wjpmr, 2021,7(3), 11 – 17.

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Research Article

ISSN 2455-3301

WJPMR

POST-OPERATIVE HIGH DOSE RATE SURFACE BRACHYTHERAPY FOR SKIN CANCER WITH FLAP APPLICATOR

***M. Hommadi, H. Bakkali, O. Houessou, M. Benlemlih, T. Elmorjani, N. Bendahou, I. LAHDIRI, S. Boutayeb, S. El Mejjaoui, H. EL Kacemi, T. Kebdani and N. Benjaafar**

Department of Radiotherapy, The national institute of Oncology, Mohammed V University in Rabat, Morocco.

***Corresponding Author: M. Hommadi**
Department of Radiotherapy, The national institute of Oncology, Mohammed V University in Rabat, Morocco.
DOI: https://doi.org/10.17605/OSF.IO/GF5VT

Article Received on 24/12/2020 **Article Revised on 14/01/2021** **Article Accepted on 04/02/2021**

ABSTRACT

Purpose: Skin cancers are the most common human malignancy with increasing incidence. Currently, surgery is standard of care treatment for non-melanoma skin cancers. However, brachytherapy (BT) is a growing modality in the management of skin cancers. In this study, we aimed to assess the outcome of patients with non-melanoma skin cancers treated by high-dose-rate (HDR) brachytherapy with FLAP Freiburg applicator in our department. **Materials and methods:** In this retrospective study, we recruited patients with Non-melanoma skin cancer (NMSC) who underwent post-operative brachytherapy during 2016-2018. Skin brachytherapy using the FLAP Freiburg applicator was indicated in all our patients. They were treated with after- loading HDR brachytherapy machine, with a total dose of 20-40 Gy in 5-8 fractions. Patients were followed to evaluate radiation toxicity, and local failures. **Results:** A total of 8 patients (75% male; median age, 70 years) were included, all of them received adjuvant brachytherapy after surgery with close or positive margins for NMSC. Fifty percent of lesions were squamous cell carcinoma (SCC) and 37.5% were basal cell carcinoma (BCC). The mean total dose was 35.6 Gy. The average follow-up was 26,4 months (17 to 39 months), low acute dermal reactions were noted for all patients, one patient present grade 3 radiodermatitis, and one patient developed skin fibrosis. One case of locoregional relapse was noted and no patient developed distant metastases, all patients are alive, one patient was lost to follow-up after the end of brachytherapy. **Conclusion:** With appropriate patient selection and choosing as lowest dose per fraction as possible, HDR brachytherapy with FLAP Freiburg applicator yields good oncological and cosmetic results for the adjuvant treatment of localized NMSC.

KEYWORDS: Skin cancer, surface Brachytherapy, Flap applicator.

I-INTRODUCTION

The incidence of skin cancer has been rising over the past decades. World Health Organization (WHO) estimates that currently 2–3 million non-melanoma skin cancers (NMSC) occur only in the United States each year with one in every three cancers diagnosed being a skin cancer.[1] It is expected that NMSC may soon start to represent a major public health problem and pose a significant burden to any health care system.[2] The most common histology of NMSC is basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). The primary goals of any treatment of NMSC are to cure the lesion with preservation of function and to optimize cosmesis. Treatment options include surgery and radiation therapy, with surgical techniques such as Mohs micrographic surgery being the most frequently used.[3-4]

Various radiotherapy techniques have been developed to treat skin cancer: superficial and orthovoltage X-rays, electron and megavoltage photon treatment, and brachytherapy (BT) .BT is an appropriate and effective treatment option for selected skin cancers, mainly NMSC that are not better served by surgical removal or external beam radiotherapy (EBRT).

There are several advantages of BT when compared with EBRT that should be considered in the decision-making process: BT is usually delivered as a hypo fractionated course, three or two times a week, rather than daily, which translates into fewer treatment visits for the patient, particularly useful for elderly and frail patients. The dose is delivered in a short period of time. A rapid fall in dose beyond radioactive source makes it possible for increased tumor control while sparing the surrounding tissue and shorter overall treatment duration reduces risk of tumor cell repopulation.

