8.01.62	Electronic Brachytherapy for Nonmelanoma Skin Cancer		
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Section:	8.0 Therapy	**Page:**	Page 1 of 16

Policy Statement

Electronic brachytherapy for the treatment of nonmelanoma skin cancer (see Policy Guidelines section) is considered **investigational.**

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Nonmelanoma skin cancer refers to squamous cell carcinoma and basal cell carcinoma. There are other less common types of skin cancer, such as T-cell lymphoma or Merkel cell tumor, which may have specific treatment options that differ from basal and squamous cell carcinomas and may need to be considered on an individual basis.

Coding

The following category III CPT code is specific for application of electronic brachytherapy to the skin surface:

- **0394T**: High dose rate electronic brachytherapy, skin surface application, per fraction, includes basic dosimetry, when performed

The following CPT code is specific for application of interstitial or intracavitary electronic brachytherapy:

- **0395T**: High dose rate electronic brachytherapy, interstitial or intracavitary treatment, per fraction, includes basic dosimetry, when performed

Any of the following codes may be used, and are considered not medically necessary: 0394T, 0395T, 77014, 77261-77263, 77280, 77285, 77290, 77295, 77300-77301, 77306-77307, 77321, 77331-77334, 77338, 77370-77373, 77385-77387, 77401, 77402, 77407, 77412, 77417, 77424-77425, 77432, 77435, 77469-77470, 77770-77772, 77778, 77790, G0339-G0340, G6001-G6017

Description

Electronic brachytherapy is a form of radiotherapy designed to deliver high-dose rate radiation to treat nonmelanoma skin cancer. This technique focuses a uniform dose of x-ray source radiation to the lesion with the aid of a shielded surface application.

Related Policies

- Radiation Oncology

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these

instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

Electronic brachytherapy systems for the treatment of nonmelanoma skin cancers are designed to deliver high-dose rate brachytherapy to treat skin surface lesions. This technique focuses a uniform dose of x-ray source radiation to the lesion with the aid of a shielded surface application. The Superficial X-Ray Radiation Therapy System (Sensus Healthcare), Esteya® Electronic Brachytherapy System (Nucletron BV), and the Xoft® Axxent® Electronic Brachytherapy System (iCAD) are systems that have been cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process. U.S. Food and Drug Administration product code: JAD.

Rationale

Background

Nonmelanoma Skin Cancer

Squamous cell carcinoma and basal cell carcinoma are the most common types of non-melanoma skin cancer in the United States, affecting between 1 million and 3 million people per year[1,2], respectively, and increasing at a rate of 3% to 8% per year.[2] Other types (e.g., T-cell lymphoma, Merkel cell tumor, basosquamous carcinoma, Kaposi sarcoma) are much less common. The primary risk factor for nonmelanoma skin cancer is sun exposure, with additional risk factors such as toxic exposures, other ionizing radiation exposure, and immunosuppression playing smaller roles.[2] Although these cancers are rarely fatal, they can impact the quality of life, functional status, and physical appearance.

Treatment

In general, the most effective treatment for nonmelanoma skin cancer is surgical. If surgery is not feasible or preferred, cryosurgery, topical therapy, or radiotherapy can be considered, though the cure rate may be lower.[3] When considering the most appropriate treatment strategy, recurrence rate, preservation of function, patient expectations, and potential adverse events should be considered.

Surgical

The choice of surgical procedure depends on the histologic type, size, and location of the lesion. Patient preferences can also play a factor in surgical decisions due to cosmetic reasons-as well as the consideration of comorbidities and patient risk factors, such as anticoagulation. Local excisional procedures, such as electrodesiccation and curettage or cryotherapy, can be used for low-risk lesions, while surgical excision is indicated for lesions that are not low risk. Mohs surgery is an excisional procedure that uses microscopic guidance to achieve greater precision and sparing of normal tissue. In patients who meet criteria for Mohs surgery, 5-year cure rates for basal cell cancer range from 98% to 99%,[4] making Mohs surgery the preferred procedure for those who qualify.

