Electronic Brachytherapy (eBx) Study

A Post-market Multi-Center Retrospective-Prospective Study to Assess Long-term Clinical Outcomes of Non-melanoma Skin Cancer Patients Treated with eBx

Protocol Number: CTPR-0019

Principal Investigator

Stephen Doggett, MD, FACR

Sponsor:
Xoft, Inc., a Subsidiary of iCAD, Inc.

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STUDY SITE PRINCIPAL INVESTIGATOR'S PROTOCOL SIGNATURE PAGE

A Post-market Multi-Center Retrospective-Prospective Study to Assess Long-term Clinical Outcomes of Non-melanoma Skin Cancer Patients Treated with eBx

The Study Site's Principal Investigator's Signature signifies acceptance of this Multi-Center Retrospective-Prospective Follow-up Study of Patients Treated with Electronic Brachytherapy for the treatment of Non-melanoma Skin Cancer (NMSC) and agrees to participate in the study in accordance with the protocol and protocol requirements stated herein:

1. Willingness to work with study project manager to facilitate study progress;
2. Adherence to applicable IRB requirements and willingness to comply with all applicable regulations and applicable good clinical practice guidelines;
3. Protocol compliance, including willingness to complete all relevant study documentation legibly;
4. Maintenance of confidentiality at all times;
5. Willingness to allow clinical research associates, at reasonable times agreed upon by the site and sponsor, to inspect all records pertaining to this trial; and
6. Willingness to agree to and sign the Investigator Agreement Page in this protocol indicating the protocol will be followed.

_____
Study Site Name

_____
Study Site Principal Investigator Signature

_____
Site Principal Investigator's Printed / Typed Name

_____
City, State, Zip

2 PROTOCOL SYNOPSIS

STUDY NAME	A Post-market Multi-Center Retrospective-Prospective Study to Assess Long-term Clinical Outcomes of Non-melanoma Skin Cancer Patients Treated with eBx
PRINCIPAL INVESTIGATOR	Stephen W. Doggett, MD, FACR
SITES	Up to 5 sites will participate
STUDY DESIGN	This is a retrospective-prospective post-market, on-label, observational study. Patients who completed eBx treatment ≥ 5 years ago since final treatment will be identified and any existing data in the patient's record will be collected in addition to conducting follow-up visits for long-term follow-up. The study will include 2 parts: 1. Retrospective Chart Review: Collect data from patient records who completed eBx treatment a minimum of five years prior to study onset. The history and demographic data will be retrospectively collected from up to 300 subjects previously treated with eBx for the treatment of NMSC. 2. Prospective Follow-up: Patients will either return for a minimum of five-year long-term follow-up visits or telehealth (video) for the investigators to assess the lesion site, document absence/presence of local recurrence and long-term skin toxicities after treatment.
SAMPLE SIZE	Up to 300 patients will return for follow-up a minimum of five years post eBx treatment.
STUDY OBJECTIVES	1. To evaluate local recurrence of eBx treated lesions in subjects with a minimum of five-year follow-up. 2. Assess long-term skin toxicities.
PRIMARY EFECTIVENESS ENDPOINT	Absence of local recurrence at ≥ 5-year follow-up at treatment site(s).
SECONDARY SAFETY ENDPOINT	Occurrence of long-term skin toxicities.
ESTIMATED STUDY PERIOD	Follow-up Visits: Estimated to occur over 6 months.
SPONSOR & FUNDING PARTY	Xoft, Inc., a Subsidiary of iCAD, Inc. 98 Spit Brook Road, Suite 100 Nashua, NH 03062
STATISTICAL ANALYSES, STUDY MANAGEMENT, EDC, MEDICAL WRITING	Eminence Clinical Research, Inc. 13521 Northgate Estates Drive Suite 150 Colorado Springs, CO 80921

3 STUDY CONTACTS

PRINCIPAL INVESTIGATOR

Stephen Doggett, MD, FACR

DrDoggett@nocancer.com

STUDY SPONSOR

Xoft, Inc., a Subsidiary of iCAD, Inc.
98 Spit Brook Road, Suite 100
Nashua, NH 03062

