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Basal Cell and Squamous Cell Skin Cancers

Clinical Practice Guidelines in Oncology

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Overview

Basal and squamous cell skin cancers, collectively known as non-melanoma skin cancers (NMSC), are the most common skin cancers.[1,2] More than 1 million cases of NMSC are estimated to be diagnosed each year in the United States and their incidence is rising rapidly.[3,4] Basal cell carcinomas are approximately 4 to 5 times more common than squamous cell carcinomas. Although rarely metastatic, basal and squamous cell cancers can produce substantial local destruction along with disfigurement, and may involve extensive areas of soft tissue, cartilage, and

NCCN Clinical Practice Guidelines in Oncology on Basal Cell and Squamous Cell Skin Cancers

Key Words

NCCN Clinical Practice Guidelines, NCCN Guidelines, non-melanoma skin cancers, skin carcinoma, sunlight and cancer, precancerous lesions, basosquamous carcinoma, Bowen's disease (*JNCCN* 2010;8:836–864)

NCCN Categories of Evidence and Consensus

Category 1: The recommendation is based on high-level evidence (e.g., randomized controlled trials) and there is uniform NCCN consensus.

Category 2A: The recommendation is based on lower-level evidence and there is uniform NCCN consensus.

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Category 3: The recommendation is based on any level of evidence but reflects major disagreement.

All recommendations are category 2A unless otherwise noted.

Clinical trials: NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Please Note

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Disclosures for the NCCN Guidelines Panel for Basal Cell and Squamous Cell Skin Cancers

At the beginning of each NCCN Guidelines panel meeting, panel members disclosed any financial support they have received from industry. Through 2008, this information was published in an aggregate statement in *JNCCN* and online. Furthering NCCN's commitment to public transparency, this disclosure process has now been expanded by listing all potential conflicts of interest respective to each individual expert panel member.

Individual disclosures for the NCCN Guidelines on Basal Cell and Squamous Cell Skin Cancers panel members can be found on page 864. (The most recent version of these guidelines and accompanying disclosures, including levels of compensation, are available on the NCCN Web site at www.NCCN.org.)

These guidelines are also available on the Internet. For the latest update, please visit www.NCCN.org.

bone. The estimated annual cost of treating these 2 diseases in the United States Medicare population exceeds $400 million.[5] However, NMSCs generally have a good prognosis.

The most significant environmental carcinogen for NMSC is sunlight.[6] Thus, individuals in Hawaii are at much greater risk than those in the northern parts of the United States. Fair-skinned individuals who have received too much sun exposure are at the greatest risk for these cancers. Most of these tumors develop on sun-exposed skin sites. The most common sites are on the head and neck area. According to a report from the Childhood Cancer Survivor Study, long-term survivors of childhood and adolescent cancers who have undergone prior radiation therapy are also at risk for developing NMSC.[7]

Actinic keratoses are sun-induced precancerous lesions.[8,9] Bowen's disease is characterized by squamous cell carcinoma in situ lesions that occur predominantly in older persons.[10] Both types of lesions, if untreated, can progress to invasive squamous cell carcinoma with the potential for metastasis.

Skin cancer preventive education should be promoted across all age groups.[11] In a recent study, organ transplant recipients who received intensive educational interventions were found to be more compliant with sun protection procedures than those who received standard education.[12] All patients should be made aware of the various resources that discuss skin cancer prevention. Some of the useful resources include:

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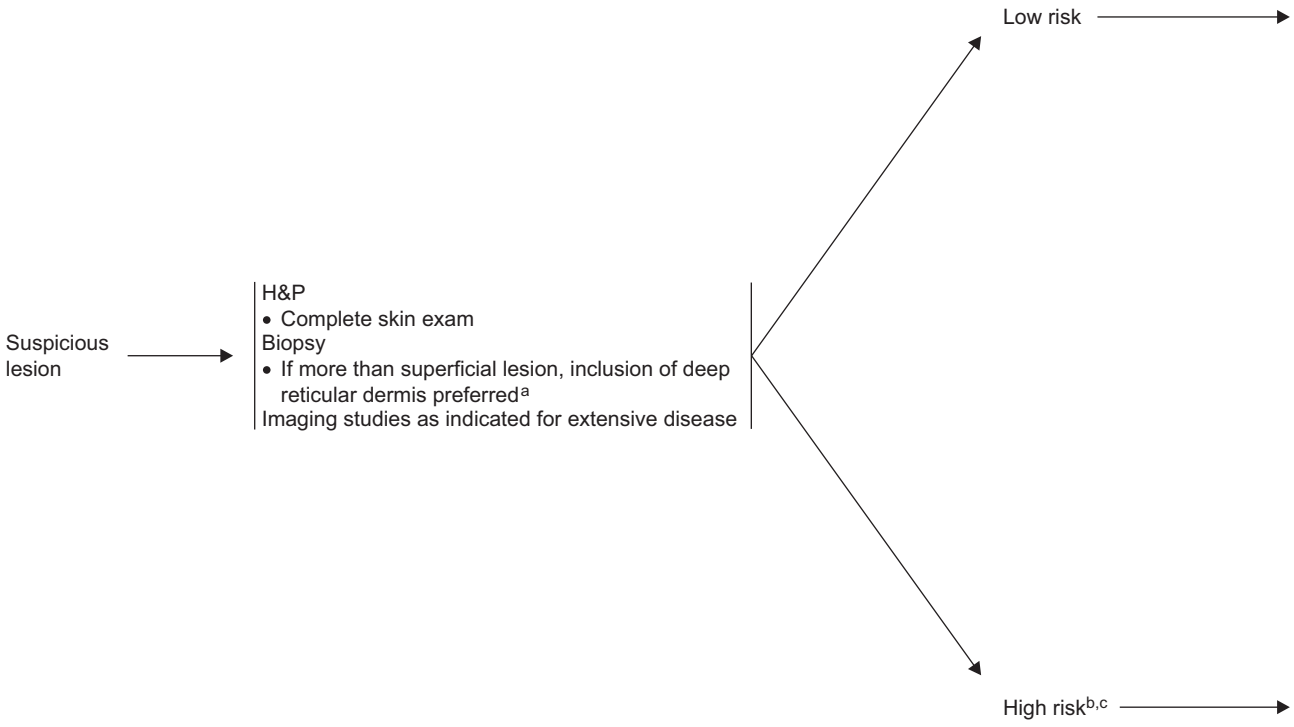

[a]See Risk Factors for Recurrence (page 840).
[b]Any high-risk factor places the patient in the high-risk category.
[c]For complicated cases, consider multidisciplinary tumor board consultation.

Clinical trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged. All recommendations are category 2A unless otherwise indicated.

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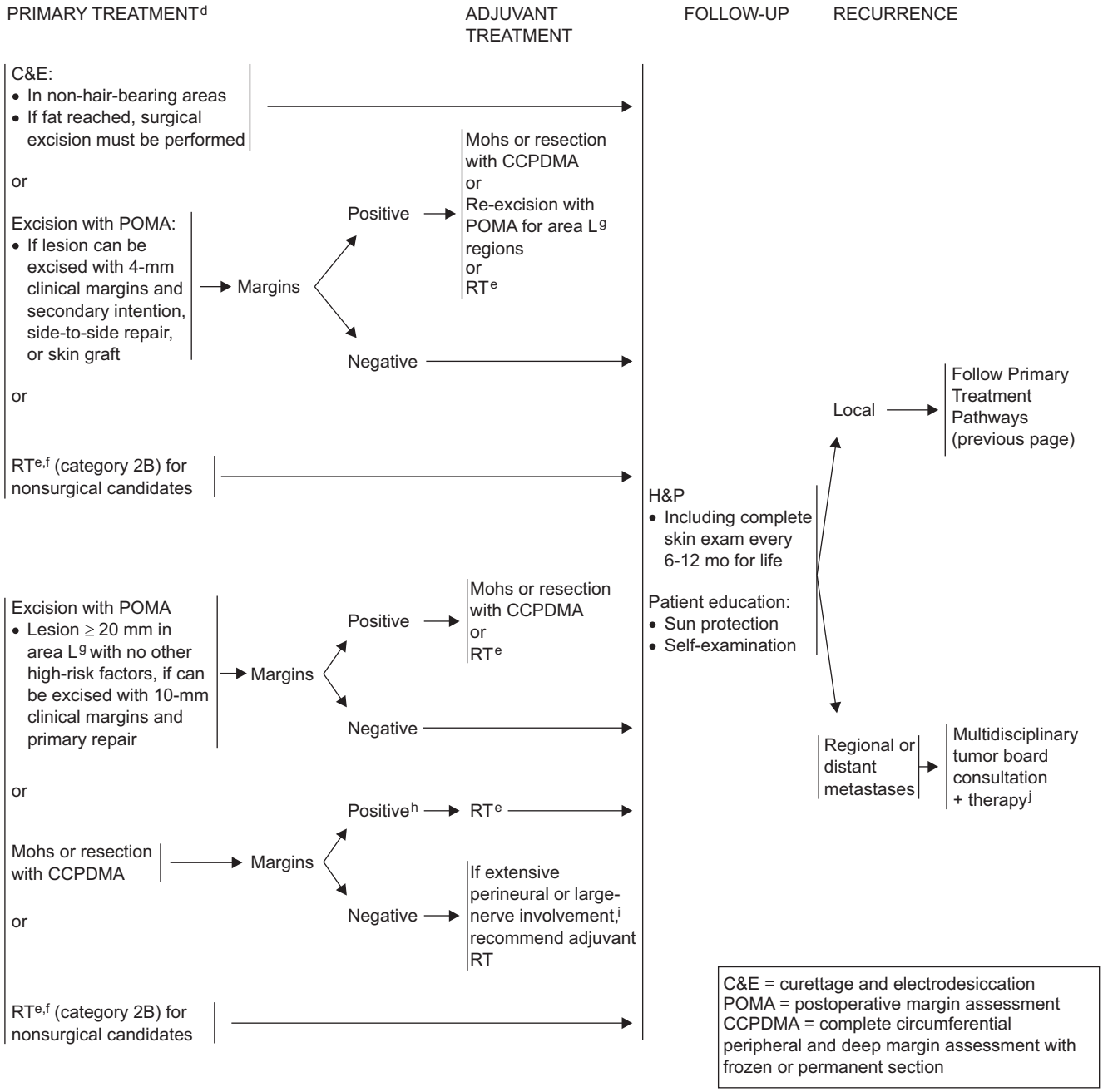