Radiotherapy

Radiotherapy is indicated for certain nonmelanoma skin cancers not amenable to surgery. In some cases, this is due to the location of the lesion on the eyelid, nose, or other structures that make surgery more difficult and which may be expected to have a less desirable cosmetic outcome. In other cases, surgery may be relatively contraindicated due to clinical factors, such as bleeding risk or advanced age. In elderly patients with a relatively large tumor that would require extensive excision, the benefit/risk ratio for radiotherapy may be considered favorable. The 5-year control rates for radiotherapy range from 80% to 92%, which is lower than that of surgical excision.[4] A randomized controlled trial by Avril et al (1997) reported that radiotherapy

for basal cell carcinoma resulted in greater numbers of persistent and recurrent lesions compared with surgical excision.[5,]

When radiotherapy is used for nonmelanoma skin cancer, the primary modality is external-beam radiotherapy. A number of different brachytherapy techniques have also been developed, including low-dose rate systems, iridium-based systems, and high-dose rate systems.[4,]

Electronic Brachytherapy
Electronic brachytherapy is a form of radiotherapy delivered locally, using a miniaturized electronic x-ray source rather than a radionuclide-based source. A pliable mold, constructed of silicone or polymethyl-methacrylate, is fitted to the tumor surface. This mold allows treatment to be delivered to nonflat surfaces such as the nose or ear. A radioactive source is then inserted into the mold to deliver a uniform radiation dosage directly to the lesion.[4,] Multiple treatment sessions within a short time period (typically within a month) are required.

This technique is feasible for well-circumscribed, superficial tumors because it focuses a uniform dose of x-ray source radiation on the lesion with the aid of a shielded surface application. Advantages of this treatment modality compared with standard radiotherapy include a shorter treatment schedule, avoidance of a surgical procedure and hospital stay, less severe side effects because the focused radiation spares healthy tissue and organs, and the avoidance of radioisotopes.[4,]

Literature Review
Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Electronic Brachytherapy for Nonmelanoma Skin Cancer
Clinical Context and Test Purpose
The purpose of electronic brachytherapy in patients who have nonmelanoma skin cancer is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of electronic brachytherapy improve the net health outcome in patients with nonmelanoma skin cancer?

The following PICO was used to select literature to inform this review.

Patients
The relevant population of interest is patients with nonmelanoma skin cancer. Nonmelanoma skin cancer refers to squamous cell carcinoma and basal cell carcinoma. There are other less

common types of skin cancer, such as T-cell lymphoma or Merkel cell tumor, which may have specific treatment options that differ from basal and squamous cell carcinomas and may need to be considered on an individual basis.

Interventions
The therapy being considered is electronic brachytherapy. Electronic brachytherapy is a form of radiotherapy delivered locally, using a miniaturized electronic x-ray source rather than a radionuclide-based source. Multiple treatment sessions within a short time period (typically within a month) are required.

Comparators
The following therapies are currently being used: surgery (excision or Mohs surgery), external-beam radiotherapy, and standard brachytherapy.

The diagnosis of nonmelanoma skin cancer involves a detailed review of medical history, a clinical exam, and a skin biopsy. Information from the diagnostic process can assess the risk of recurrence, which informs the choice of treatment. Location and size of the skin cancer are also factors in choosing the treatment strategy. Brachytherapy is considered when lesions are located on anatomic curves or are near critical organs.

Outcomes
The general outcomes of interest are survival, recurrence rates, and treatment-related morbidity. Follow-up to adequately detect nonmelanoma skin cancer recurrence should be at least 5 years.

Review of Evidence
Systematic Reviews
Delishaj et al (2016) published a systematic review of studies on high-dose rate brachytherapy, including electronic brachytherapy, for the treatment of nonmelanoma skin cancer.[6] A literature review conducted through May 2019 identified 10 case series with sample sizes of 20 patients or more that reported on nonoverlapping patients. Findings were reported for 1870 patients (N=1870 lesions). Most lesions (65%) were basal cell carcinoma and the second largest group (35%) was squamous cell carcinoma. Reviewers did not pool study findings, reporting that the rates of local control ranged from 83% to 100%. After median follow-up ranging from 9 months to 10 years, recurrence rates ranged from 0% to 17%. Seven of the 10 studies reported recurrence rates of less than 5%, 2 had recurrence rates of 8% to 9%, and 1 study had a recurrence rate of 17%. The 2 studies with recurrence rates in the 8%-to-9% range used Leipzig applicators and the study with a 17% recurrence rate used high-dose rate brachytherapy with surface applicators or custom-made surface molds.

