Original paper

Long-term clinical outcomes of non-melanoma skin cancer patients treated with electronic brachytherapy

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Abstract

Purpose: High-dose-rate electronic brachytherapy (eBx) is a non-surgical treatment option for non-melanoma skin cancer (NMSC) patients. This study assessed long-term effectiveness and safety of eBx for the treatment of NMSC.

Material and methods: A chart review was conducted to identify subjects who had five or more years since their last eBx treatment fraction. Subjects meeting these criteria were contacted to determine their interest in participating in a long-term follow-up study. Those who agreed, underwent a follow-up visit where consent was obtained, and their lesions were clinically assessed for recurrence and long-term skin toxicities. History and demographic data were retrospectively collected, and treatment method was verified.

Results: 183 subjects with 185 lesions were enrolled into this study at four dermatology centers in two practices in California. Three subjects in the analysis were less than 5 years from the last treatment to follow-up visit. All lesions were stage 1 basal cell carcinoma, squamous cell carcinoma, or squamous cell carcinoma *in situ*. Recurrence rate for the 183 subjects was 1.1%. Long-term skin toxicities were reported in 70.0% of the subjects. Hypopigmentation grade 1 was observed in 65.9% of the lesions, telangiectasia grade 1 was seen in 22.2%, scarring grade 1 in two subjects (1.1%), hyperpigmentation grade 1 in two subjects (1.1%), and induration grade 2 in one patient (0.5%). The induration grade 2 was located on the upper back and did not limit instrumental activities of daily living (ADLs).

Conclusions: Electronic brachytherapy for the treatment of non-melanoma skin cancer is safe and effective, showing excellent long-term 98.9% local control through a median follow-up of 7.6 years (n = 183), with minimal long-term toxicities.

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Key words: electronic brachytherapy, non-melanoma skin cancer, squamous cell carcinoma, local control, basal cell carcinoma.

Purpose

It is estimated that 5.4 million cases of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are diagnosed annually in the United States [1]. About 80% of non-melanoma skin cancers (NMSC) are basal cell carcinoma [2]. Treatment options for patients with NMSC include Mohs micrographic surgery (MMS), curettage with electro-desiccation, surgical excision, 5-fluorouracil (topical, intralesional, intravenous), cryotherapy, toll-like receptor 7 activator (imiquimod), Hedgehog (Hh) pathway inhibitors (vismodegib, sonidegib), PD-1 blockers (pembrolizumab, nivolumab, cemiplimab), photodynamic therapy, and radiation therapy [3-11].

A Cochrane database review concluded that surgical interventions have the lowest recurrence rates among all reviewed therapies, and that non-surgical treatments may be less effective than surgical therapies, but have superior cosmetic outcomes and acceptable recurrence rates [7]. European consensus-based interdisciplinary guidelines note that radiotherapy represents a valid alternative to surgery for facial BCC, especially in elderly patients [8].

European consensus-based interdisciplinary guidelines also notes that radiation therapy represents an alternative to surgery in the treatment of small SCCs in low-risk areas [9]. Lesion recurrence rate for patients at five years after MMS varies depending on primary vs. recurrent lesion, lesion location (high-risk 'mask' areas), treatment modality, size, depth, histologic differentiation, perineural involvement, and immune status [3-6, 10-12]. Five-year recurrence rates reported by Rowe *et al*. and Kauvar *et al*. were both of 1% [3, 5]. Network meta-

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analysis by Drucker *et al*. showed recurrence rate of 3.8% in those treated with MMS [14]. Recurrence rates for primary SCCs reported were 3.1% to 5.3% [4, 6, 15].

A non-surgical treatment option for patients with NMSC, studied previously in a matched-pair cohort study and compared to MMS, is electronic brachytherapy (eBx). The mean follow-up for the eBx arm was 3.3 years with a local control rate of 99.5%, and the MMS arm had a local control rate of 100% [16].

This real-world, multi-center, non-randomized study assessed long-term clinical outcomes of non-melanoma skin cancer (NMSC) patients treated with Axxent® electronic brachytherapy (eBx) system (Xoft, Inc. – a subsidiary of iCAD, Inc., San Jose, CA, USA). Prior to retrospective data collection and prospective follow-up visits, patients who were identified to have completed eBx treatment a minimum of five years ago, and who were available for a prospective long-term follow-up visit, were included in the present study. At the prospective follow-up visit assessment of local control and long-term skin toxicities at the treatment site were collected to determine the durability and long-term safety of eBx for the treatment of NMSC.

