Clinical Review Criteria

Superficial Radiation Therapy
(Electronic Brachytherapy for Non-Melanoma Skin Cancer)

- “Xoft” Skin Treatments

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Criteria
For Medicare Members

<table>
<thead>
<tr>
<th>Source</th>
<th>Policy</th>
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<tbody>
<tr>
<td>CMS Coverage Manuals</td>
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<td>National Coverage Determinations (NCD)</td>
<td>None</td>
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<td>Local Coverage Determinations (LCD)</td>
<td>Brachytherapy: Non-intracoronary (L24281)</td>
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<td>Local Coverage Article</td>
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For Non-Medicare Members

There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or provides better long-term outcomes than current standard services/therapies.

The following information was used in the development of this document and is provided as background only. It is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

Background
Nonmelanoma skin cancer (NMSC) is the most common malignancy in the Caucasian population and its incidence continues to rise. It is estimated that more than two million Americans are affected by NMSC each year. Basal cell carcinoma (BCC) represents approximately 75% of NMSCs and squamous cell carcinoma (SCC) 25%. These cancers have a low mortality rate and are rarely life threatening, but can be disfiguring when not diagnosed and treated in a timely manner. They also have a significant impact on the health care delivery system (Alam 2011, Bhatnagar 2010 & 2013).

Treatment options for NMSC include surgery, radiation therapy, chemotherapy, and photodynamic therapy. Surgery is considered the gold standard therapy; it provides the highest cure rates and has satisfactory cosmetic results. Surgical techniques include excision, curettage with electrodesication, and Mohs micrographic surgery. The choice of procedure depends on the histologic type, size, and location of the lesion. Some patients however, are not suitable candidates for surgery because of their age, health condition, or potential disfigurement due to the location or type of cancer. Radiation therapy has been used for selected skin cancers, typically reserved as a second-line therapy for patients with surgical contraindications or as adjuvant therapy for high-risk lesions. It may also be a good alternative to surgery for lesions located in areas where surgery may be more difficult, lead to disfigurement, or affect structural function e.g. eyelid, ear, or nose. Radiation therapy techniques used for NMSC include superficial x-rays, orthovoltage x-rays and megavoltage photons, electron beam irradiation, and high-dose rate (HDR) brachytherapy with surface applicators or surface molds. HDR brachytherapy works via a precise, radioactive seed that delivers high dose radiation within specialized catheters to a targeted area within a shielded room. It is also commonly used for breast, lung, prostate and gynecologic cancers (Bhatnagar 2010 & 2013, Frakulli 2015, Linos 2015, Safigholi 2015).

Electronic brachytherapy (EBT) is a form of HDR brachytherapy that brings an electronic brachytherapy source in close proximity to the cancerous site. EBT has the potential benefit of providing shorter and more convenient form of radiotherapy without the use of radioactive isotopes, linear accelerators, or dedicated treatment vault, and with
minimal shielding requirements due to the low energy used. Currently there are three different EBT systems available for clinical application: Axxent by Xoft Inc. (Fremont, CA), the Intrabeam Photon Radiosurgery Device by Carl Zeiss Surgical (Oberkochen, Germany), and the Esteya by Elekta (Esteya EBS, Elekta AB-Nucletron, Stockholm, Sweden). The main component in these systems is a miniature X-ray tube that produces bremsstrahlung (electromagnetic) radiation using electron energies ranging from 20-70keV. Treatment of skin cancers by these systems is performed using conical applicators developed by the manufacturers and provided in different sizes (1cm, 2 cm, 3.5 cm, and 5 cm) Bhatnagar 2013, Safigholi 2015).

Medical Technology Assessment Committee (MTAC)