Prospective Cohort Study
Patel et al (2017)[7] published preliminary results from a multi-center prospective matched pair cohort study NCT03024866acomparing clinical outcomes of nonmelanoma skin cancer treated with electronic brachytherapy (EBT) or Mohs micrographic surgery (MMS). Patients from 4 treatment centers who had already received treatment for NMSC with EBT and met eligibility criteria were invited to participate. A retrospective chart review was used to individually match patients with patients who had received MMS for NMSC based on patient age (±15 years), lesion size, type and location, and treatment dates. All MMS treated subjects treated in the same time-frame were considered for matching and the final pair was selected based on the closest match of demographics and lesion characteristics. A total of 369 patients were included for study representing 208 matched lesion pairs. Additional eligibility criteria included:

- completion of EBT or MMS for NMSC ≥3 years prior
- age > 40 yrs
- diagnosis of squamous cell carcinoma (SCC) or basal cell carcinoma (BCC)
- cancer stage 0-2

Exclusion criteria included:

- target area adjacent to burn scar
- surgical resection of the cancer prior to EBT
- presence of actinic keratosis
- known metastatic disease

Patients were evaluated for follow-up at 2.3 to 5.0 years post-treatment. Treatment with EBT was performed with a miniature, HDR electronic X-ray source using standard surface applicators. A dose of 40.0 Gy in 8 fractions (5 Gy twice weekly) was used to delivered to a depth of 2-3 mm but in some cases a customized dose, depth, or schedule. MMS was performed by clinicians according to guidelines of the American College of Mohs Surgery. Matching of patients based on lesion characteristics was based on histopathology of basal cell carcinoma (BCC) or squamous cell carcinoma (SCC), cancer staging (Stage 0, Stage 1, Stage 2), size (≤ 1 cm, >1 cm and ≤ 2 cm, > 2 cm and ≤ 3 cm), and location (head, ear, eyelid, face/neck, lip, scalp, nose, torso, lower extremity, upper extremity). The mean follow-up length was 3.3 years for the EBT group and 3.5 years for the MMS group. The primary outcome was absence of NMSC recurrence at follow-up. Secondary outcomes included late toxicities, cosmetic outcomes, and patient satisfaction with treatment. All patients completed all evaluations.

The main characteristics and results are summarized in Table 1.

Table 1. Prospective Cohort Study of Electronic Brachytherapy for Nonmelanoma Skin Cancer

Population	N	MFU, years (median; range)	Treat-ment	Outcomes			
Patients receiving EBT for NMSC	188		EBT				
Lesions receiving EBT for NMSC (number of lesions, %)	208	3.3 ± 0.4(3.2; 2.6-4.3)	EBT	Absence of Local Recurrence at Follow-Up (number of lesions, %, 95%CI)	Cosmesis Grade at Follow-Up (number of lesions, %, CI)a	Long-term Toxicities Present at Follow-Up (number of lesions, %)	Results of Patient Satisfaction Questionnaire at Follow-Up (mean ± SD; median, [10-60])b
• Lesions with BCC (113, 54.3%) • Lesions with SCC (95, 45.7%)	208	3.3 ± 0.4(3.2; 2.6-4.3)	EBT	207 (99.5%, 97.4-100%)	Clinician Cosmesis Grade • Excellent/Good (203, 97.6%, 94.5-99.2%) • Excellent (133, 63.9%) • Good (70, 33.7%) • Fair (1, 0.5%) • Poor (4, 1.9%) Subject Cosmesis Grade • Excellent (140, 67.3%) • Good (48, 23.1%) • Fair (15, 7.2%) • Poor (5, 2.4%)	No changes, relatively invisible scar (138, 66.7%) Late toxicities: • Hypopigmentation (124, 59.6%) • Hyperpigmentation (11, 5.3%) • Erythematous scar (6, 2.9%) • Telangiectasia (65, 31.4%) • Hair loss (8, 3.9%) • Fibrosis (3, 1.4%) • Atrophy (12, 5.8%) • Loss of subcutaneous tissue (7, 3.4%)	54.0 ± 9.0; 58.0 Individual Questions • Treatments were convenient (4.3 ± 1.1) • Satisfied with how well treatment worked (4.5 ± 1.1) • Satisfied with appearance of the treated area (4.4 ± 1.0) • If another cancer, would use same treatment (4.1 ± 1.4)

