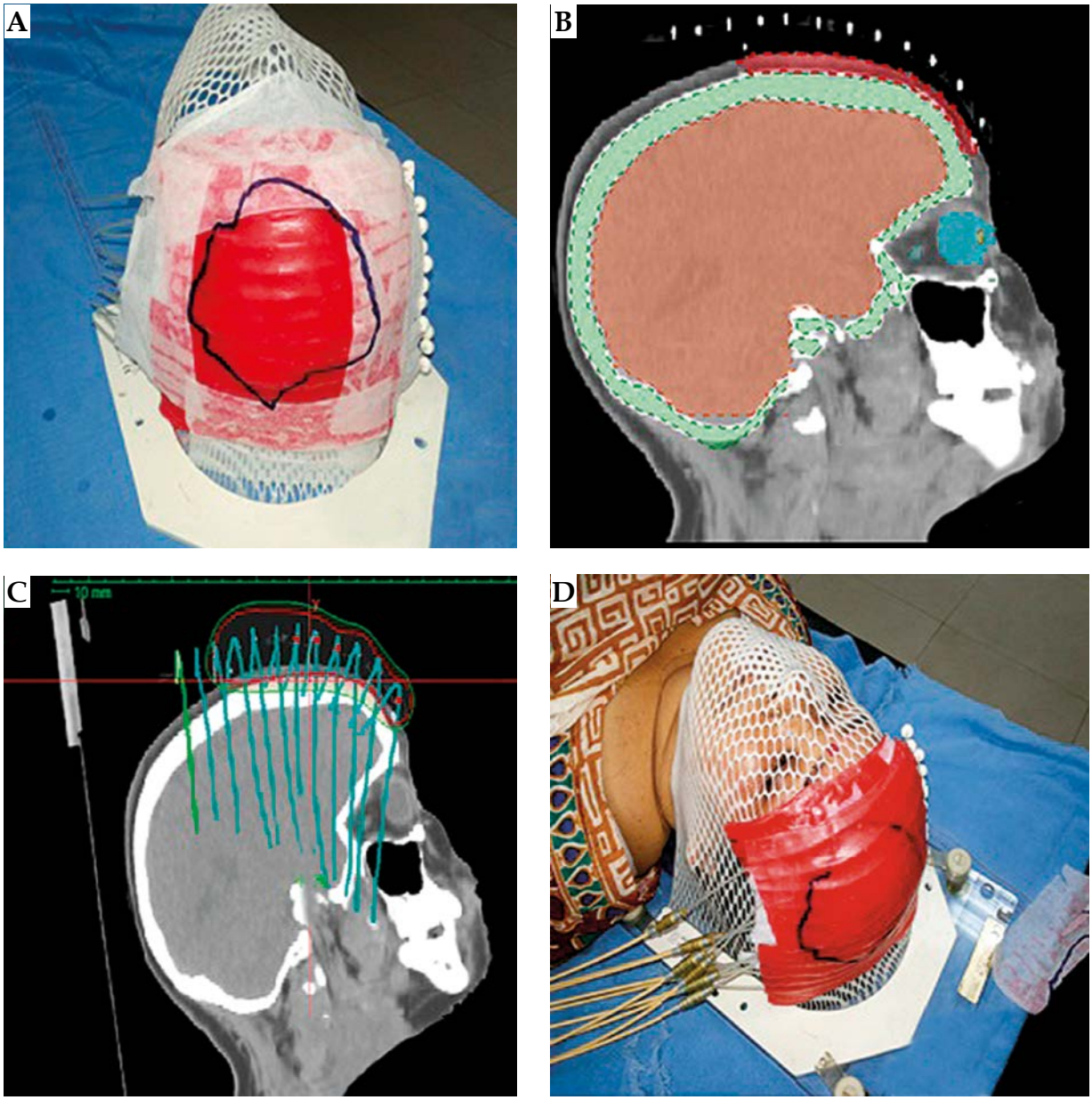

Fig. 3. A) Shows customized mold with plastic brachytherapy catheters *in situ*. B) Planning CT scan acquired with customized mold. Orange arrow shows the brachytherapy catheters with lead wire and green arrows show the lead wire around the lesion placed to delineate the treatment area. C) Isodose lines (green color shows 80% and red color shows 100% isodose lines) for the treatment. D) Shows patient being treated on remote after loading HDR brachytherapy unit

dose of 0.39 Gy/fraction and dose to whole brain was 0.07 Gy/fraction of treatment. Rest of the dosimetric data has been summarized in Table 1. Treatment was administered using an Iridium-192 source (Microselectron HDR, Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden) (Fig. 3D). Treatment time was 10 minutes per fraction including treatment set up time. Patient tolerated the treatment well without any interruption. Figure 2B shows the clinical picture at completion of the treatment. At 2 weeks after completion of the treatment (Fig. 2C), healthy granulation tissue with partial resolution of the lesion was appreciable along with alopecia in the adjacent area. Figure 2D shows complete resolution of the lesion at 8 weeks of treatment. Alopecia was resolved in the adjacent area and there is no evidence of radiation dermatitis or ulceration.

Patient is asymptomatic 14 months post treatment and reports cosmesis as excellent. However, in view of chances of late recurrences and secondary malignancy, she needs to be on long term follow up.

Discussion

The treatment of Bowen's disease ranges from observation, topical therapies, surgery to radiotherapy [4] based on a number of factors including lesion site, lesion size,

thickness of lesion, patient's age, and preference, availability of therapeutic modalities, and physician's choice of treatment. Of the local therapies, 5% Fluorouracil cream [12,13] and 5% Imiquimod [14,15] usually is sufficient in most of the patients. These topical therapies are not equally tolerated by all patients. Thirty-eight percent of patients in a study by Mackenzie-Wood *et al*. [16] discontinued 5% Imiquimod because of side effects of treatment.