CLINICAL STUDY CONTACTS

Patricia Rohne-McCarthy, RN, RCES
Eminence Clinical Research, Inc.
Sr. Clinical Research Associate
Phone : 719-400-7463
Email: pmccarthy@ecr-inc.com

Grace Millholland, PhD
Eminence Clinical Research, Inc.
Clinical Trial Assistant
Phone : 719-400-7463
Email: gmillholland@ecr-inc.com

SPONSOR CONTACT

Crystal Leonard, CCRP
Xoft, Inc., a Subsidiary of iCAD, Inc.
Phone: (937) 503-8588
cleonard@icadmed.com

4 INTRODUCTION AND BACKGROUND

More than one million skin cancer cases occur annually.[1] Most of these forms of skin cancers are curable. Carcinoma is a medical word for a cancer that starts in a lining layer of cells such as the skin or the lining cells of the digestive system. There are many types of keratinocyte cancer, but two types of epithelial skin cancers are most common, basal cell carcinoma (BCC) and squamous cell carcinoma (SCC).

Epithelial skin cancer is a common neoplasm that affects more than a half of a million people each year. The most serious of skin cancers is melanoma, which was diagnosed in approximately 60,000 people in 2007. However, the majority of these lesions, estimated to be eighty to ninety percent, are basal cell cancers and the remainder is categorized as squamous cell.

Both types of malignancies are related to ultraviolet light exposure from the sun.[1-3] Basal cell cancer begins in the lowest layer of the epidermis, the basal cell layer. About eight out of ten skin cancers are BCCs. They usually begin on areas exposed to the sun, such as the head and neck. BCC was once found mostly in middle-aged or older people, in the fourth decade of life and beyond. But now it is also being seen in younger people. This may be because people are spending more time in the sun without protecting their skin. BCC tends to grow slowly. It is very rare for a basal cell cancer to metastasize. But if left untreated, it can grow into nearby areas and spread into the bone or other tissues beneath the skin.

SCCs are more likely to spread into fatty tissues just beneath the skin. They are also more likely to spread to lymph nodes or to distant parts of the body than are BCCs, but this is not common. With thorough screening these neoplasms can be identified at an early stage. With the selection of the appropriate treatment option, these cancers can result in excellent local control with excellent cosmesis results.[1, 2]

There has been a diverse variety of modalities developed for the treatment of basal cell and SCC over the years, from surgical excision to Mohs micrographic surgery, to radiation therapy. The location of the cancer and the extent of the disease effect the treatment options available to patients.[3] The following section provides an overview of the different treatment modalities published in the literature.

Lovett et al reported on 339 patients who were consecutively treated for histologically confirmed basal cell (71%) and squamous cell (29%) carcinoma.[5] A retrospective study was performed to assess local recurrence. The majority of the basal cell lesions (93%) and 97% of the SCCs were on the head. Radiation therapy was the initial treatment modality in 212 patients, and 127 patients were treated with radiation therapy after the initial surgical excision failed. Tumor control was analyzed by the type of external beam radiation therapy administered. The local control for superficial x-ray ranged from 91 to 100% reported categorically by tumor size.

Electron beam ranged from 70 to 75% local control. Patients were stratified into groups by the type of radiation beam used on the treatment. Excellent to good cosmesis was seen in 97% of the patients treated with superficial X-rays and in 78% of the patients treated with electrons, 78% of the patients treated with mixed beams, and in 80% of the patients treated with megavoltage photons. The overall complication rate (complications were defined as grade 4 toxicities[4]) for the 310 patients whose data was available was 5.5%. Of the 217 previously untreated patients, the complication rate was 3.2%.[5]

Silva et al report on a retrospective review of radiation therapy treatment for basal cell, squamous cell, and basal-SCC from 313 patients with 334 lesions treated. The objective of this study was to assess local control and late toxicities in patients treated with radiation therapy for the treatment of cancer of the pinna of the ear. For 270 patients, radiation therapy was the primary treatment, 50 patients received radiation therapy for recurrent cancer that had not previously undergone resection, and 12 patients received radiation therapy as an adjuvant treatment.[6]