Material and methods

The NMSC long-term follow-up study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, in accordance with local regulatory requirements, and was approved by an independent central institutional review board Advarra IRB, number: Pro00060222 (Columbia, MD, USA). This study included both a retrospective chart review, and a prospective collection and analysis of follow-up data. Chart reviews were conducted at the sites to determine potential participants who could be contacted for participation in the prospective visits by confirming that the last treatment date was a minimum of five years ago. Once this was confirmed, data was not collected until the patients who were willing to participate returned for their follow-up visit. Follow-up visits were scheduled, and patients had the option of returning to the site for an in-person visit, or attend a video conference for remote participation, a common method for conducting visits by dermatology offices in the USA [13].

For this study, a participant was required to provide verbal consent on video, and this was documented in the informed consent form. If a treated area was in question based on appearance, the study participant was required to undergo a biopsy. For in-person visits, participants provided written informed consent. Once the prospective follow-up visit was completed, retrospective data were collected from electronic medical record. Retrospective data collection included eligibility criteria, demographics and history, verification of the treatment regimen, lesion information, including stage, histology, location, and local control at the treated area. Prospective visits consisted of examination of the previously treated skin lesion for local control at the treatment site. Skin toxicities were assessed according to the Common Terminology Criteria Adverse Events (CTCAE version 5.0) [17].

Patient selection

Patients treated with eBx five or more years ago, who met eligibility criteria, and were willing to undergo a follow-up visit, were selected for this study at four West Coast centers in the United States. The majority of subjects in the study were included in the eBx arm of a prior study conducted by Xoft, Inc. [16].

Inclusion criteria were previously completed treatment for non-melanoma skin cancer using Xoft Axxent electronic brachytherapy system according to standard of care, a minimum of five years prior to the follow-up visit in this study; patient provided informed consent; greater than 40 years of age; pathological diagnosis confirmed as squamous cell carcinoma, squamous cell carcinoma *in situ*, or basal cell carcinoma prior to treatment; and staging. Patients were excluded if the target area was adjacent to a burn scar, if there was any prior definitive surgical resection of the cancer, such as MMS, known perineural invasion, diagnosis of actinic keratosis, known spread to regional lymph nodes, and known metastatic disease. Lesions were staged as Tis, T1, or T2.

Treatment methods

Surface applicators sizes were 10 mm, 20 mm, 35 mm, and 50 mm in diameter. Surface applicator size was selected based on lesion diameter, which allowed for a 2 mm to 5 mm margin. Prescription dose was 40.0 Gy administered over 8 fractions (5.0 Gy twice weekly), delivered to the skin surface, as previously reported [16, 21, 25].

Study endpoints

The primary effectiveness endpoint was the local control at a minimum of five years from the last eBx treatment, while the primary safety endpoint was long-term skin toxicities at the target treatment site at the time of the follow-up visit. Most common long-term primary toxicities reported are hypopigmentation and telangiectasias [16]. Data for the primary effectiveness endpoint were collected retrospectively once it was determined that the subject could be available for a long-term follow-up visit in this study, and the follow-up visit would be five years or more since the last treatment. Follow-up visits occurred prospectively. Data for the secondary safety endpoint were collected prospectively at the time of the follow-up visit in this study, to identify long-term toxicities.

Statistical analysis

The objective of this study was to report the number and percentage of subjects who had local recurrence, and the number and percentage of subjects who showed a long-term skin toxicity at the follow-up visit. Data were analyzed and reported as descriptive statistics, both categorical and continuous variables, as appropriate.

Results

Patient demographics and lesions characteristics

In total, 183 subjects with 185 lesions were enrolled in this long-term follow-up study from March 9, 2022

to July 18, 2022, at four study centers in Northern and Southern California, out of 307 potential participants who were called. There were three subjects who had less than five years between the last treatment and the follow-up visit. Of the remaining 180 subjects with 182 lesions, all patients met all inclusion criteria and none of the exclusion criteria. The mean age was 82.3 years, with a range of 63 to 96 years; 61.7% were male and 98.9% were white non-Hispanic subjects (Table 1). All lesions were 4 cm in diameter or smaller. The results of 180 and 183 subjects are presented in Tables 1-4. The mean follow-up in this study was 7.5 years (median, 7.6 years; range, 5-9.5 years). All lesions were stage 0, 1, or 2. The majority of the lesions (n = 131, 70.8%) were above the clavicles. If the results include the three subjects who were excluded due to less than 5-year follow-up, the male to female ratio was the same, race and ethnicity was the same, and the three subjects excluded were diagnosed with BCC stage 2. Tables 1-5 demonstrate all the results for both the groups.