Population	N	MFU, years (median; range)	Treat-ment	Outcomes			
						• Hypertrophy (excessive fibrosis) or keloid (0, 0%) • Poor healing, ulceration, erosion (4, 1.9%)	• Have not had any skin problems with treated area (4.5 ± 1.2) • Since treatment, frustrated about appearance of treated site (4.5 ± 1.1) • Since treatment, embarassed about appearance of treated site (4.6 ± 0.9) • Since treatment, depressed about appearance of treated site (4.5 ± 1.1) • Treatment prevented me from participating in daily activities (4.6 ± 0.9) • Treatment made it hard to work or do what I enjoy (4.7 ± 0.7) • Would recommend treatment to others (4.4 ± 1.3) • Always followed instructions related to care of treated area (4.9 ± 0.4)
Patients receiving MMS for NMSC	181	---	MMS	Outcomes			
Lesions receiving MMS for NMSC (number of lesions, %)	208	3.5 ± 0.5(3.4; 2.3-5.0)	MMS	Absence of Local Recurrence at Follow-Up (Number of lesions, %, 95% CI)	Cosmesis Grade at Follow-Up (Number of lesions, %, 95% CI)a	Long-term Toxicities Present at Follow-Up (Number of lesions, %)	Results of Patient Satisfaction Questionnaire at Follow-Up (mean ± SD; median, [10-60])b
• Lesions with BCC (113, 54.3%)	208	3.5 ± 0.5(3.4; 2.3-5.0)	MMS	208 (100%, 98.2-100%)	Clinician Cosmesis Grade • Excellent/Good (199, 95.7%, 92.0-98.0%)	No changes, relatively invisible scar (143, 68.8%) Late toxicities:	56.0 ± 5.3; 59.0 • Treatments were convenient (4.7 ± 0.6)

Population N	MFU, years (median; range)	Treat-ment	Outcomes			
• Lesions with SCC (95, 45.7%)			• Excellent (142, 68.3%) • Good (57, 27.4%) • Fair (9, 4.3%) • Poor (0, 0.0%) Subject Cosmesis Grade • Excellent (148, 71.1%) • Good (50, 24.0%) • Fair (10, 4.8%) • Poor (0, 0.0%)	• Hypopigmentation (109, 52.4%) • Hyperpigmentation (4, 1.9%) • Erythematous scar (15, 7.2%) • Telangiectasia (23, 11.1%) • Hair loss (7, 3.4%) • Fibrosis (2, 1%) • Atrophy (9, 4.3%) • Loss of subcutaneous tissue (6, 2.9%) • Hypertrophy (excessive fibrosis) or keloid (3, 1.4%) • Poor healing, ulceration, erosion (0, 0.0%)	• Satisfied with how well treatment worked (4.8 ± 0.5) • Satisfied with appearance of the treated area (4.6 ± 0.7) • If another cancer, would use same treatment (4.6 ± 0.7) • Have not had any skin problems with treated area (4.7 ± 0.6) • Since treatment, frustrated about appearance of treated site (4.6 ± 1.0) • Since treatment, embarrassed about appearance of treated site (4.7 ± 0.7) • Since treatment, depressed about appearance of treated site (4.6 ± 0.8) • Treatment prevented me from participating in daily activities (4.6 ± 0.9) • Treatment made it hard to work or do what I enjoy (4.6 ± 0.8) • Would recommend treatment to others (4.7 ± 0.7) • Always followed instructions related to care of treated area (4.7 ± 0.5)

MFU: mean follow-up; SD: standard deviation; EBT: electronic brachytherapy; MMS: Mohs micrographic surgery; NMSC: nonmelanoma skin cancer

a Standardized scale adapted from Cox et al (1995).[8]
b A score of 5 represents the maximum positive or favorable response to each question.

No statistically significant difference was found between EBT (97.6%) and MMS (95.7%) groups for local recurrence absence (p = 1.000). However, 1 recurrence was reported in the EBT group at 1 year post-treatment. No recurrences occurred in the MMS group. No statistically significant differences were noted for secondary endpoints of cosmesis (p = 0.277) and patient satisfaction with both groups demonstrating predominantly excellent cosmesis grades and high patient satisfaction scores. Late toxicities appeared at similar rates with telangiectiasa being reported slightly more in the EBT vs MMS group (31.4% vs 11.1%).

