DERMATOLOGY ASSOCIATION of RADIATION THERAPY™

Appropriate Use Criteria for the Treatment of Basal Cell Carcinoma (BCC) Using Image-Guided Superficial Radiation Therapy

(Version 1.2024)

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I. BACKGROUND AND STANDARDS

Use of Multidisciplinary Team

Radiotherapy has recently experienced a renaissance in the treatment of nonmelanoma skin cancer (NMSC). The gold standard treatment that has emerged is called Image-Guided Superficial Radiation Therapy (IGSRT). IGSRT combines high-resolution dermal ultrasound (HRDUS) imaging with superficial radiation therapy.

To optimize patient outcomes, IGSRT should be delivered in the dermatology setting by a board-certified dermatologist with a multidisciplinary team (MDT) in accordance with the Dermatology Association of Radiation Therapy (DART) Appropriate Use Guidelines. The MDT must include a board-certified radiation therapist (RTT) for treatment delivery of IGSRT under the supervision of the prescribing dermatologist. The MDT must also include access to a board-certified radiation oncologist, a medical physicist, and organized weekly national Grand Rounds. Grand Rounds assist dermatologists with complex scenarios such as dose decay calculations, inverse square calculations, and review of beam parameters and field placement to determine whether the anatomic location of the current NMSC overlaps with previously radiated fields, as well as the latest clinical data and research regarding the optimal indications and contraindications in the treatment of NMSC of all modalities. Dermatologists and their RTTs must be trained in how to utilize IGSRT and how to present challenging cases to Grand Rounds so that they can access the support of the MDT at any time. Once this training is accomplished, the dermatologist has met all qualifications necessary to safely and effectively perform IGSRT with ongoing support from the MDT.

The 2024 National Comprehensive Cancer Network (NCCN) guidelines suggest that "the determination of the appropriateness of radiation therapy (RT) should be determined by a radiation oncologist".[1] DART notes that this NCCN suggestion does not apply to dermatologists supported by a MDT, as long as that MDT includes general access to a radiation oncologist.

The treatment of NMSC has long been a substantial component of clinical practice for dermatologists who are well versed in the numerous available therapeutic options including, but not limited to, superficial radiation therapy (SRT).[2] Dermatologists are widely regarded as the skin cancer experts who have safely and effectively used office-based SRT to treat NMSC for over a century.[2] Supporting these skin cancer experts with a MDT provides more than enough expertise to "determine the appropriateness of RT".[1]

II. BCC CRITERIA

BCC tumors must be Tis, T1 or T2 lesions according to the American Joint Committee on Cancer (AJCC) guidelines 8th ed.[3] (NB While AJCC 8th Ed.)[3]

BCC Tumors Can Be Low or High Risk According to 2024 NCCN Guidelines[1]

RISK OF RECURRENCE FOR BCC TUMORS[1]		
	Low-Risk Factors	**High-Risk Factors***
Location/size	Trunk or extremities with <2.0 cm diameter	Trunk or extremities with ≥2.0 cm diameter Tumors of any size located on the head, neck, hands, feet, pretibial, and anogenital area
Borders	Well defined	Poorly defined
Tumor occurrence	Primary	Recurrent
Immunosuppression	No	Yes
Prior radiation therapy	No	Yes, if current tumor is located at same site as prior treatment
Histologic subtypes	Nodular, superficial, keratotic, infundibulocystic, fibroepithelioma of Pinkus	Basosquamous, infiltrative, sclerosing/morpheaform, micronodular, carcinosarcomatous
Perineural Involvement (PNI)	No	Yes

*Any high-risk factor places the patient in the high-risk category.[1]

Advanced/Neglected BCCs are only appropriate for IGSRT after surgical debulking or shrinkage via hedgehog inhibitors (HHIs), such as vismodegib or sonedegib, until tumor depth is confirmed via HRDUS imaging to be 2.0 mm or less in thickness. Modified dosing of HHIs to reduce side effects is appropriate per NCCN.[1,4]

III. CONTRAINDICATIONS

ABSOLUTE CONTRAINDICATIONS[1,4]

Gorlin's Syndrome
(Basal Cell Nevoid Syndrome)