NMSC recurrence

The retrospective data analysis revealed the recurrence rate of the 180 subjects with a mean of 7.5 year follow-up (1.1%) (Table 3). Two subjects diagnosed with BCC had one lesion with a recurrence, one subject's lesion was located on the nasal sidewall, and the recurrence was diagnosed at 2.7 years after treatment. The other subject's lesion was located on the nasal tip, and the recurrence was diagnosed at 6.5 years after treatment. Both recurrences were treated with MMS. For all 183 subjects, including those who did not meet the minimum of 5 years from last treatment to the follow-up visit in this study, the recurrence rate was 1.1%. There were no recurrences in the 183 subjects newly discovered at the time of the prospective follow-up.

Table 1. History and demographic data

Demographic data	n = 180 subjects n (%) ≥ 5.0 years of follow-up	n = 183 subjects n (%) ≥ 4.4 years of follow-up
Gender		
Male	111 (61.7)	113 (61.7)
Female	69 (38.3)	70 (38.3)
Race		
White	179 (99.4)	182 (99.5)
Asian	1 (0.6)	1 (0.5)
Ethnicity		
Hispanic	4 (2.2)	4 (2.2)
Non-Hispanic	176 (97.8)	179 (97.8)
Diagnosis		
BCC	91 (50.6)	94 (51.4)
SCC	89 (49.4)	89 (48.6)
Cancer stage		
Stage 0	9 (5.0)	9 (4.9)
Stage 1	166 (92.2)	169 (92.3)
Stage 2	5 (2.8)	5 (2.7)
Age (years)		
Mean ±SD	82.3 ±6.5	82.3 ±6.5
Minimum-maximum	63-96	63-96
Median (IQR)	83.0 (77.0-86.5)	83.0 (77.0-87.0)

Safety and skin toxicities

Skin toxicities (Table 4) were reported in 71.1% of the subjects. Hypopigmentation grade 1 was the most com-

Table 2. Lesion locations

Lesion location	n = 182 lesions n (%)	n = 185 lesions n (%)
Scalp	17 (9.3)	17 (9.2)
Temple	6 (3.3)	6 (3.2)
Forehead	11 (6.0)	11 (5.9)
Cheek	21 (11.5)	22 (11.9)
Chin	2 (1.1)	2 (1.1)
Neck	4 (2.2)	4 (2.2)
Pre-auricular	2 (1.1)	2 (1.1)
Eyelid	3 (1.6)	3 (1.6)
Lip	1 (0.5)	1 (0.5)
Nasal dorsum	2 (1.1)	3 (1.6)
Nasal sidewall	21 (11.5)	21 (11.4)
Nasal ala	11 (6.0)	11 (5.9)
Nasal tip	17 (9.3)	17 (9.2)
Back	3 (1.6)	3 (1.6)
Chest	2 (1.1)	2 (1.1)
Upper arm	3 (1.6)	3 (1.6)
Forearm	3 (1.6)	3 (1.6)
Hand	17 (9.3)	18 (9.7)
Helix	1 (0.5)	1 (0.5)
Antihelix	1 (0.5)	1 (0.5)
Earlobe	8 (4.4)	8 (4.3)
Tragus	1 (0.5)	1 (0.5)
Lower leg	22 (12.1)	22 (11.9)
Foot	3 (1.6)	3 (1.6)
Summary of adverse events by location	**n = 182 lesions n (%)**	**n = 185 lesions n (%)**
Head, neck, above the clavicles	129 (70.9)	131 (70.8)
Torso (front and back)	5 (2.7)	5 (2.7)
Upper extremity and hand	23 (12.5)	24 (12.9)
Lower extremity and foot	25 (13.7)	25 (13.7)