A summary of the EBT study relevance limitations is provided in Table 2.

Table 2. Electronic Brachytherapy Study Relevance Limitations

Study (year)	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Patel et al (2017)[7]	2 - Rationale for inclusion and exclusion criteria unclear	2 - Version used unclear		6 - Clinical significant difference not supported	1 - Not sufficient duration for benefit

a Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use
b Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest
c Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively
d Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not established and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported
e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms

A summary of the EBT study design and conduct limitations is provided in Table 3.

Table 3. Electronic Brachytherapy Study Design and Conduct Limitations

Study (year)	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Patel et al (2017)[7]	3 - Allocation concealment unclear in matching procedure	3 - Outcome asesed by treating physician	2-3 - Evidence of selective reporting and publication	5 - Unclear whether patients with metastatic disease should be excluded or whether age exclusion is clinically relevant	1,2 - Power calculations not reported or reported for primary outcome	

a Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias
b Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded to treatment outcome; 3. Outcome assessed by treating physician
c Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication
d Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. No intent to treat analysis (per protocol for non-inferiority trials)
e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference
f Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated

Major limitations of this study include the presence of selective publication and lack of blinding as patients were clinically evaluated for follow-up by the physician who had administered EBT or

MMS. The study is registered but result submissions have been canceled twice and have not been submitted as of January 2019. Since some patients received customized treatments, all intervention characteristics are unclear. Eligibility and exclusion criteria seemed to introduce bias with regard to age and low tumor stage. No statistically significant outcomes were reported for the use of EBT compared to MMS in NMSC.

Case Series

Evidence also includes uncontrolled studies. The main characteristics and results of published case series are summarized in Table 4.

Table 4. Case Series of Electronic Brachytherapy for Nonmelanoma Skin Cancer

Study	Population	N	MFU, mo	Treatment	Outcomes	
					Recurrence	Toxicity, %
Paravati et al(2015)[9]	Basal, squamous, or basosquamous cell carcinoma	127	16.1	• Axxent Xoft system • Total dose: 40 Gy in 8 fractions delivered 2 times weekly	1.2%[c](2/154)	Acute: • Grade 0-1=53 • Grade 2=34.4 • Grade 3=13 Late: • Grade 0-1=94 • Grade 2=6
Delishaj et al(2015)[10]	Nonmelanoma skin cancer	39	12	• Valencia applicator • Total dose: 40 Gy in 8 fractions	0%	Acute: • Grade 1=58 • Grade 2=5 Late: • Grade 1=19 • Grade 2=2
Tormo et al (2014)[11]	Basal cell carcinoma	32	47	• Valencia applicator • Total dose: 42 Gy in 6-7 fractions	3.1%	• Grade 1=NR • Grade 2=0 • Grade 3=0
Bhatnagar (2013)[1];Bhatnagar & Loper (2010)[12,a]	Nonmelanoma skin cancer	122	10.0	• Axxent Xoft system • Total dose: 40 Gy in 8 fractions delivered twice weekly	0%	• Grade 1=11 • Grade 2=13 • Grade 3=0
Gauden et al (2013)[13]	Small nonmelanoma skin cancers	200	66[b]	• Leipzig applicator • Total dose: 36 Gy in 12 fractions delivered daily	2%[c](4/236)	• Grade 1=71 • Grade 2=34 • Grade 3=0
Giux et al (2000)[14]	Basal or squamous cell carcinoma	136	60	• Brock applicator • Total dose: 60-65 Gy in 33-36 fractions	2.2%	NR ("no severe complications")

Gy: gray; MFU: mean follow-up; NR: not reported.
[a] Overlapping case series; results from larger, more recent publication reported.
[b] Median.
[c] Calculated based on number lesions not patients.

The largest series was published by Gauden et al (2013) and included 200 patients with 236 lesions (121 basal cell, 115 squamous cell).[13] Brachytherapy was the primary treatment modality in 69% of the lesions, while in the remaining 31% (74/236) brachytherapy was a follow-up treatment to surgery when there were positive margins. Outcomes included treatment efficacy, as measured by local recurrence rate, skin toxicity measured using Radiation Therapy Oncologic Group criteria, and cosmetic outcome using the Radiation Therapy Oncologic Group Cosmesis Scale. After a median follow-up of 66 months, there were recurrences in 2% (4/236) of treated lesions. Cosmetic outcome was judged to be excellent or good in 88% (208/236) of treated lesions. Grade 1 skin toxicity was common (71% of treated lesions); grade 2 toxicity was less common (34%); and no instances of grade 3 or higher toxicities were noted. Late hypo-pigmentation of treated skin was reported in 5.5% (13/236) of treated lesions.