Xeroderma Pigmentosum

Ataxia Telangiectasia

Previous ionizing radiation at proposed treatment site

RELATIVE CONTRAINDICATIONS[1,4]

Ehlers-Danlos Syndrome

Scleroderma

Mixed Connective Tissue Disease

Systemic Lupus Erythematosus

IV. DIAGNOSIS, STAGING AND USE OF IGSRT

BCC Tumors - Role of HRDUS Imaging in Diagnosis and Staging

Pathology reports are often prone to sampling error, i.e., "tumor is transected at the base, so a deeper component cannot be ruled out in these sections". These "partial" pathology reports should be considered preliminary diagnoses. HRDUS imaging is performed on the anatomic site to measure depth and evaluate tumor shape and morphology after the biopsy. The HRDUS images are evaluated in the context of the preliminary histologic diagnosis to see if the findings match (confirmatory) or differ (revelatory).

Confirmatory HRDUS Imaging

A pathology report diagnoses a superficial BCC, transected at the base. HRDUS imaging shows a thin "ribbon-shaped" tumor without an invasive border. This image has confirmed that the diagnostic subtype is indeed superficial BCC.

Revelatory HRDUS Imaging

A pathology report diagnoses a superficial BCC, transected at the base. HRDUS imaging shows a round tumor without an invasive border. This image has revealed that the diagnostic subtype is actually a nodular BCC.

EXAMPLE 1

Pathology report #1 diagnoses a superficial BCC, transected at the base. Post-biopsy HRDUS imaging shows a residual round tumor, without an infiltrative/invasive border that is 1.8 mm deep. This image has revealed that the diagnostic subtype is definitely not a superficial BCC because it lacks a "thin ribbon" morphology. The round tumor shape on the HRDUS imaging is most consistent with a diagnosis of nodular BCC. The absence of an infiltrative or invasive morphology makes a sclerotic/morpheaform BCC less likely.

The depth of 1.8 mm is classified as low risk without the presence of high-risk factors. The patient is an IGSRT candidate.

EXAMPLE 2

Pathology report #2 diagnoses a superficial BCC, transected at the base. Post-biopsy HRDUS imaging shows a residual tumor with an infiltrative/invasive border that is 3.0 mm deep. This image has revealed that the diagnostic subtype is definitely not a superficial BCC. The presence of an infiltrative or invasive morphology makes a sclerotic/morpheaform BCC the most likely diagnosis. In either case, we know the exact depth and the infiltrative morphology of this BCC prior to starting IGSRT.

The depth of 3.0 mm and infiltrative morphology means the BCC is classified as high risk. The patient is an IGSRT candidate, as long as the 3.0 mm depth of the tumor is surgically or medically debulked to a depth of ≤2.0 mm prior to treatment initiation.

Two Methods for Debulking BCCs With Depth Measurements >2.0 mm

BCC tumors deeper than 2.0 mm post-biopsy that are not located in cosmetically- or functionally-sensitive anatomic areas can be surgically debulked via shave removal or electrodessication and curettage (ED&C) until the pre-treatment depth of 2.0 mm or less is confirmed by HRDUS imaging.

BCC tumors deeper than 2.0 mm post-biopsy that are located in cosmetically- or functionally-sensitive anatomic areas can be medically debulked via several months of pre-treatment with hedgehog inhibitors (HHIs), such as vismodegib, sonedegib or PD-1 inhibitors like cemiplimab. Once tumor depth is reduced to 2.0 mm or less, the patient may discontinue HHI and/or PD-1 therapy and begin IGSRT treatment. It is strongly recommended that the patient be given only 3 weeks of HHI medication at a time to insure compliance, with follow-up HRDUS imaging performed every 3 weeks to measure tumor shrinkage.