Orthovoltage X-ray radiation therapy (100-250 kV) was used in 83% of the patients, and electron radiation therapy was used in approximately 12%. The rest were treated with megavoltage X-rays (primarily ^{60}Cobalt). The prescriptions were as follows: 17.5 Gy-20 Gy in one fraction, 35 Gy in five fractions with 7 Gy per fraction, 42-45 Gy in ten fractions with 4.2 to 4.5 Gy per fraction, and 50 to 60 Gy divided among 20 to 30 fractions with less than 3 Gy per fraction. Thirty-five (35) Gy was prescribed for 124 of the 313 patients. The follow-up ranged from 0.12 to 13.37 years. The primary endpoint was time to local failure, and the secondary endpoint was significant grade 4 late toxicities. Local control rate was reported to be 9% for patients who present with early-stage cancer with tumor size 2cm or less in diameter. Orthovoltage X-ray radiation therapy has been shown to be efficacious primary treatment for squamous cell and BCC.[6]

Chan et al report on a single center experience for the treatment of basal cell and SCCs. They studied 1005 lesions treated with single fraction radiotherapy. This retrospective chart review took place ten years later to allow for follow-up. All patients were treated with 45-100 kV X-ray. The radiation doses administered were 22.5 Gy, 20 Gy and 18 Gy. The 18 Gy prescription was reserved for patients who were considered frail or had very small tumors. The study endpoints were recurrence and late necrosis over a ten-year period. There was no difference in the recurrence rate for the group treated with 20 Gy versus 22 Gy, but there was a significant increase in late skin necrosis rate ($p=0.002$). Most tumors were in the head and neck regions. One subgroup in this study, patients who received radiation therapy for the treatment of cancer of the inner canthus of the ear, showed a higher recurrence rate because of the concavity, or standoff, of the treatment area. Chan concluded that a standoff of 0.5 cm-1.5 cm would cause the radiation dose to decrease by six to 23%.[2]

Guix et al. published their series of 136 patients with basal cell or SCC of the skin of the face treated with surface molds and Ir-192 HDR brachytherapy with 98% 5-year local control rate with no severe early or late complications detected.[7]

Other treatment options for patients with basal cell or SCCs include curettage, Mohs surgery and conventional surgery. Curettage has been said to be quick, requires minimal equipment, and is associated with a cure rate of 90% or better for select low-risk skin cancers. With this strategy, however, there is no margin control, and healing and cosmesis can be variable; moreover, it is not a very effective treatment for high-risk tumors and tumors in certain locations.[3, 5, 6]

A common treatment for non-melanoma skin cancer (NMSC) has been Mohs surgery, which uniquely orients, maps, and processes removed tissue, permitting the microscopic evaluation of virtually 100% of the specimen margins. The completeness of this margin control permits the accurate identification and removal of all tumor extensions under the microscope. Tissues in Mohs surgery are processed as modified frozen sections which allow the accurate and rapid interpretation of most skin cancers.[6,9] For those patients where surgical resection is not an option, primary treatment with radiation therapy was selected for patients whose data will be collected in this study. The treatment approach was individualized based on specific risk factors, and patient characteristics for the most acceptable cosmetic and functional outcome.[10, 11]

5 STUDY RATIONALE

Non-melanoma skin cancers, BCC and SCC, are the most prevalent of all skin cancers. Multiple publications have shown that radiation therapy using kilovoltage X-rays is a viable option for the treatment of BCC and SCC but treatment must be individualized to determine if radiation therapy should be an adjuvant therapy following surgical resection or if the radiation therapy is the primary treatment for skin cancer. Local recurrence rate varies depending on the histology, BCC versus SCC. SCC has a higher recurrence rate than BCC; deaths have been attributed to the recurrence of SCC.[2, 5, 6, 11-14]

Brachytherapy has the advantage of delivering a high dose to the tumor while sparing the surrounding normal tissues. With proper case selection and delivery technique, high-dose rate (HDR) brachytherapy has great promise, allows short treatment times, and can be performed on an outpatient basis.[15] The Xoft Axxent Electronic Brachytherapy (eBx) System allows for the administration of high dose rate brachytherapy treatments using an electronic source. The Xoft Axxent System Controller and Source are cleared by the United States Food and Drug Administration to deliver high dose rate X-ray radiation for brachytherapy.