Bhatnager (2013) published a case series using a commercially available device (Axxent eBx System).[1] The series included 122 patients with 171 nonmelanoma skin lesions. Most patients had either basal cell carcinoma (53%) or squamous cell carcinoma (41%); 10 (5.8%) patients had other types of cancer. Outcome measures included recurrence rates, adverse events using version 3.0 of the Common Terminology Criteria for Adverse Events, and cosmetic results using a standardized Cosmesis Scale. After a mean 10-month follow-up, there were no local recurrences. Dermatitis and pruritus were common early adverse events, occurring in 83% and 18% of the treated lesions, respectively. Skin hypopigmentation was the most common late adverse event, occurring in 10.9% of lesions at 1 year. Other late complications included rash (6.5%), alopecia (2.2%), and dry desquamation (2.2%). All patients had their cosmetic outcomes rated as good or excellent.

Summary of Evidence
For individuals who have nonmelanoma skin cancer who receive electronic brachytherapy, the evidence includes a systematic review and case series. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related morbidity. No controlled trials were identified that have compared electronic brachytherapy with alternative treatment options. A 2016 systematic review of case series found local control rates ranging from 83% to 100% and recurrence rates ranging from 0% to 17%. In most studies, the recurrence rate was less than 5%. In the absence of controlled studies, conclusions cannot be drawn about the efficacy and safety of electronic brachytherapy compared with other treatments for non-melanoma skin cancer. Controlled trials are needed in defined populations that compare electronic brachytherapy with alternatives, specifically other forms of radiotherapy or surgical approaches. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information
Practice Guidelines and Position Statements

National Comprehensive Cancer Network
The National Comprehensive Cancer Network guidelines on basal cell carcinoma (v.1.2020)[15] and squamous cell skin cancer (v.1.2020)[16] both contain the following statement on electronic brachytherapy: "There is insufficient long-term efficacy and safety data to support the routine use of electronic surface brachytherapy."

American Academy of Dermatology
In 2018, the American Academy of Dermatology published guidelines on the management of basal cell carcinoma[3] and the management of squamous cell carcinoma.[17] Electronic brachy-therapy was rated as a C recommendation, with the level of evidence of II and III. By comparison, surgery, cryosurgery, topical therapies, and photodynamic therapies are rated as A and B recommendations.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 5.

Table 5. Summary of Key Ongoing Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT03024866[a]	Electronic Brachytherapy: A Multi-Center Retrospective-Prospective Matched Pairs Cohort Study to Assess Long Term Clinical Outcomes of Nonmelanoma Skin Cancer Patients Treated with eBx Compared to Nonmelanoma Skin Cancer Patients Treated with Mohs Surgery	500	Jan 2018 (ongoing)*
NCT01016899[a]	Xoft Electronic Brachytherapy Clinical Protocol for the Primary Treatment of Non-Melanoma Skin Cancer	100	Feb 2018 (ongoing)**
NCT02131805	A Multicenter Pilot Study of Electronic Skin Surface Brachytherapy for Cutaneous Basal Cell and Squamous Cell Carcinoma	34	May 2021 (ongoing) ***

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.
*=Last updated clinicaltrials.gov January 2017-update for 2020-results not posted (status: unknown; preliminary results published but not submitted)
**=Last update posted to clinicaltrials.gov September 2017-update 2020-results not posted (status: active, not recruiting)
***=Last update to clinicaltrials.gov March 2020 (status: recruiting)

