Electronic Brachytherapy for Nonmelanoma Skin Cancer

BY LAUREN D. STEGMAN, MD, PHD, DABR

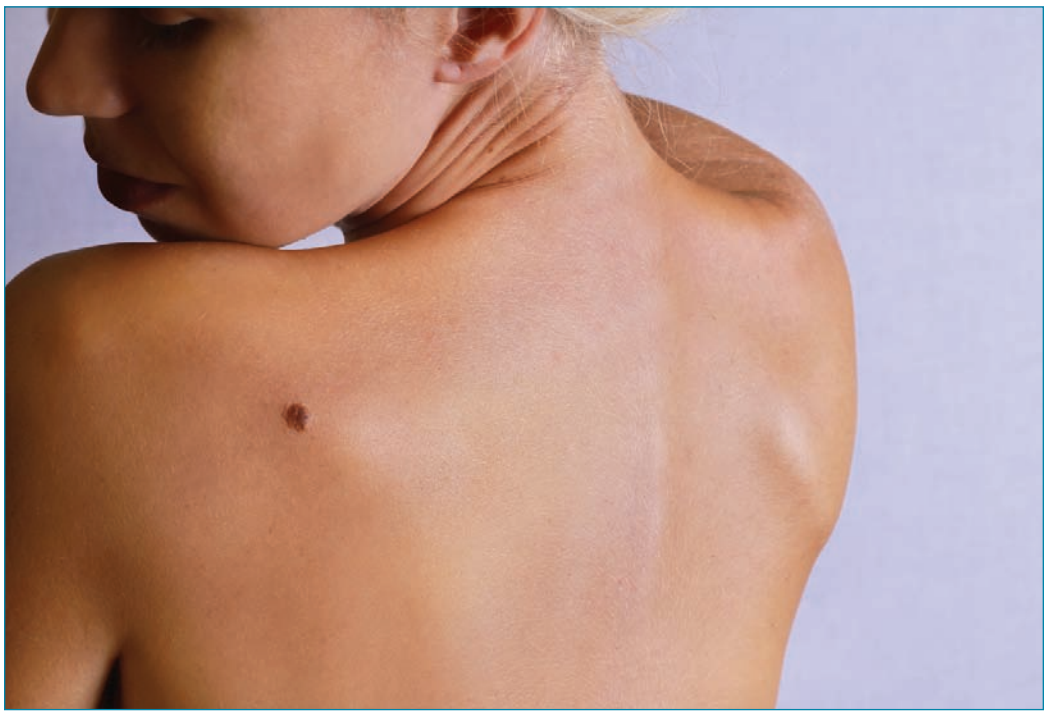
Rates of nonmelanoma skin cancer (NMSC), including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), have risen to epidemic levels in recent years (*JAMA Dermatol* 2015;151(10):1081-1086, *Semin Cutuan Med Surg* 2011;30(1):3-5).

Given that approximately 3 million Americans are diagnosed with NMSC each year and almost half of those who live to age 65 will have BCC or SCC at least once, it is essential for clinicians to continually review and assess emerging advances in treatment that have the potential to improve patient comfort and outcomes.

Standard Treatments

Mohs micrographic dermatologic surgery is considered the standard-of-care for treatment of NMSC. The technique has become widely adopted as an alternative to excision, electrodessication, cryosurgery, and traditional radiation therapy.

However, despite its prevalence and clinical efficacy, it can result in serious disfigurement depending on size and anatomical location of a tumor. In severe cases, some patients may require corrective plastic surgery procedures following Mohs surgery, resulting in additional costs and an increased risk for potential infections or complications.



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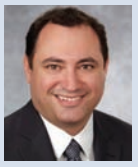
Radiation therapy is another treatment option that has been used for decades for treatment of NMSC. High-quality data from a randomized controlled trial of radiotherapy versus Mohs are not yet available; however, most experts agree that tumor control rates are generally equivalent to surgery.

Recent retrospective reviews and two meta-analyses have reported 5-year local control rates above 90 percent for both BCC and SCC (*Int J Dermatol* 2005;44(6):513-517, *J Dtsch Dermatol Ges* 2006;4(2):124-130, *Int J Radiat Oncol Biol Phys* 2000;47(1):95-102). These data validate guidelines from the National Comprehensive Cancer Network (NCCN) that include radiation therapy as a reasonable alternative to surgery for many patients.

The best candidates are patients with lesions in anatomically challenging locations (ear, nose, scalp, neck, shin, elbow), patients who may have trouble with wound healing, patients who are on anticoagulants, or those with medical comorbidities that may preclude them from surgery.