Current skin applications in brachytherapy can be classified in two modalities: Superficial, also called contact brachytherapy and interstitial BT with the insertion of plastic tubes or rigid needles. Superficial modalities involve moulds and flaps for larger lesions,

and radionuclide based shielded applicators and electronic based shielded applicators for small volume lesions. Interstitial BT is applied to deeper located and/or very irregular tumors.

Indications for BT are: radical (mono) BT of T1-2N0 tumors (primary lesions, recurrences after surgery and/or radiotherapy); adjuvant therapy after non-radical surgery; as a boost after EBRT for (T2–T3) cases or for palliative treatment for locally advanced skin tumors.[5]

contraindications for brachytherapy are: Malignant melanoma of the skin which is not radiosensitive, skin cancers invading bony structures; upper eyelid lesions, tumor involving ear conduct or any other site where the anatomical situation makes the source positioning needed to provide adequate covering of the target volume impossible.

We present our experience with high dose rate brachytherapy using Flap applicator for complex neoplastic lesions of the facial skin and the scalp.

2. MATERIALS AND METHODS

a) Patients characteristics

Between January 2016 and December 2018, we report the experience of eight patients with skin cancer of the face and scalp treated in the radiotherapy department at the National Institute of Oncology of Rabat Morocco by high-dose brachytherapy with FLAP Freiburg applicator. All patients underwent excision surgery with positive or close margins with impossibility of surgical recovery, hence the indication for additional treatment with brachytherapy.

b) Applicator

Flap applicators are prefabricated custom molds with desirable geometry. They can help minimize the inconsistencies sometimes found in custom molds. The Nucletron Freiburg flap consists of attached 10-mm silicon spheres with catheters, 10 mm apart, embedded in the material at 5 mm from the surface of the sphere. These applicators can be used for all types of superficial lesions (size and shape). The most common flaps being used clinically are the Freiburg flap (Elekta). (image 1). These applicators can be cut to any size to fit the target area. In some cases, with large and curved surfaces, such as the scalp or shin, it is common to use multiple attached pieces of flap to better conform to the surface.

c) Simulation

Each patient had a computed tomography (CT) scan to plan the brachytherapy treatment with the flap in place (image 2). The tumoral bed was represented on the skin by a metal wire, for this we use pre-operative imaging. To assure the reproducibility of applicator positioning, we used thermoplastic masks, that kept the imprint of the applicator and the patients in the same position.

d) Target volume delineation, treatment planning and dose prescription

For each patient no gross tumoral volume (GTV) was defined, because all of cases was postoperative, the clinical target volume (CTV) was represented on the skin by a metal wire, 0.5cm margin were added to the surgical bed to perform the CTV, lateral limits were the metal wires and deep limits depended of the location, for a scalp lesion, the CTV depth corresponded to the bony structure and for a facial lesion it correlated with the fascia ,the planning target volume was equal to the CTV. Planning was performed with Oncentra software. Since the catheters were placed parallel and equidistant from each other, the prescription dose points were placed, in a median plan at the middle of each pair of catheters, like in the Paris brachytherapy system. For each plan, prescription was made on an isodose line where V100 (CTV receiving 100% of the prescribe dose) was superior or equal to 95%. (image 3)

e) Treatment delivery

Patients were positioned identically as during the simulation, they had their treatment twice a week. Irradiation was delivered by the Brachytherapy Afterloading Platform Flexitron in our brachytherapy dedicated room with audio and video monitoring (image 4).

f) Follow-up

Patients will be followed 15 days after brachytherapy, 1 month and then every 3 months during 2 years to evaluate the efficiency and toxicity of the procedure. The major endpoint of this study was the local control and toxicity. Results are presented as median or mean value for quantitative parameters. Frequencies and percentages were computed for qualitative parameters.

3. RESULTS

Between January 2016 and December 2018, eight patients were treated in our department, six men and two women. The median age was 70 years (39-84 years), the predominant histological type was squamous cell carcinoma in 4 patients, 3 patients had basal cell carcinoma and one patient had a malignant tumor of the peripheral nerve sheaths. The predominant tumor location was the scalp in 4 patients, one patient had a frontal location, one in the nose one patient had a left sub orbital location and one had nasogenous localization. The tumor was classified according to seventh edition of TNM staging: T3 in 5 patients and T2 in the 3 others. Results are reported in table 1.