References

1. Bhatnagar A. Nonmelanoma skin cancer treated with electronic brachytherapy: results at 1 year. Brachytherapy. Mar-Apr 2013; 12(2): 134-40. PMID 23312675
2. Madan V, Lear JT, Szeimies RM. Non-melanoma skin cancer. Lancet. Feb 20 2010; 375(9715): 673-85. PMID 20171403
3. Kim JYS, Kozlow JH, Mittal B, et al. Guidelines of care for the management of basal cell carcinoma. J Am Acad Dermatol. Mar 2018; 78(3): 540-559. PMID 29331385
4. Alam M, Nanda S, Mittal BB, et al. The use of brachytherapy in the treatment of nonmelanoma skin cancer: a review. J Am Acad Dermatol. Aug 2011; 65(2): 377-388. PMID 21496952
5. Avril MF, Auperin A, Margulis A, et al. Basal cell carcinoma of the face: surgery or radiotherapy? Results of a randomized study. Br J Cancer. 1997; 76(1): 100-6. PMID 9218740
6. Delishaj D, Rembielak A, Manfredi B, et al. Non-melanoma skin cancer treated with high-dose-rate brachytherapy: a review of literature. J Contemp Brachytherapy. Dec 2016; 8(6): 533-540. PMID 28115960
7. 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. Aug 2017; 9(4): 338-344. PMID 28951753
8. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys. Mar 30 1995; 31(5): 1341-6. PMID 7713792
9. 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. Nov-Dec 2015; 5(6): e659-64. PMID 26432680

10. Delishaj D, Laliscia C, Manfredi B, et al. Non-melanoma skin cancer treated with high-dose-rate brachytherapy and Valencia applicator in elderly patients: a retrospective case series. J Contemp Brachytherapy. Dec 2015; 7(6): 437-44. PMID 26816500
11. Tormo A, Celada F, Rodriguez S, et al. Non-melanoma skin cancer treated with HDR Valencia applicator: clinical outcomes. J Contemp Brachytherapy. Jun 2014; 6(2): 167-72. PMID 25097557
12. Bhatnagar A, Loper A. The initial experience of electronic brachytherapy for the treatment of non-melanoma skin cancer. Radiat Oncol. Sep 28 2010; 5: 87. PMID 20875139
13. Gauden R, Pracy M, Avery AM, et al. HDR brachytherapy for superficial non-melanoma skin cancers. J Med Imaging Radiat Oncol. Apr 2013; 57(2): 212-7. PMID 23551783
14. Guix B, Finestres F, Tello J, et al. Treatment of skin carcinomas of the face by high-dose-rate brachytherapy and custom-made surface molds. Int J Radiat Oncol Biol Phys. Apr 01 2000; 47(1): 95-102. PMID 10758310
15. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Basal Cell Skin Cancer. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf. Accessed July 6, 2020.
16. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Squamous Cell Skin Cancer. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf. Accessed July 6, 2020.
17. Kim JYS, Kozlow JH, Mittal B, et al. Guidelines of care for the management of cutaneous squamous cell carcinoma. J Am Acad Dermatol. Mar 2018; 78(3): 560-578. PMID 29331386
18. Blue Cross Blue Shield Association. Medical Policy Reference Manual, No. 8.01.62 (July 2020).

Documentation for Clinical Review

- No records required

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	0394T	High dose rate electronic brachytherapy, skin surface application, per fraction, includes basic dosimetry, when performed
	0395T	High dose rate electronic brachytherapy, interstitial or intracavitary treatment, per fraction, includes basic dosimetry, when performed
	77261	Therapeutic radiology treatment planning; simple
	77262	Therapeutic radiology treatment planning; intermediate
	77263	Therapeutic radiology treatment planning; complex
	77280	Therapeutic radiology simulation-aided field setting; simple
	77285	Therapeutic radiology simulation-aided field setting; intermediate