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The traditional methods of offering radiation therapy for skin cancer can be cumbersome for both providers and patients and have contributed to limitations in its use. First, traditional brachytherapy, orthovoltage, and electron beam treatment machines require a significant capital investment in equipment and shielded treatment vaults.

Second, these treatments often require custom-made shielding devices, bolus, a special material placed on the skin over the lesion to ensure delivery of the full treatment dose to the skin surface and help minimize the dose delivered with the subcutaneous tissues, and special immobilization devices.

These can be time-consuming for the treatment team to make and can be uncomfortable for the patient to wear during treatments. Moreover, these modalities require the patient be in the treatment room alone for 10-20 minutes for each treatment session. Finally, most traditional radiation treatment regimens consist of 15-33 treatment sessions over 4-7 weeks, which can be logistically difficult.

Electronic Brachytherapy

In 2009, a new method of delivering radiotherapy for NMSC was introduced called high-dose rate (HDR) electronic brachytherapy (eBx). It uses a miniaturized electronic X-ray source rather than a radionuclide-based source.

Practical advantages for providers include less capital investment, no required special shielding of the treatment room, a mobile treatment platform without worries about protecting a radioactive source, and a streamlined system of applicators that do not require bolus and facilitate treatment delivery.

Patients appreciate that members of the treatment team may remain with them in the treatment room during the treatment. This is reassuring and allows the use of less-restrictive immobilization devices. No bolus is needed, which also likely increases patient comfort. An additional advantage is that the very rapid dose fall off below the skin allows more radiation to be given in each session, which generally shortens the total number of treatment sessions to 8-10 doses in most eBx treatment regimens.

Several recent surveys have demonstrated that eBx is well-rated by both patients and doctors. In one study, a majority of patients surveyed between 32 and 73 months after treatment said that eBx did not hinder their daily activities and they were satisfied with how well the modality worked. Patients unanimously agreed the treatment was convenient, and most patients said they would recommend the treatment to a friend with NMSC (*Int J Radiat Oncol Biol Phys* 2000;47(1):95-102). In a survey of doctors, the majority reported they prefer eBx over traditional external beam radiation therapy due to its shorter treatment course, conformality of treatment for irregular or curved targets, and shallow dose deposition (*Brachytherapy* 2016; doi:10.1016/j.brachy.2016.10.006).

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ELECTRONIC BRACHYTHERAPY

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eBx for the treatment of NMSC is both painless and non-invasive, and can offer many patient benefits including added convenience, fewer treatments compared to traditional radiotherapy, and excellent clinical results. It can be delivered on an outpatient basis in a dermatologist's office, hospital, or cancer center under the direction of a supervising physician. A growing body of evidence supports the use of eBx for NMSC patients who meet specific selection criteria. Research on the use of this modality has been conducted by leading clinicians and positive clinical results have been presented at important medical meetings and published in leading peer-reviewed journals.

In my clinical practice, we recently introduced technology to offer eBx to appropriate patients. The entire system is mobile and can be wheeled easily from room to room. In addition, radiation from an electronic source rather than a radionuclide-based source reduces the need for a shielded vault to protect health care professionals from repeat exposure to radiation. The technology is FDA-cleared for the treatment of cancer anywhere in the body, including eBx for NMSC, making it a cost-effective investment for medical practices that treat different types of cancers.

While NCCN guidelines still suggest that the standard-of-care in treatment of NMSC is surgery and eBx does not yet have the long-term follow-up data of other radiation modalities, the significant level of clinical data showing that eBx treatment is safe and effective positions it well to be an increasingly utilized option for patients. As with the use of all medical technologies, decisions regarding the use of eBx to treat NMSC should be made by treating physicians in close consultation with the patient. OT

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Noninvasive Imaging Test Shown Accurate in Ruling Out Kidney Cancers

The latest in a series of studies led by researchers at Johns Hopkins Medicine, Baltimore, shows that addition of a widely available, noninvasive imaging test called 99mTc-sestamibi SPECT/CT to CT or MRI increases the accuracy of kidney tumor classification. The research team reports that the potential improvement in diagnostic accuracy will spare thousands of patients each year in the U.S. alone from having to undergo unnecessary surgery.

In a recent report on ongoing work to improve kidney tumor classification, the team reports that the sestamibi SPECT/CT test adds additional diagnostic information in conjunction with conventional CTs and MRI and improves physicians' ability to differentiate between benign and malignant kidney tumors (*Clinical Nuclear Medicine* 2017;42(3):e166-e167).