All patients underwent surgical excision, the limits of excision were marginal less than 2 mm in 5 patients and 3 patients had a tumoral limit. Skin brachytherapy using the FLAP Freiburg applicator was indicated in all our patients, only one patient received external beam radiotherapy with a dose of 20 Gy before BT. The protocol used was 8x 5Gy in 5 patients,6 x5 Gy in 2 patients, and 5x5 Gy in one patient. The patients are treated, twice a week.

The patients were followed until January 2020. The average follow-up was 26,4 months (17 to 39 months). Low acute dermal reactions were noted in all patient, one case of grade 3 radiodermatitis was observe (image 5),

for late complication one patient developed skin fibrosis. One case of locoregional relapse was noted and no patient developed distant metastases, all patients are alive, one patient was lost to follow-up after the end of brachytherapy.

Table 1: Clinical characteristics of patients and methods of treatment received.

Population	Age: 70 years (39-84 years) Gender : Male: 6 (75%) Female: 2 (25 %)
Histology	SSC: 4 (50%) BCC: 3 (37%) OTHER: 1 (12,5)
Tumor	SIZE: 4,4cm (2-9cm) TNM: T2: 3 (37,5%) T3 : 5 (62,5%)
Localization	SCALP: 4 (50%) FRONTAL: 1 (12,5%) NASO-GENIEN: 1 (12,5%) SUB ORBITAL: 1(12,5%) NOSE: 1(12,5%)
Treatment	SURGERY: 8 (100%) TUMORAL LIMITES: 4 (50%) MRGINAL LIMITES: 4 (50%) EBRT: 1(12,5%) DOSE: 20Gy DOSE/FRACTION: 2Gy/fr
Brachytherapy	TOTAL DOSE: 35,6Gy (25-40Gy) DOSE/FRACTION: 5Gy/fr PROTOCOLE: 8X5Gy: 5(62,5%) 6X5Gy: 2(25%) 5X5Gy: 1(12,5%) Dose max Skin: 123% (102%-160%) D100: 5Gy Spread of BT: 21 days (11-27days)
Follow up	**Follow up:** 26,4 months (17 to 39 months) **Acute complication:** Radiodermite Grade I+II: 8 (100%) Grade III: 1 (12,5%) Grade IV: 0 (0%) **Late complication** fibrosis: 1 (12,5%) **Relapse** local: 1 (12,5%) distant: 0 (0%)

Table 2: Recommandations for skin cancer brachytherapy (source: Greater Poland Cancer Center, Poznan, Poland).

Treatment	Indications	Technique	Fraction dose (range)	Total dose (range)
Radical	Primary, recurrences. Diameter < 5–6 cm, technically possible application, thickness < 2 cm	HDR	5.0–10.0 Gy	50–60.0 Gy
		PDR	1.0 Gy (pulse)	50–60.0 Gy (in 2–3 fractions)
Radical, after surgery	Typically, after non-radical surgery (suggested by pathological diagnosis), healthy tissue margin < 5 mm	HDR	5.0–10.0 Gy	50–60.0 Gy
		PDR	1.0 Gy (pulse)	50– 60.0 Gy (in 2–3 fractions)
Palliative	Inoperative tumors, size preventing coverage with curative dose, thickness > 2 cm	HDR	5.0–10.0 Gy	20–40.0 Gy
		PDR	1.0 Gy (pulse)	20–40.0 Gy (in 1–2 fractions)