Type	Code	Description
	77290	Therapeutic radiology simulation-aided field setting; complex
	77295	3-dimensional radiotherapy plan, including dose-volume histograms
	77300	Basic radiation dosimetry calculation, central axis depth dose calculation, TDF, NSD, gap calculation, off axis factor, tissue inhomogeneity factors, calculation of non-ionizing radiation surface and depth dose, as required during course of treatment, only when prescribed by the treating physician
	77301	Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications
	77306	Teletherapy isodose plan; simple (1 or 2 unmodified ports directed to a single area of interest), includes basic dosimetry calculation(s)
	77307	Teletherapy isodose plan; complex (multiple treatment areas, tangential ports, the use of wedges, blocking, rotational beam, or special beam considerations), includes basic dosimetry calculation(s)
	77316	Brachytherapy isodose plan; simple (calculation[s] made from 1 to 4 sources, or remote afterloading brachytherapy, 1 channel), includes basic dosimetry calculation(s)
	77317	Brachytherapy isodose plan; intermediate (calculation[s] made from 5 to 10 sources, or remote afterloading brachytherapy, 2-12 channels), includes basic dosimetry calculation(s)
	77318	Brachytherapy isodose plan; complex (calculation[s] made from over 10 sources, or remote afterloading brachytherapy, over 12 channels), includes basic dosimetry calculation(s)
	77321	Special teletherapy port plan, particles, hemibody, total body
	77331	Special dosimetry (e.g., TLD, microdosimetry) (specify), only when prescribed by the treating physician
	77332	Treatment devices, design and construction; simple (simple block, simple bolus)
	77333	Treatment devices, design and construction; intermediate (multiple blocks, stents, bite blocks, special bolus)
	77334	Treatment devices, design and construction; complex (irregular blocks, special shields, compensators, wedges, molds or casts)
	77338	Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan
	77370	Special medical radiation physics consultation
	77401	Radiation treatment delivery, superficial and/or ortho voltage, per day
	77402	Radiation treatment delivery, => 1 MeV; simple
	77407	Radiation treatment delivery, => 1 MeV; intermediate
	77412	Radiation treatment delivery, => 1 MeV; complex
	77417	Therapeutic radiology port image(s)
	77470	Special treatment procedure (e.g., total body irradiation, hemibody radiation, per oral or endocavitary irradiation)
HCPCS	G6001	Ultrasonic guidance for placement of radiation therapy fields
	G6002	Stereoscopic x-ray guidance for localization of target volume for the delivery of radiation therapy
	G6003	Radiation treatment delivery, single treatment area, single port or parallel opposed ports, simple blocks or no blocks: up to 5 mev
	G6004	Radiation treatment delivery, single treatment area, single port or parallel opposed ports, simple blocks or no blocks: 6-10 mev

Type	Code	Description
	G6005	Radiation treatment delivery, single treatment area, single port or parallel opposed ports, simple blocks or no blocks: 11-19 mev
	G6006	Radiation treatment delivery, single treatment area, single port or parallel opposed ports, simple blocks or no blocks: 20 mev or greater
	G6007	Radiation treatment delivery, two separate treatment areas, three or more ports on a single treatment area, use of multiple blocks: up to 5 mev
	G6008	Radiation treatment delivery, two separate treatment areas, three or more ports on a single treatment area, use of multiple blocks: 6-10 mev
	G6009	Radiation treatment delivery, two separate treatment areas, three or more ports on a single treatment area, use of multiple blocks: 11-19 mev
	G6010	Radiation treatment delivery, two separate treatment areas, three or more ports on a single treatment area, use of multiple blocks: 20 mev or greater
	G6011	Radiation treatment delivery, three or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, electron beam; up to 5 mev
	G6012	Radiation treatment delivery, three or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, electron beam; 6-10 mev
	G6013	Radiation treatment delivery, three or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, electron beam; 11-19 mev
	G6014	Radiation treatment delivery, three or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, electron beam; 20 mev or greater
	G6015	Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session
	G6016	Compensator-based beam modulation treatment delivery of inverse planned treatment using three or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session
	G6017	Intra-fraction localization and tracking of target or patient motion during delivery of radiation therapy (e.g., 3D positional tracking, gating, 3D surface tracking), each fraction of treatment

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
09/30/2015	BCBSA Medical Policy adoption
01/01/2016	Coding update
09/01/2016	Policy revision without position change
09/01/2017	Policy revision without position change
09/01/2018	Policy revision without position change
09/01/2019	Policy revision without position change
10/01/2020	Annual review. No change to policy statement. Literature review updated. Coding update.

Effective Date	Action
11/20/2020	No change to policy statement. Policy guidelines updated.
06/01/2021	No change to policy statement. Policy guidelines updated. Coding update.
08/01/2021	Annual review. No change to policy statement.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
Electronic Brachytherapy for Nonmelanoma Skin Cancer 8.01.62 **Policy Statement:** Electronic brachytherapy for the treatment of nonmelanoma skin cancer (see Policy Guidelines section) is considered **investigational.**	**Electronic Brachytherapy for Nonmelanoma Skin Cancer 8.01.62** **Policy Statement:** Electronic brachytherapy for the treatment of nonmelanoma skin cancer (see Policy Guidelines section) is considered **investigational.**