A matched pairs study was completed previously comparing eBx treatment outcomes to Mohs surgery outcomes. The median follow-up was three years. Local recurrence, toxicities, and cosmesis were the endpoints.[16] Because of the excellent cosmetic outcomes evident in this study at three years, the physicians rated cosmesis as “excellent” or “good” in 97.6% of EBx-treated

lesions, and 95.7% of MMS-treated lesions, cosmetic outcomes in this study will not be collected.[16] It is most important to understand the long-term recurrence rates for this treatment option. The rationale for this retrospective data collection study is to understand longer-term outcomes in patients treated with eBx for the treatment of both BCC and SCC NMSC.

6 STUDY PURPOSE

The purpose of this retrospective-prospective study is to evaluate lesions after treatment for BCC or SCC NMSC in order to gain a better understanding of the durability of the treatment, and risk of late toxicities for this patient population.

7 STUDY DESIGN, ENROLLMENT, AND DURATION

7.1 Study Design

This is a retrospective-prospective study design. The study is post-market, on-label observational study for the treatment of NMSC. Patients who completed treatment at least five years from the last treatment will be identified and existing data as required by this protocol in the patient's record will be collected in addition to conducting office visits or telehealth visits (video) for long-term follow-up.

The study will include:
Identifying patients, retrospectively, who completed treatment a minimum of five years from the last treatment. The history and demographic data will be collected from up to 300 subjects previously treated with eBx for the treatment of NMSC. Patients will have an office visit or telehealth visit in order for the investigators to assess the lesion site, document absence of recurrence, treatment for recurrence (if applicable), and long-term toxicities at the time of the prospective visit.

7.2 Sample Size

Up to 300 subjects treated with eBx will have data collected retrospectively from the patient's medical records, and prospectively at the time of the follow-up visit for those who agree to participate in this study. Up to three lesions per subject may be included in this study. The sample size will include those who were treated previously with eBx per the standard of care treatment as published in Patel et al and Doggett et al.[16-17]

7.3 Study Objective

Evaluate long-term local recurrence (≥ 5 years post-treatment) of eBx treated lesions at follow-up.

7.4 Primary Effectiveness Endpoint

Absence of local recurrence at ≥ 5-year follow-up at treatment site(s).

7.5 Secondary Safety Endpoint

Occurrence of long-term skin toxicities at the prospective follow-up visit.

7.6 Eligibility Criteria

7.6.1 Inclusion Criteria All answers must be YES to have lesions included in this study.

1. Previously completed treatment for non-melanoma skin cancer using Xoft eBx Electronic Brachytherapy System according to standard of care;[16]
2. Provides informed consent;
3. Greater than 40 years of age;
4. Pathological diagnosis confirmed to be squamous cell carcinoma, or squamous cell carcinoma-in-situ, or basal cell carcinoma prior to treatment;
5. Cancer Staging included in this study:
    - Stage 0: Tis, N0, M0
    - Stage 1: T1a, b, c, N0, M0
    - Stage 2: T2a, N0, M0

7.6.2 Exclusion Criteria

All answers must be NO to have lesions included in this study.

1. Target area is adjacent to a burn scar;
2. Any prior definitive surgical resection of the cancer, prior to Radiation Treatment;
3. Known perineural invasion;
4. Actinic Keratosis;
5. Known spread to regional lymph nodes;
6. Known metastatic disease;
7. Lesion treated with Mohs surgery.

8 METHODOLOGY

8.1 Identifying the Population

The first phase of this study will be to identify patients who completed treatment with eBx at least five years ago prior to study onset and collect history and demographic data, and eligibility data retrospectively from the patient records and on source worksheets.

This phase will include a review of the site's medical records to determine if the source documentation contains the variables that are needed to determine eligibility, and which will be used in the endpoint analyses.