Table 3. Recurrences

Recurrence by subject	*n* = 180 subjects *n* (%) ≥ 5.0 years of follow-up	*n* = 183 subjects *n* (%) ≥ 4.4 years of follow-up
All	2 (1.1)	2 (1.1)
Nasal tip	1 (0.6)	1 (0.5)
Nasal sidewall	1 (0.6)	1 (0.5)
Recurrence by lesion	***n* = 182 lesions** ***n* (%)**	***n* = 185 lesions** ***n* (%)**
All	2 (1.1)	2 (1.1)

mon skin toxicity, observed in 65.9% of the patients. Telangiectasia grade 1 was observed in 22.5% of the subjects. Other toxicities noted included scarring grade 1 in two subjects (1.1%), hyperpigmentation grade 1 in two subjects (1.1%), and induration grade 2 in one subject (0.5%). In this case, the indurated site was located on the upper back, and did not limit instrumental activities of daily living (ADL). In the overall population, the toxicity rate was 70.1% in the group with 180 subjects, and it was similar (70.0%) in the group with 183 subjects. The types of skin toxicities and severity were equal across both the groups.

Discussion

W.C. Roentgen reported the discovery of X-rays in December, 1895, and within four years, X-rays were being used successfully for the treatment of skin cancers [22]. High energy linear accelerators and high-dose-rate afterloading iridium-192 (^{192}Ir) replaced the low penetrating X-rays of the Roentgen era. These devices required heavy room shielding and protracted courses of treatment. Radiation therapy has been reported to result in low recurrence rates for both primary BCC (7.4%) and recurrent BCC (9.5%) [20-23].

More recently, use of hypofractionation of radiations has been shown to have comparable cosmesis over standard, lengthy treatment schedules. In a meta-analysis of 344 articles utilizing external beam radiation therapy or brachytherapy for BCC/SCC, fewer than 8% of patients experienced poor cosmesis, independent of dose or fractionation regimen [24].

Previous eBx studies showed excellent durable local control and minimal long-term toxicity. These studies utilized low penetrating X-rays of 50 KeV, as opposed to 6 million eV of linear accelerators and 330 KeV of Ir^{192} brachytherapy. Doggett *et al*. reported a study of 524 lesions treated with eBx showing a 0.8% failure at 1.04 years follow-up [25]. Bhatnagar reported outcomes for 297 lesions with up to 63 months follow-up (mean, 16.5 months; range, 1-63 months) [21], with one recurrence and excellent cosmesis in 100% of patients at years 4-5. No acute toxicities were reported, and late toxicities occurred in 2% of patients. Paravati *et al*. retrospectively analyzed 157 NMSC lesions treated with eBx with 3.4 to 34.8 months of follow-up, and two recurrences were noted (at 6.3 and

Table 4. Visit types and skin toxicities according to CTCAE [8]

Follow-up visit type by subject	*n* = 180 subjects *n* (%) ≥ 5.0 years of follow-up	*n* = 183 subjects *n* (%) ≥ 4.4 years of follow-up
In person visit	117 (65.0)	119 (65.0)
Remote telemedicine visit	63 (35.0)	64 (35.0)
Safety endpoint: skin toxicities by subject	***n* = 180 subjects** ***n* (%)** **≥ 5.0 years of follow-up**	***n* = 183 subjects** ***n* (%)** **≥ 4.4 years of follow-up**
Yes	128 (71.7)	130 (71.0)
No	52 (28.9)	53 (29.0)
Safety endpoint: skin toxicities by lesion	**Occurrence** ***n* = 182, *n* (%)**	**Occurrence** ***n* = 185, *n* (%)**
Hypopigmentation grade 1	120 (65.9)	122 (65.9)
Telangiectasia grade 1	41 (22.5)	41 (22.2)
Scar grade 1	2 (1.1)	2 (1.1)
Hyperpigmentation grade 1	2 (1.1)	2 (1.1)
Induration grade 2	1 (0.5)	1 (0.5)

Table 5. Follow-up

Follow-up in years	*n* = 180 subjects *n* (%) ≥ 5.0 years of follow-up	*n* = 183 subjects *n* (%) ≥ 4.4 years of follow-up
Mean (±SD)	7.4 ±1.4	7.4 ±1.4
Median (range)	7.7 (5.0-9.5)	7.6 (4.4-9.5)
Q1 (25th percentile), Q3 (75th percentile)	6.8, 8.6	6.2, 8.6

7.3 months) [26]. Excellent cosmesis was rated in 94.2% of the cases. A matched-pair cohort study with 188 patients in the eBx arm demonstrated that 99.5% were free of recurrence at a mean of 3.4 years post-treatment. Physicians rated cosmesis as "excellent" or "good" in 97.6% of EBT-treated lesions, and 95.7% of MMS-treated lesions [16].