Electronic Brachytherapy for Non-Melanoma Skin Cancer

04/21/2014: MTAC REVIEW

Evidence Conclusion: The published study on EBT for the treatment of NMSC was identified by the literature search as a small case series with no control or comparison group (evidence table 1). A total of 122 patients with 171 NMSC lesions (from July 2009 to April 2012) received EBT to a dose of 40 Gy in eight fractions, delivered twice weekly. Patients were assessed for acute and late toxicities, cosmesis, and local control. In 2010 Bhatnagar and Loper retrospectively reported on the short-term (median 4.1 months) results of 37 patients (44 lesions); and in 2013, Bhatnagar published the outcomes of 42 patients (46 lesions) with one or more year follow-up data. The author reported that all lesions resolved with treatment, with no recurrences. The early side effects of the therapy were rash dermatitis (83% of the lesions) and pruritus (18%). Late adverse events included grade 1 hypopigmentation in 10% of the lesions, rash dermatitis (6.5%), as well as alopecia, and dry desquamation that occurred at lower rates (2.2%) each. One-year cosmetic evaluation was performed for 42 of the 46 lesions; 39 (92.9%) were graded as excellent, and 3/42 (7.1%) were good. Two-year outcome data for 22 lesions in 21 patients (Bhatnagar 2012) showed that cosmesis was excellent for 20 evaluable lesions, and good for 1. Based on these results the authors concluded that EBT provides a convenient nonsurgical option for NMSC patients. The study was a case series with its limitations and potential biases. EBT was not compared any other surgical procedure or radiation therapy; it had a short follow-up duration, and the authors did not discuss how patients were selected for the procedure, and whether there were any dropouts.

Bhatnagar A, the principal investigator of the study received a research grant from the industry sponsoring the study. Conclusion: There is insufficient published evidence to determine the safety and efficacy of EBT for the treatment of NMSC. There is an ongoing clinical trial “Electronic Brachytherapy for the Treatment of NMSC” (NLM Identifier NCT01016899) with the objective of recording the recurrence in patients treated for nonmelanoma (basal cell and squamous cell carcinomas) skin cancer using the Xoft Axxent Electronic Brachytherapy System. The trial will also evaluate the cosmetic outcomes and skin toxicities related to the treatment.


The use of electronic brachytherapy for non-melanoma skin cancer does not meet the Kaiser Permanente
Medical Technology Assessment Criteria.

03/21/2016: MTAC REVIEW

Electronic Brachytherapy (EBT) for the treatment of non-melanoma skin cancer (NMSC)

Evidence Conclusion: There is insufficient published evidence to determine whether the safety and efficacy outcomes of electronic brachytherapy for NMSC are as good or superior to the outcomes of alternative treatment options. There are no published randomized or non-randomized controlled trials that compared EBT to an alternative therapy for the treatment of NMSC. The available published evidence consists of case series that used different systems for the delivery of HDR. The largest series (Bhatnagar 2010 & 2013) that used one of the three commercially available devices (the Axxent system, Xoft Inc. Sunnyvale, CA) was reviewed by MTAC earlier in 2014, and did not provide sufficient evidence on the long-term efficacy or safety of the procedure. The more recent case series identified by the search were small retrospective series with no comparison groups, and do not provide additional evidence to support the use of EBT for NMSC. In a recently published article, Linos and colleagues (2015), expressed their concern regarding the increase in the use of EBT for skin cancer. The authors analyzed Medicare claims data and found that EBT use for skin cancer is increasing rapidly in the Medicare population. They indicated this may be attributable to marketing by the manufacturers, and that there is insufficient long-term data on the efficacy and safety of the therapy to cover the period during which recurrence and radiation sequelae would be expected (Linos, 2015).
**Articles:** The updated literature search for the use of electronic brachytherapy in the treatment of NMSC did not identify any controlled trial that compared the therapy with an alternative mode of treatment. The search only identified a number of small retrospective case series and a systematic review of the observational studies reporting on the outcomes of low-dose or high-dose brachytherapy used for the treatment of NMSC of the eyelid (Frakulli 2015).

The use of electronic brachytherapy for non-melanoma skin cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

There is insufficient long-term efficacy and safety data to support the routine use of electronic surface brachytherapy.

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<tr>
<th>Date Created</th>
<th>Date Reviewed</th>
<th>Date Last Revised</th>
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<td>05/06/2014</td>
<td>05/06/2014&lt;sup&gt;MPC&lt;/sup&gt;, 03/03/2015&lt;sup&gt;MPC&lt;/sup&gt;, 01/05/2016&lt;sup&gt;MPC&lt;/sup&gt;, 11/01/2016&lt;sup&gt;MPC&lt;/sup&gt;</td>
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<sup>MPC</sup> Medical Policy Committee

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<tr>
<th>Revision History</th>
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<tr>
<td>04/05/2016</td>
<td>Added MTAC review</td>
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<tr>
<td>04/25/2017</td>
<td>Added NCCN Guideline</td>
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**Codes**
CPT: 0182T, 0394T, 77401