These variables include:

Patient Age

Pathology report for evidence of:

- Lesion size (cm) / TNM stage
- Lesion diagnosis (BCC, SCC)

Last treatment date for each location

Lesion location (e.g. face, extremities, neck, nose, scalp, torso)

Data Collected Prospectively:

Recurrence of cancer at prospective follow-up visit

Recurrence occurred prior to prospective follow-up visit

Long term skin toxicity (graded according to CTCAE v.5)

8.2 Long-term Follow-up Visits

Patient Selection: Patients who are due for their annual skin assessment with a minimum of five years since their last eBx treatment will be selected to call for an appointment. The patients who were in prior studies will be called from a list kept at the study sites. Additional patients who were not in the previous studies will be contacted if they meet eligibility criteria. The patient will be told about the study and asked if they would be willing to participate in the Xoft study through an on-site or remote telehealth appointment.

On-site Visits: Patients agreeable to participating that return for an office visit for prospective data collection will be offered $100.00 compensation for his/her time and effort required to participate in this study. Written informed consent will be required for participation in the study.

Remote Visits: Patients agreeable to participating that choose a remote visit by video, such as Zoom or Web-Ex or another video conference platform will be offered $100.00 compensation for his/her time and effort to participate in this study. Verbal informed consent documented by the study staff will be required for participation in the study. Signed informed consent will be waived.

9 ADVERSE EVENTS - SAFETY

The late skin toxicities that potentially occur in these subjects are primarily mild and typically hypopigmentation and telangiectasia. All late skin toxicities at the time of the visit will be documented and graded according to CTCAE current version.

10 RISKS

Given the nature of this trial there are no risks related to the eBx treatment in this trial, as the treatment occurred previously, five or more years ago. The only risk is to confidentiality of information. The study sites will maintain confidentiality at all times. No subject identifiers will be published or presented from this study. The sponsor and sponsor representatives shall maintain confidentiality at all times.

11 STUDY MANAGEMENT

11.1 Site Requirements and Selections

Study sites will be those that previously participated in the matched pair study with a retrospective-prospective study design. Sites will be associated with and under the approval of an Institutional Review Board (IRB) [45 CFR 46.10(b)]

Sites selected have expressed an interest in the conduct of a controlled study to collect and report long-term outcomes of eBx for the treatment of non-melanoma skin cancer. Each site will execute a clinical trial agreement with the sponsor. The contract will be executed prior to first subject enrollment at the site.

Case report forms will be used to collect data for the prospective visits. These will also be considered source documentation for data not in the patient medical record.

11.2 Principal Investigator

Stephen W. Doggett, MD, FACR – San Diego Dermatology and Laser Institute, San Diego, CA.

11.3 Investigator Responsibilities

The following responsibilities are required for investigators participating in this study:

1. Have adequate experience in skin cancer treatment and therapies as documented on the physician's Curriculum Vitae (CV).
2. Be familiar with all regulatory requirements associated with the conduct of a clinical investigation and have the desire and time to comply with the requirements of this study.
3. Have access to an appropriate medical facility, staff, training, and equipment necessary for the conduct of this study.
4. Always observe confidentiality throughout this study.
5. Conduct research under an IRB that oversees the conduct of research studies.
6. Have primary responsibility and oversight of this study for the accuracy, legibility and security of all subject data.
7. Have an adequate patient population to meet study requirements.
8. Follow the protocol procedures and provide the clinical monitor with accurate data in a timely manner.

9. Provide direct access to complete patient medical records for the purposes of conducting source document verification by monitoring, audits, IRB review and regulatory inspections(s) throughout the duration of the study.
10. Provide current (signed and dated) CV to the Sponsor at time of site qualification.
11. Provide current medical license to the Study Management at time of site qualification.
12. Sign and date the Protocol Signature Page to signify agreement to participate in this study and comply with all protocol requirements.
13. Attend the Site Initiation Visit as provided by CRO (web-based presentation or on-site) to ensure understanding of the study requirements, case report forms, and data collection.
14. Identify a study coordinator for this study. Working with and under the authority of the Principal Investigator, the study coordinator assures that all study requirements are fulfilled and is the contact person at the site for all aspects of study administration.
15. Maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.