A review of 21 tele-dermatology studies indicated that some studies show a high accuracy of tele-dermatologic diagnoses [13]. Appropriate used criteria previously published by Miller *et al*. described how the application of eBx can be incorporated into an outpatient dermatology clinic [28].

Our study provides further evidence of the similarity of eBx to Mohs micrographic surgery in terms of local control and mild long-term toxicities. The mean follow-up in this study is now the longest of all previously published eBx studies for the treatment of NMSC [5, 17-19].

Study limitations

This study was designed to address the insufficient long-term efficacy and safety data for the treatment of NMSC with electronic brachytherapy. Although mean follow-up in our study was 7.5 years, which is the longest reported eBx result to date, this was not a randomized controlled trial designed to compare eBx with MMS in subjects with long-term follow-up. 59.6% of the 307 potential participants contacted did participate in the study. The remainder of the potential participants could not be contacted. No contacted potential participant declined to participate in the study.

Comparative studies of surgery vs. radiation therapy report short follow-ups. The Cochrane comprehensive analysis of skin cancer therapies subset comparing radiotherapy against surgical excision (with or without frozen section margin control) extended out only to 4-years [7].

The 7.5 years of follow-up in the current study may be insufficient to identify the true local failure rate for eBx, as a 7.3% of 15-year recurrence rate for primary BCCs treated surgically with whole specimen intra-operative frozen section analysis has been reported [31]. In our study, 51.4% of the lesions were BCC in comparison with the 80% rate of BCC occurrence in the general population, as showed by the American Society of Clinical Oncology [2]. The skewing of lesion numbers toward SCC in this study may mask a higher local control due to the higher failure rate of treated SCC compared with treated BCCs [3-6, 11, 14, 15].

Pathology in this study was not always reported as to the various sub-types of BCC, which may confound reporting of long-term results. BCC is divided into multiple sub-types, such as superficial, nodular, pigmented (low-risk of recurrence) and sclerosing, morphoeic, infiltrating, and basosquamous (high-risk of recurrence). More than one histological sub-type can be detected within a single BCC [30].

Thirty-five per cent of the follow-up visits were performed by tele-dermatology rather than in person due to patients' fears regarding in-office COVID-19 exposure. While concern might be raised regarding the accuracy of diagnosis based on telemedicine images, a review of 21 tele-dermatology studies indicates that some studies show a high accuracy of diagnosis [13].

Conclusions

This study was designed to address the insufficient long-term efficacy and safety data for the treatment of NMSC with electronic brachytherapy. Electronic brachytherapy for the treatment of non-melanoma skin cancer is safe and effective, showing excellent long-term 98.9% of local control, with a median follow-up of 7.6 years (n = 183) and minimal long-term toxicities. These results of a non-surgical treatment for NMSC provide further support for the use of eBx for the treatment of NMSC.

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Disclosure

The authors report no conflict of interest.

References

1. https://www.cancer.org (accessed August 20, 2022).
2. https://www.cancer.net/cancer-types/skin-cancer-non-melanoma/statistics (accessed August 20, 2022).
3. Rowe DE, Carroll RJ, Day CL Jr. Long-term recurrence rates in previously untreated (primary) basal cell carcinoma: implications for patient follow-up. *J Am Acad Dermatol* 1989; 15 (3): 315-328.
4. Rowe DE, Carroll RJ, Day CL Jr. Prognostic factors for local recurrence, metastasis, and survival rates in squamous cell carcinoma of the skin, ear, and lip. Implications for treatment modality selection. *J Am Acad Dermatol* 1992; 26 (4): 976-990.
5. Kauvar ANB, Cronin T Jr, Roenigk R et al. Consensus for non-melanoma skin cancer treatment: basal cell carcinoma, including a cost analysis of treatment methods. *Dermatol Surg* 2015; 41: 550-571.
6. Kauvar ANB, Arpey CJ, Hruza G et al. Consensus for non-melanoma skin cancer treatment, part II: squamous cell carcinoma, including a cost analysis of treatment methods. *Dermatol Surg* 2015; 41: 1214-1240.
7. Thomson J, Hogan S, Leonardi-Bee J et al. Interventions for basal cell carcinoma of the skin. *Cochrane Database Syst Rev* 2020; 11.
8. Peris K, Fargnoli MC, Garbe C et al. Diagnosis and treatment of basal cell carcinoma: European consensus-based interdisciplinary guidelines. *Eur J Cancer* 2019; 118: 10-34.
9. Stratigos A, Garbe C, Lebbe C et al. Diagnosis and treatment of invasive squamous cell carcinoma of the skin: European consensus-based interdisciplinary guideline. *Eur J Cancer* 2015; 51: 1989-2007.
10. Gniadecki R, Glud M, Mortensen K et al. Favorable results of Mohs micrographic surgery for basal cell carcinoma. *Dan Med J* 2015; 62: A5171.
11. Burns CA, Brown MD. Imiquimod for the treatment of skin cancer. *Dermatol Clin* 2005; 23: 151-164.
12. Dika E, Scarfi F, Ferracin M et al. Basal cell carcinoma: a comprehensive review. *Int J Mol Sci* 2020; 21: 5572.