BCC Subtypes and Appropriate Margins

Dermoscopy: Can be used if available to improve the accuracy of identifying the clinical diameter/peripheral edges of the BCC tumor prior to radiation delivery

Superficial BCC: 5.0 mm margin around clinically apparent tumor. Strong consideration of using 7.0 mm to 10.0 mm margins with margins can be reduced to not less than 4.0 mm at adjacent critical structure (i.e., eye, acanthus)

Nodular BCC: 5.0 mm margin around clinically apparent tumor. Strong consideration of using 7.0 mm to 10.0 mm margins with margins can be reduced to not less than 4.0 mm at adjacent critical structure (i.e., eye, acanthus)

Keratotic BCC: 5.0 mm margin around clinically apparent tumor. Strong consideration of using 7.0 mm to 10.0 mm margins with margins can be reduced to not less than 4.0 mm at adjacent critical structure (i.e., eye, acanthus)

Pigmented BCC: 5.0 mm margin around clinically apparent tumor. Strong consideration of using 7.0 mm to 10.0 mm margins with margins can be reduced to not less than 4.0 mm at adjacent critical structure (i.e., eye, acanthus)

Infundibulocystic BCC: 5.0 mm margin around clinically apparent tumor. Strong consideration of using 7.0 mm to 10.0 mm margins with margins can be reduced to not less than 4.0 mm at adjacent critical structure (i.e., eye, acanthus)

Fibroepithelioma of Pinkus: 5.0 mm margin around clinically apparent tumor. Strong consideration of using 7.0 mm to 10.0 mm margins with margins can be reduced to not less than 4.0 mm at adjacent critical structure (i.e., eye, acanthus)

Infiltrative BCC: Strong consideration of using 7.0 mm to 10.0 mm margins with margins can be reduced to not less than 5.0 mm at adjacent critical structure (i.e., eye, acanthus)

Multifocal/Micronodular BCC: Strong consideration of using 7.0 mm to 10.0 mm margins with margins can be reduced to not less than 5.0 mm at adjacent critical structure (i.e., eye, acanthus)

Sclerotic/Morpheaform BCC: Strong consideration of using 7.0 mm to 10.0 mm margins with margins can be reduced to not less than 5.0 mm at adjacent critical structure (i.e., eye, canthus)

Basosquamous: See IGSRT for SCC Appropriate Use Criteria[5]

BCC with carcinosarcomatous differentiation: Not appropriate for IGSRT

V. RATIONALE AND IGSRT PROTOCOL GUIDELINES

The IGSRT protocol is based on HRDUS imaging of tumor depth, which changes regularly. Depth intervals are measured in millimeters from lowest to highest. Each depth interval corresponds to similarly increasing intervals of energy (kV) and time, dose, fractionation (TDF). Prior to delivering radiation, the depth is measured and the corresponding interval is selected, clearly defining the appropriate energy (kV) and TDF to use. For NMSC tumors that have increased in depth, adaptive increases in kV and TDF serve to optimize efficacy. For NMSC tumors that have decreased in depth, adaptive decreases in kV and TDF serve to minimize toxicity. The adaptive nature of the IGSRT protocol has proven in multiple retrospective studies to consistently deliver 99% cure rates for NMSC with minimal toxicity.[4, 6-10]

Rationale for HRDUS Imaging and Adaptive Changes Prior to Each Fraction

92% of NMSC tumors undergoing IGSRT exhibit measurable changes in the depth of invasion compared to that of the previous image.[11] Because these measurements are collected immediately prior to treatment, they allow for the opportunity to implement adaptive changes in treatment parameters, such as kV, TDF, and dose/boost. These adaptive changes are necessary in approximately 40% of cases, directly benefitting patients by maximizing efficacy and minimizing toxicity.[11]

HRDUS Imaging, Adaptive Changes and Efficacy

Any measured increase in NMSC depth is clinically significant during treatment with IGSRT as it may change the tumor coverage based on the percentage depth dose (PDD) initially selected for that lesion. A lower energy PDD means significantly less radiation is delivered to the deepest tumor cells compared to a higher energy PDD. This results in comparatively diminished therapeutic efficacy if the tumor becomes deeper (at times due to tissue edema) during the treatment. Thus, by performing HRDUS depth measurements prior to every fraction, dermatologists and RTTs know exactly when to make adaptive increases in kV, TDF, and dose/boost. This ensures that every NMSC tumor is adequately and uniformly radiated to achieve a 99% cure rate.[4, 6-10]