[d] See Principles of Treatment for Basal Cell Skin Cancer (page 841).
[e] See Principles of Radiation Therapy for Basal Cell Skin Cancer (page 841).
[f] RT generally reserved for patients older than 60 y because of concerns about long-term sequellae.
[g] Area L = trunk and extremities (see page 840).
[h] Negative margins unachievable by Mohs surgery or more extensive surgical procedures.
[i] If large-nerve involvement is suspected, consider MRI to evaluate extent and rule out skull involvement.
[j] Clinical trials of chemotherapy or biologic modifiers are recommended for metastatic basal cell carcinoma. Combination chemotherapy has produced useful responses (cisplatin and cyclophosphamide, cisplatin and vinblastin, cisplatin and doxorubicin, or cisplatin and paclitaxel).

RISK FACTORS FOR RECURRENCE

H&P	Low Risk	High Risk
Location/size	Area L < 20 mm	Area L ≥ 20 mm
	Area M < 10 mm	Area M ≥ 10 mm
	Area H < 6 mm[1]	Area H ≥ 6 mm[1]
Borders	Well-defined	Poorly defined
Primary vs. recurrent	Primary	Recurrent
Immunosuppression	(-)	(+)
Site of prior RT	(-)	(+)
Pathology		
Subtype	Nodular, superficial	Aggressive growth pattern[2]
Perineural involvement	(-)	(+)

Area H = "mask areas" of face (central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermillion], chin, mandible, preauricular and postauricular skin/sulci, temple, ear), genitalia, hands, and feet.
Area M = cheeks, forehead, scalp, and neck.
Area L = trunk and extremities.

[1] Location independent of size may constitute high risk in certain clinical settings.
[2] Having morpheaform, sclerosing, mixed infiltrative, or micronodular features in any portion of the tumor.

PRINCIPLES OF TREATMENT FOR BASAL CELL SKIN CANCER

- The goal of primary treatment for basal cell skin cancer is the cure of the tumor and the maximal preservation of function and cosmesis. All treatment decisions should be customized to account for the particular factors present in the individual case and for patient's preference. Customary age and size parameters may have to be modified.
- Surgical approaches often offer the most effective and efficient means for accomplishing cure, but considerations of function, cosmesis, and patient preference may lead to choosing radiation therapy as primary treatment to achieve optimal overall results.
- In certain patients at high risk for multiple primary tumors, increased surveillance and consideration of prophylactic measures may be indicated.
- In patients with low-risk superficial basal cell skin cancer, in whom surgery or radiation is contraindicated or impractical, topical therapies such as 5-fluorouracil, imiquimod, photodynamic therapy (e.g., porfimer sodium, topical amino levulinic acid [ALA]), or vigorous cryotherapy may be considered, even though the cure rate may be lower.