13. Finnane A, Dallest K, Janda M et al. Tele-dermatology for the diagnosis and management of skin cancer: a systematic review. *JAMA Dermatol* 2017; 153: 319-327.
14. Drucker AM, Adam GP, Rofeberg V et al. Treatments of primary basal cell carcinoma of the skin. *Ann Intern Med* 2018; 169: 156-166.
15. Van Lee CB, Roorda BM, Wakkee M et al. Recurrence rates of cutaneous squamous cell carcinoma of the head and neck after Mohs micrographic surgery vs. standard excision: a retrospective cohort study. *Br J Dermatol* 2019; 181: 338-343.
16. Patel R, Strimling R, Doggett S et al. Comparison of electronic brachytherapy and Mohs micrographic surgery for the treatment of early-stage non-melanoma skin cancer: a matched pair cohort study. *J Contemp Brachytherapy* 2017; 9: 338-344.
17. US Department of Health and Human Services, National Institutes of Health, National Cancer Institute. Common Terminology Criteria Adverse Events (CTCAE) Version 5.0. November 27, 2017.
18. Squamous Cell Skin Cancer: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) v.2.2022 (accessed September 23, 2022).
19. Kasper ME, Chaudhary AA. Novel treatment options for non-melanoma skin cancer: focus on electronic brachytherapy. *Med Devices (Auckl)* 2015; 26: 493-502.
20. Caccialanza M, Piccinno R, Moretti D et al. Radiotherapy of carcinomas of the skin overlying the cartilage of the nose: results in 405 lesions. *Eur J Dermatol* 2003; 13: 462-465.
21. Bhatnagar A. Electronic brachytherapy for the treatment of non-melanoma skin cancer: results up to four years. *Int J Radiat Oncol Biol Phys* 2014; 90 Suppl: S756.
22. Orton CG. Uses of therapeutic x rays in medicine. *Health Phys* 1995; 69: 662-676.
23. Silverman MK, Kopf AW, Gladstein AH et al. Recurrence rates of treated basal cell carcinomas. Part 4: X-ray therapy. *J Dermatol Surg Oncol* 1992; 18: 549-554.
24. Zaorsky NG, Lee CT, Zhang E. Hypo-fractionated radiation therapy for basal and squamous cell skin cancer: A meta-analysis. *Radiother Oncol* 2017; 125: 13-20.
25. Doggett S, Willoughby M, Willoughby C et al. Incorporation of electronic brachytherapy for skin cancer into a community dermatology practice. *J Clin Aesthet Dermatol* 2015; 8: 28-32.
26. Paravati AJ, Hawkins PG, Martin AN et al. Clinical and cosmetic outcomes in patients treated with high-dose-rate electronic brachytherapy for nonmelanoma skin cancer. *Pract Radiat Oncol* 2015; 5: e659-e664.
27. Bittner GC, Cerci FB, Kubo EM et al. Mohs micrographic surgery: a review of indications, technique, outcomes, and considerations. *Ann Bras Dermatol* 2021; 96: 263-277.
28. Miller K. Electronic brachytherapy: understanding the technology and identifying appropriate use. *Pract Dermatol* 2015; 47-48.
29. Scholten LA, Kedilioglu MA, Huizinga PM et al. LT recurrence rates of whole specimen intraop frozen section analysis in BCC face with WIFSA. *J Surg Oncol* 2019; 119: 103-108.
30. Seidl-Philipp M, Frischhut N, Höllweger N et al. Known and new facts on basal cell carcinoma. *J Dtsch Dermatol Ges* 2021; 19: 1021-1041.