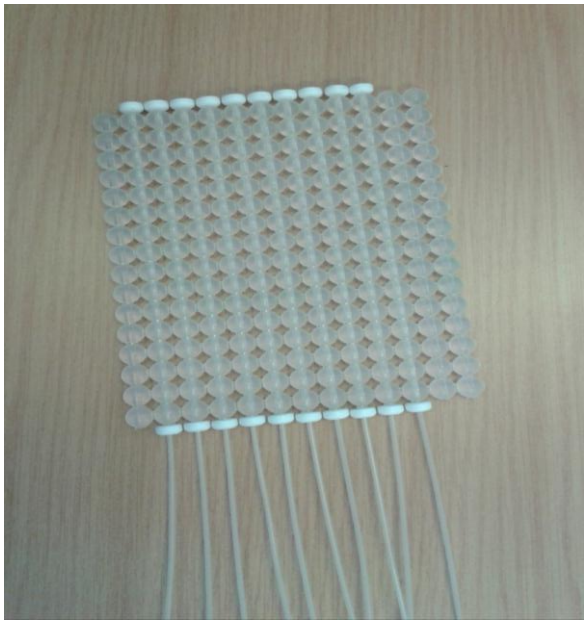

Image 1: Freiburg FLAP Applicator with Catheters in Place.

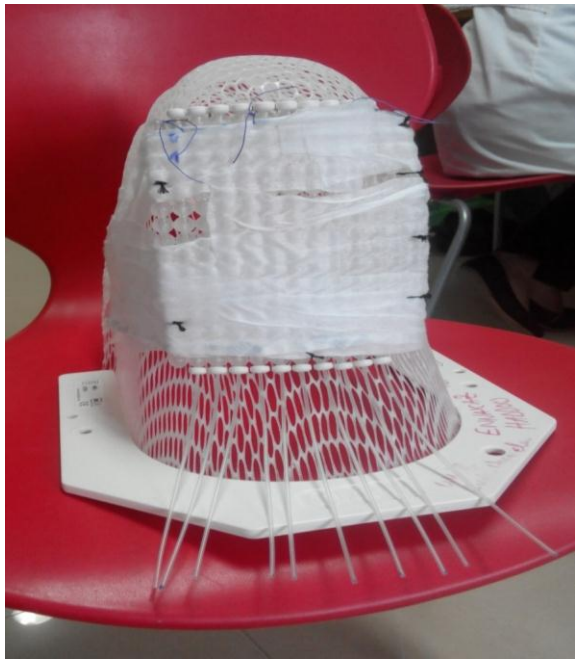

Image 2: FLAP applicator stuck to the thermoformed mask.

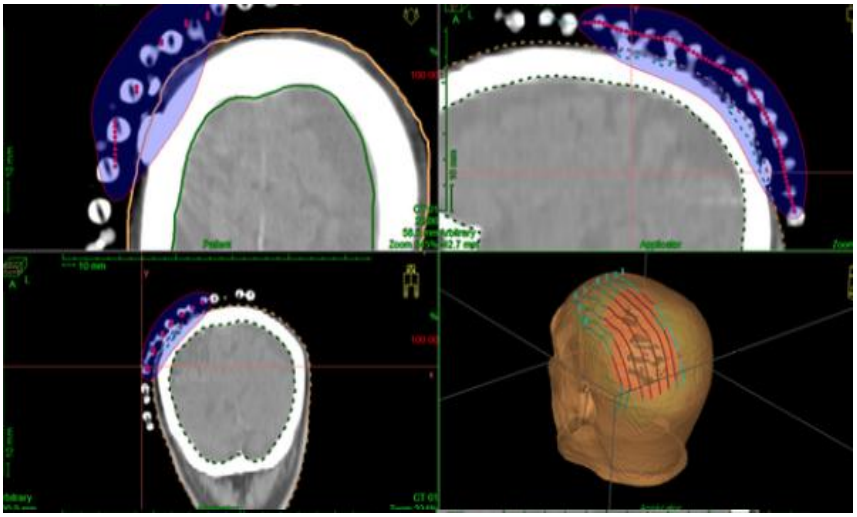

Image 3: Brachytherapy plan in axial and sagittal viewing for a scalp lesion using Freiburg FLAP Applicator.