Treatment of Bowen's disease of scalp, which is refractory to topical therapies is challenging. Surgical resections, particularly of large lesions are not only cosmetically unacceptable, but are also associated with increased wound complication rates [7]. Chemotherapy or other systemic therapies are usually not indicated for localized premalignant or malignant lesions of scalp. Radiation therapy remains an underutilized treatment option for this disease and is often called in to action when all other treatment options have failed or is not possible.

Radiation therapy for Bowen's disease is not new and is particularly suited for the patients with large, recurrent or multiple tumors at cosmetically sensitive body sites, and more so in patients who refuse surgery or are predisposed to keloids. Radiotherapy has its own advantages and limitations. All the body sites don't tolerate radiation well. Radiation therapy for lower extremity has been associated with poor wound healing. In a study by Dupree *et al*. [10,17], 25% of the patients had unhealed lesions after radiotherapy and all of them belonged to lower extremity. Scalp is a difficult site to be treated with radiation therapy owing to its irregular convex contour and its predisposition towards poor wound healing. These limitations are more so in case of lesion involving large areas of scalp.

Limited studies have explored the role of external beam radiotherapy for Bowen's disease of scalp. Twenty percent patients (9 patients) in the study by Lukas VanderSpek *et al*. [9] had lesions of scalp. Patients in this study were treated with orthovoltage X-rays. The median biologically effective dose used in this study was 49.3 Gy (range: 26.4-65.3 Gy). All patients had complete response except one. Radiation therapy has been used in doses ranging from 25-70 Gy with dose per fraction ranging from 2-5 Gy [8]. Dose per fraction more than 4 Gy [9] has been associated with impaired healing and a dose per fraction less than this should always be encouraged. We, in our study, used a dose of 35 Gy at 3.5 Gy per fraction and achieved an excellent outcome.

Treatment of superficial skin tumors with mold brachytherapy technique dates back to 1989 by Ashby *et al*. [18]. These authors treated 642 patients of non-melanoma skin malignancies using wax molds loaded with radon sources. Mold brachytherapy has been tried for sites like oral cavity [19] and mold based surface brachytherapy has been used for scalp irradiation for leukemic infiltrates of the scalp by Liebmann *et al*. [20]. Gauden *et al*. [21] reported their experience of 200 patients of non-melanoma skin cancers treated with HDR brachytherapy using a special applicator (Leipzig surface applicator), and reported an excellent local control rate (98%) and good to excellent cosmesis (88%) at a median follow up of 66 months (range 25-121 months). Tormo *et al*. [22] described results of 32 patients (with 45 non-melanoma skin cancers) treated with Valencia applicator with HDR brachytherapy and reported a 98% local control rate at a median follow up of 47 months.

Table 1. Doses values to the OARs

OARs	Dose (D_{max})
Left eye	36.84%
Left optic nerve	22.89%
Brainstem	16.82%
Right eye	18.89%
Right optic nerve	19.45%
Skull bone	90.78%

OARs – organ at risk, D_{max} – maximum point dose received by organ

Kowalik *et al*. [23] described CT based HDR surface mold brachytherapy technique for three unfavorably localized malignant lesion and have described in detail the process of manufacturing individual applicator. Similarly, we in our study used CT based plan optimization. Computed tomography based plan helps to more clearly visualize the coverage of intended treatment area and also evaluate irradiation of underlying critical structure.

The time points of evaluation of toxicities and cosmesis in HDR surface mold brachytherapy is also important. Study by Guix *et al*. [24] illustrates the temporal patterns of treatment complication and cosmesis. Skin erythema and varying degrees of skin ulceration is a rule rather than exception. Skin toxicities should be evaluated at longer time points of 6-12 weeks, as most of the reactions settle and cosmesis is best evaluated. In this study by Guix *et al*. [24], cosmesis was good or excellent in only 38% of patients at 2 weeks and was 98% at 3 months post completion of treatment. Also, no definite guidelines exist to grade reactions in surface mold brachytherapy. However, the definition used by Lukas VanderSpek *et al*. [9] seems to be reasonable to use. Grade 4 toxicity in this study was defined as necrosis (cartilage/bone damage) and/or ulceration for a duration of > 3 months. In our patient also, the reaction subsided only by 4 weeks of treatment and complete resolution was seen roughly 6 weeks after the completion of treatment.

Yet another innovative approach to treat areas of face (eyelids, nose, lips etc.) is the application of a specially designed radioactive skin patch coated with high energy beta-emitter holmium-166. Chung *et al*. [25] used this approach to treat Bowen's disease of face in eight patients (29 sites) with complete resolution in all patients at 1-5 months. The patches were topically applied for 30-60 minutes for a total radiation dose of 35 Gy. All patients developed desquamation, erythema or erosion after 1-2 weeks of treatment, but all at good functional and cosmetic outcomes later on.

In conclusion, based on the available evidence, radiation therapy is a highly effective therapy for Bowen's disease of the scalp. Customized CT based HDR surface mold brachytherapy with Iridium-192 is well tolerated,

highly reproducible, suited for accurate dose calculation and optimization, is associated with acceptable short term radiation morbidity, and an excellent outcome in terms of local control and cosmesis. It's non-hesitant use should be considered in all patients responding poorly to topical therapies, particularly for cosmetically sensitive areas of body like scalp.

Disclosure

Authors report no conflict of interest.

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