"Sestamibi SPECT/CT lets radiologists and urologists 'see' the most common benign kidney tumor, something CT and MRI have not succeeded in doing alone," said Mohamad E. Allaf, MD, MEA Endowed Professor of Urology at the Johns Hopkins University School of Medicine. "This noninvasive scan may prevent patients with a potentially benign kidney tumor from having to undergo a surgery to remove the tumor or potentially the entire kidney, along with its associated risks and high costs. At Johns Hopkins, use of this test has already spared a number of our patients from unnecessary surgery and unnecessary removal of a kidney that would require them to be on dialysis. These results are hugely encouraging, but we need to do more studies."

Defining Malignant Tumors

For this study, 48 patients who were diagnosed with a kidney tumor on conventional CT or MRI were imaged with sestamibi SPECT/CT at Johns Hopkins prior to surgery. Radiologists, who were not allowed to talk to each other or know the results of the surgeries, graded the conventional and sestamibi SPECT/CT images benign or malignant using a 5-point scale (1=definitely benign, 5=definitely cancerous).

Following surgery, similarly "blinded" pathologists analyzed the tumors without knowing the radiologists' imaging results. Pathology results of surgically removed tumors showed that eight of the 48 were benign. The remaining 40 were classified as a variety of other tumor types, including malignant renal cell carcinomas.

Reviewing sestamibi SPECT/CT scan results in conjunction with CT or MRI changed the initial rating levels from cancerous (score 3, 4, 5) toward benign (score 1 and 2) in nine cases, and changed reviewers' score from likely cancerous (score 4) to definitely cancerous (score 5) in five cases, or about 10 percent of all cases. The addition of sestamibi SPECT/CT increased the reviewers' diagnostic certainty in 14 of the 48 patients, or in nearly 30 percent of all cases.

Overall, the investigators said, adding sestamibi SPECT/CT helped identify seven of nine benign tumors, and conventional imaging with added sestamibi SPECT/CT outperformed conventional imaging alone, as measured by a statistical analysis that measures tradeoffs between sensitivity and specificity. On this measure, a value of 0.50 indicates that a diagnostic test is no better than chance. Conventional imaging combined with sestamibi SPECT/CT had a value of 0.85, while conventional imaging alone had a value of 0.60.

Even for patients whose tumors were not reclassified, the addition of sestamibi SPECT/CT increased physicians' ability to more confidently classify malignant tumors, which reduces the risk of misdiagnosis and unnecessary surgery for all patients, according to researchers.

Alternative to Surgery

Radiologists and urologists have been frustrated for decades by the inability of conventional imaging tests, such as CT and MRI, to distinguish benign from malignant kidney tumors. At Johns Hopkins, multispecialty teams work together to determine the best care for patients and as partners on research innovations and quality improvement initiatives.

"This collaborative venue enabled two then-residents [Drs. Michael Gorin and Steven Rowe] from different departments and specialties to design a clinical trial based on a few reports in the literature suggesting a potential role for sestamibi SPECT/CT in this diagnostic conundrum, and their hypothesis proved correct," noted Mehrbod Som Javadi, MD, Assistant Professor of Radiology at Johns Hopkins University School of Medicine and the senior author on the paper. Pamela T. Johnson, MD, Associate Professor of Radiology at the Johns Hopkins University School of Medicine, added, "These types of advances are critical to our precision medicine initiative, Hopkins inHealth, designed for individualized patient management, and to our mission of high-value health care, where the highest quality care is safely delivered at the lowest personal and financial cost to the patient."

"As radiologists, we have struggled to find noninvasive ways to better classify patients and spare unnecessary surgery, but this has not been easy," said Steven P. Rowe, MD, PhD, one of the two former residents who developed this approach, and now Assistant Professor of Radiology and Radiological Science at the Johns Hopkins University School of Medicine. "Sestamibi SPECT/CT offers an inexpensive and widely available means of better characterizing kidney tumors, and the identical test is now being performed as part of a large trial in Sweden, for which the first results have just recently been published and appear to confirm our conclusions."

Although further study is needed to validate the accuracy of sestamibi SPECT/CT, this test appears to be a less-expensive, faster, noninvasive alternative to surgery, concluded Michael A. Gorin, MD, the other resident involved in developing this approach and now Chief Resident with The James Buchanan Brady Urological Institute of the Johns Hopkins University School of Medicine. "In the absence of diagnostic certainty, surgeons tend to remove kidney tumors in an abundance of caution, leading to an estimated 5,600 surgically removed benign kidney tumors each year in the U.S." OT