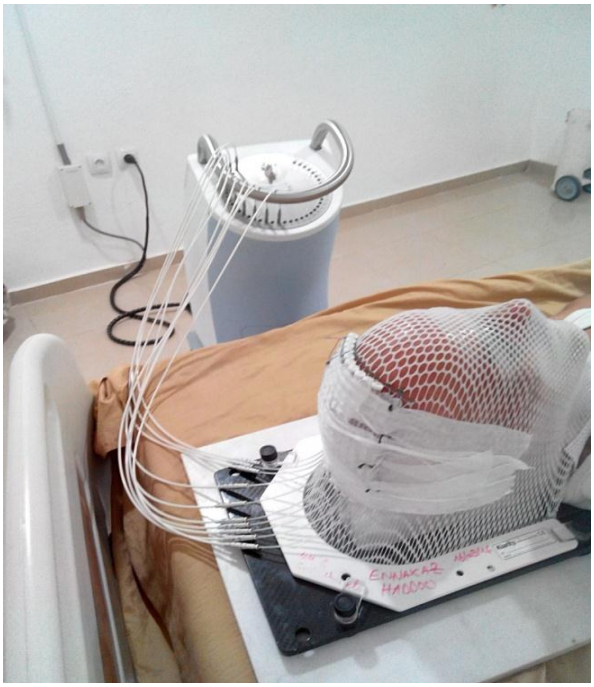

Image 4: Irradiation delivered by the Brachytherapy Afterloading Platform Flexitron.

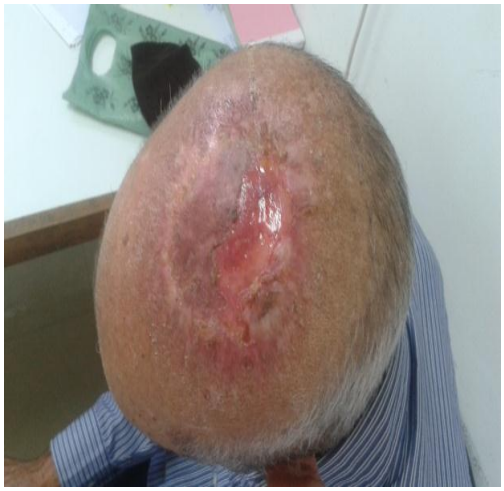

Image 5: Radiodermatitis grade 3 two weeks after the end of radiotherapy.

4-DISCUSSION

Surgical techniques remain the primary treatment option of NMSC, especially when occurring on areas of skin allowing uncomplicated excision. BT is used in tree clinical situations: Primary treatment of non-resected tumor after biopsy, adjuvant treatment of excised lesions with close or positive surgical margins, and for palliative cases (table 2). The absolute contraindications for the use of BT in NMSC are invasion of the bone, genetic diseases such as ataxia- telangiectasia or other related diseases of DNA repair, suspected extension in the orbit or deep extension along fascial planes and perineural invasion. BT in NMSC is usually limited to older patients (>50 years) decreasing possibility of long-term sequelae.[6]

In the above-described study, we showed that high dose rate brachytherapy using the Freiburg Flap from ELEKTA is highly efficient for complex facial skin or scalp lesions after non-radical surgery. We noted only one local recurrence on the tumor bed of a frontal BCC whose initial depth of invasion was> 1.5 cm and a marginal deep surgical limit with some perineural invasion on the excision. It is important to underline the tolerance of this technique with absence of major toxicity during and after treatment.

Many published studies confirm the high percentages of the cure rate using skin BT. Guix *et al.*[7] in a serie of 136 patients with primary and recurrent cancers treated using superficial BT showed that the probability of a local cure is 99% and 87%, respectively. The percentage of early and late complications was low. Arenas et al.[8] showed, in a retrospective study based on 114 patients, the efficiency and tolerance of high dose rate brachytherapy with Leipzig applicator or mold applicators. They treated 134 basal cell or squamous cell carcinomas of the face, scalp or extremities. The mean lesion diameter was 14.5 mm. The total dose varied according to histology (45–57 Gy) and treatment had been delivered in 3 Gy per fraction. The overall disease-free survival at 5 years was 93.4%. Gauden et al.[9] presented in a cohort of 200 patients treated for superficial NMSC a local control rate of 98% at 66 months using HDR BT with the Leipzig surface applicator. Montero et al.[10] showed an absence of local relapse at a mean follow-up of 15 months in a cohort of 9 patients, treated for NMSC with HDR BT with custom-made moulds.