11.4 Sponsor Responsibilities

Xoft is the manufacturer of the Axxent® eBx System and the Sponsor of this study. Xoft has overall responsibility for the study and shall delegate study management to the CRO:

1. Select qualified Principal Investigators and study sites.
2. Select qualified monitors.
3. Provide the Protocol and any subsequent amendments to the centers.
4. Provide appropriate information and training to Investigators and study staff.
5. Ensure that all variations from the protocol are reviewed with the appropriate investigator(s), where appropriate, are reported to the relevant authorities and IRBs.
6. Ensure uniform data collection and protocol compliance.
7. Provide site initiation training (remote or on-site) that will include review of the protocol, Case Report Form (CRFs), CRF completion guidelines,
8. Retain ownership of all clinical data generated in this study and control the use of the data.
9. Protect patient confidentiality.
10. Collect, store and keep secure the following documents:
    a. A current, signed, and dated Curriculum Vitae for each site PI
    b. Current medical license for each site PI
    c. The IRB opinions and/or approvals, in writing, and relevant correspondence
    d. IRB approved informed consent form
    e. Protocol signature page signed by the PI at each site

11.5 Monitor Responsibilities

Study site monitoring (remote or on-site) will be performed by the CRO. Each site will be monitored on-site or remotely on a regular schedule to ensure that the study is conducted in

compliance with sponsor requirements, the protocol, GCP, and the applicable regulations. The monitor will also ensure that the data reported is consistent with the information found in the subject's medical records (source data verification) and in source documents. Monitoring will include the assessment of the site's overall progress, including but not limited to the site's ability to keep accurate records and to report study-related data to the sponsor in a timely fashion. Monitoring of each site will be performed according to the CRO's Interim Monitoring Visits Standard Operating Procedure (SOP) and the monitoring plan. In order to appropriately monitor the progress of the study, the site will provide the sponsors and/or its designees access to all source documents and other information necessary to ensure investigator compliance with the protocol and applicable rules and regulations, and to assess the progress of this study.

The sponsors designees will maintain contact with the investigator and staff throughout the duration of the study by phone, e-mail, and remote or on-site visits. The monitor will compile and file a monitoring report for each visit. Monitoring will ensure continued protocol compliance, adequate patient enrollment, and accurate data reporting.

The monitor will verify:

1. Informed Consent Forms (ICF)s for on-site visits will be obtained from each subject prior to the participation in this study, and the ICF process is clearly and contemporaneously documented in the medical record.
2. For remote visits, informed consent will be provided verbally by the participant prior to commencing with the prospective data collection at the time of the visit. The signature on the informed consent will be waived for remote visits.
3. The data in the CRF are completed and recorded and provided to the study management team (CRO), in a timely manner.
4. Findings of non-compliance are reviewed with the Investigator(s) and disclosed in a written monitoring report
5. Source Data Verification – Risked based monitoring will be implemented, and source data verification will be performed according to the monitoring plan for the Xoft Study.
6. Site Close-Out: At the time of the site close-out visit, the site monitor will collect all outstanding study documents, ensure that the investigator's files are accurate and complete, review record retention requirements with the investigator, and ensure that all applicable requirements are met for the study.
7. Study Materials: Each Site will receive all the necessary materials needed to initiate and participate in this clinical study. The materials include, but are not limited to:
    - Regulatory Binder and Contents
        1. Protocol
        2. Delegation of Authority Log
        3. Subject Screening Log
        4. Training Log
    - Subject Binder
        1. CRFs
        2. Tab for ICF

12 INFORMED CONSENT PROCESS: ON-SITE VISITS AND REMOTE VISITS

12.1 On-site Visits Informed Consent

Potential study subjects will be called to determine interest in participation in the Xoft follow-up study. Should the person be interested, the patient will be scheduled for a follow-up appointment that is in line with the next clinic visit required by insurance or Medicare. Once the patient arrives at the office, the study will be explained, and the consent will be reviewed and any questions the patient may have will be answered. Should the patient agree to be a participating study subject, the informed consent will be signed and dated by the patient and the person providing informed consent. The subject will receive a copy of the consent and proceed with the visit. The investigator (MD or other healthcare professional) who is qualified to participate as an investigator shall assess the treatment locations and document if there is a local recurrence or late toxicity and grade the late toxicity according to CTCAE criteria. Once this is complete the subject has completed study participation.