HRDUS Imaging, Adaptive Changes and Toxicity

Any measured decrease in NMSC depth is clinically significant during treatment with IGSRT as it is an opportunity to decrease unnecessary radiation and minimize toxicity. The guiding principle of radiation safety is ALARA, which stands for “as low as reasonably achievable”. ALARA means avoiding exposure to radiation that does not have a direct benefit to the patient, even if the dose is small. Thus, by performing HRDUS depth measurements prior to every fraction, dermatologists and RTTs know exactly when to make adaptive decreases in kV, TDF, and dose/boost. This ensures that the safety of every NMSC patient is optimized by reducing radiation toxicity whenever possible.[12]

Procedures and Protocol

Tumor depth measurements should be recorded prior to every fraction to optimize efficacy.

RTOG scores should be recorded after every 5 fractions to monitor radiation toxicity.

Rationale for imaging and adaptive changes 3- to 6-weeks after IGSRT is completed:
Patients and dermatologists need visual confirmation of BCC eradication once therapy has been completed. If no residual BCC is identified, IGSRT has successfully cured the BCC.

Suggested Follow Up Protocol

If the possibility of residual BCC is visualized, the recommended course of action is to wait an additional 3- to 4-weeks (total of 6- to 10-weeks after completion of treatment) for a second follow-up evaluation and perform follow-up HRDUS imaging. If no residual BCC is identified, IGSRT has successfully cured the BCC.

If after waiting the additional 3- to 4-weeks for the second follow-up evaluation, the HRDUS imaging is still suspicious for residual tumor, the case should be presented to MDT/Grand Rounds so that the radiation oncology/dermatology experts can review the case and make specific recommendations regarding boost doses if possible or recommended.

After boost dosing is completed, follow up using HRDUS imaging is necessary to visually confirm that IGSRT has successfully cured the resistant portion of the BCC tumor. If a small localized "stubborn" residual portion of the BCC tumor persists 6-weeks or longer after boost dosing, it may be injected with 5-FU or bleomycin while the area is healing. It is advisable to wait 2- to 3-months before starting intralesional injections unless the tumor is obviously progressing. Such injections often assist in the resolution of radioresistant BCC, which is often preferable to surgery. If the BCC does not resolve with injections, it can be salvaged with Mohs micrographic surgery after 4- to 6-months of healing, unless the tumor is obviously progressing. All decisions are based on the clinical judgement of the dermatologist.

HOW TO USE THESE GUIDELINES AND DISCLAIMER

These guidelines were developed by the Dermatology Association of Radiation Therapy (DART) and its panel of experts from its education committee to provide clinicians, patients, and policy makers with an orientation as to how to inform patients and assess and treat certain medical conditions. These guidelines were developed by an expert panel that critically appraised, summarized, and interpreted recent and relevant clinical evidence to provide recommendations that can be applied to patient care. Healthcare providers should exercise their own clinical judgment and discretion when utilizing these guidelines in the care of patients. Individual patient circumstances may vary and adherence to these guidelines does not guarantee specific outcomes. The ultimate judgment regarding a specific therapy must be made by the physician and the patient in light of all the circumstances presented by the individual patient and the biological variability of their disease. The content in these guidelines should not be used as a substitute for professional medical advice, diagnosis or treatment. Users of these guidelines are encouraged to review updates and revisions regularly, as medical knowledge is constantly evolving.

DART guidelines are reviewed and updated periodically to ensure alignment with the latest advances in evidence-based care, treatment technologies, and clinical research. Clinicians and healthcare providers seeking to consult on DART guidelines may contact info@DermAssociationRT.org.

APPROVAL	DATE
DART Education Committee	**June 12, 2024**
Subcommittee on SRT/IGSRT *Reviewed and approved by:* Jeff Stricker, DO, FAOCD, FAAD Liqiao Ma, MD, FAAD Clay Cockerell, MD, FAAD Blake Robbins, DO, FAOCD, FAAD Ashwin Patel, MD, DABR Daniel Ladd, DO, FAOCD, FAAD Lio Yu, MD, DABR	**June 12, 2024**
Board Approval/Membership Approval	**Approved**

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