Our results are concordant with these studies. One bias of this study is its retrospective nature and the fact that it is based on a small number of patients. The short follow-up must be also pointed out.

5-CONCLUSION

HDR BT with FLAP Freiburg applicator for facial skin and scalp lesions is efficient and safe. It is a good modality to treat complex lesions in patients unfit for invasive treatment, specifically, wen interstitial brachytherapy with hypodermic needles cannot be installed.

Abbreviations list

BT: brachytherapy
HDR: high-dose-rate
NMSC: Non-melanoma skin cancer
SCC: squamous cell carcinoma
BCC: basal cell carcinoma
WHO: World Health Organization
EBRT: external beam radiotherapy
CT: computed tomography
GTV: gross tumoral volume
CTV: clinical target volume

Ethics approval and consent to participate

Informed consent (verbal) was obtained from all participants. This study was submitted to and approved by research and ethics committee of the national institute of oncology of Rabat.

Competing interests

We (authors) declare that we have no conflict of interest.

Authors' Contribution

M. HOMMADI, H. BAKKALI, performed research and share the first position in this manuscript; O. HOUESSOU, M. BENLEMLIH collected the clinical data, H. BAKKALI, I. LAHDIRI, S. BOUTAYEB, S. EL MEJJAOUI, H. KACEMI, T. KEBDANI, N. BENJAAFAR designed and coordinated research and drafted the manuscript. All authors read and approved the final manuscript.

ACKNOWLEDGEMENT

All the authors are thankful for providing the necessary facilities for the preparation the manuscript. Special thanks are due to the Faculty of Medicine and Pharmacy of Rabat; the source(s) of funding for all authors.

BIBLIOGRAPHY

1. Rogers HW, Wenstock MA, Harris AR, et al. Incidence estimate of nonmelanoma skin cancer in the United States, 2006. Arch Derma- tol, 2010; 146: 283e287.
2. Lo A, Leonardi-Bee J, Bath-Hextall F. A systematic review of worldwide incidence of nonmelanoma skin cancer. Br J Dermatol, 2012; 166: 1069e1080.
3. Macfarlane L, Waters A, Evans A et al. Seven years' experi- ence of Mohs micrographic surgery in a UK centre, and de- velopment of a UK minimum dataset and audit standards. *Clin Exp Dermatol*, 2013; 38: 262-269.
4. Nguyen TH, Ho DQ. Nonmelanoma skin cancer. *Curr Treat Options Oncol*, 2002; 3: 193-203.
5. Ouhib Z, Kasper M, Perez Calatayud J et al. Aspects of dosimetry and clinical practice of skin brachytherapy: The American Brachytherapy

Society working group report. *Brachytherapy*, 2015; 14: 840-858.
6. Skowronek J, Chicheł A, Piotrowski T. Brachyterapia HDR nowotworów skóry – doświadczenie Wielkopolskiego Centrum Onkologii. Contemp Oncol (Poznan), 2005; 8: 347-54.
7. Guix B, Finestres F, Tello JI, et al. Treatment of skin carcinomas of the face by high-dose-rate brachyterapy and custom made surface molds. Int J Radiat Oncol Biol Phys, 2000; 47: 95-102.
8. Arenas M, Arguís M, Díez-Presa L, Henríquez I, Murcia-Mejía M, Gascón M, et al. Hypofractionated high dose rate plesiotherapy in non-melanoma skin cancer treatment. Brachytherapy, 2015; 14: 859–65.
9. Gauden R, Pracy M, Avery A-M, Hodgetts I, Gauden S. HDR brachytherapy for superficial non-melanoma skin cancers. J Med Imaging Radiat Oncol, 2013; 57: 212–7.
10. Montero A, Hernanz R, Capuz AB, Fernández E, Hervás A, Colmenares R, et al. High dose rate (HDR) plesiotherapy with custom-made moulds for the treatment of non-melanoma skin cancer. Clin Transl Oncol, 2009; 11: 760–4.