12.2 Remote Visits Informed Consent

Potential study subjects who choose to participate remotely by a video conference will be scheduled for a call that meets the regulatory requirements of a visit. The video will start with the delegated site personnel reviewing the elements of the informed consent for this study. Once the consent has been provided verbally, the visit may begin. In this scenario, the waiver of informed consent documentation applies. The study site personnel will document that they provided informed consent and that the patient provided verbal approval and consent to participate, with a written informed consent form being waived for these subjects. All California sites will be required to obtain subject acknowledgement/signature in agreement with the California Bill of Rights. The investigator (MD or healthcare provider) who is qualified to participate as an investigator shall remotely assess the treatment locations and document if there is a local recurrence or late toxicity and grade the late toxicity if applicable. Once this is complete, the subject has completed study participation.

Should there be a situation where the lesion on a remote participant is suspect for a recurrence development, the site will proceed with standard of care.

13 STATISTICAL CONSIDERATIONS

13.1 Data Collection

Data will be collected at the study site on case report form and will be entered into the online database by site and/or ECR personnel. The EDC system for the on-line database will be HIPAA compliant and 21 CFR compliant. The data entry personnel will be

separate from the monitoring personnel. Double data entry will take place to ensure accuracy. The following data collection requirements are listed below:

Table 1. Case Report Forms

Form Name	Retrospective Chart Review	Prospective Follow-up and Data Collection
Demographics and History	X	
Eligibility	X	
Assessment of Local Recurrence		X
Assessment of Late Skin Toxicities		X
Grading of Late Skin Toxicities		X

13.2 Statistical Analyses

This is a multi-center, retrospective-prospective study comparing non-melanoma skin cancer treatment (basal cell carcinoma and squamous cell carcinoma) using Xoft electronic brachytherapy (eBx) results. The primary endpoint is freedom from recurrence at five-year follow-up or longer. The secondary safety endpoint is late skin toxicities as assessed at the time of the prospective follow-up visit. This study is not powered, as it is for the purpose of reporting the number and percent of subjects who had a recurrence and the number and percent of subjects who showed a late skin toxicity at the follow-up visit. The data will be analyzed and reported by subject and by lesion. The final analysis from the study will be reported as descriptive statistics, both categorical and continuous variables, as appropriate.

14 PUBLICATIONS AND PRESENTATIONS

The analyses from this study shall be published and presented by the sponsor. Should an investigator from a study site wish to publish or present the data, this must be pre-approved by the study sponsor. The sponsor has the right to present the data first prior to sites presenting site data and multi-center data.

15 GLOSSARY

TERM OR ABBREVIATION	DEFINITION	
BCC	Basal Cell Carcinoma	
21 CFR Part 11	Title 21, Code of Federal Regulations Part 11: Electronic Records, Electronic Signatures https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=11	
CRF	Case Report Form	
CRO	Contract Research Organization	
CTCAE	Common Terminology Criteria Adverse Events	
eBx	Electronic brachytherapy treatment with Xoft	
EDC	Electronic Data Capture	
N0	No lymph node involvement	
M0	No metastases	
SCC	Squamous Cell Carcinoma	
Tis	Tumor in stage 0; abnormal cells are found in the squamous cell or basal cell layer of the epidermis; also called carcinoma in situ.	
Tumor Stages	8th Edition	7th Edition[18]
T1a	Lesions ≤ 1cm	Lesions ≤ 2cm
T1b	Lesions >1 and ≤ 2cm	Lesions >2 and ≤ 3cm
T1c	Lesions >2 and ≤ 3cm	N/A
T2a	Lesions > 3 and ≤ 4cm	Lesions > 3cm, lesions must be ≤ 4cm

16 REFERENCES

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