PRINCIPLES OF RADIATION THERAPY FOR BASAL CELL SKIN CANCER

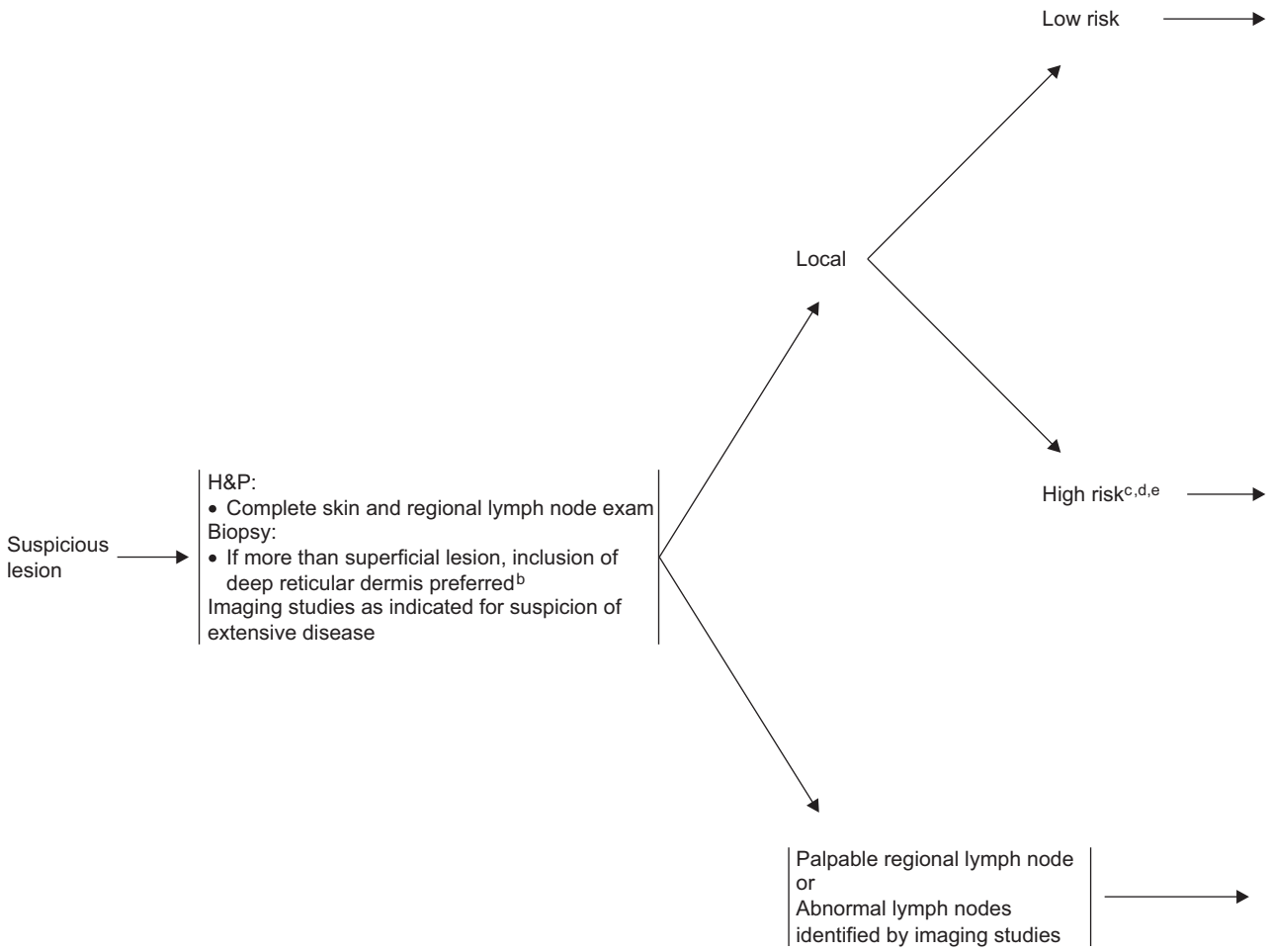
Dose and Field Size

Tumor Size	Margins	Examples of Electron Beam Dose and Fractionation
< 2 cm	1-1.5 cm[1]	64 Gy in 32 fractions over 6-6.4 wk[2] 55 Gy in 20 fractions over 4 wk 50 Gy in 15 fractions over 3 wk 35 Gy in 5 fractions over 5 d
≥ 2 cm	1.5-2 cm[1]	66 Gy in 33 fractions over 6-6.6 wk 55 Gy in 20 fractions over 4 wk
Postoperative adjuvant		50 Gy in 20 fractions over 4 wk 60 Gy in 30 fractions over 6 wk

- Protracted fractionation is associated with improved cosmetic results.
- Radiation therapy is contraindicated in genetic conditions predisposing to skin cancer (e.g., basal cell nevus syndrome, xeroderma pigmentosum) and connective tissue diseases (e.g., scleroderma).

[1] When using electron beam, wider field margins are necessary than with orthovoltage x-rays because of the wider beam penumbra. Tighter field margins can be used with electron beam adjacent to critical structures (e.g., the orbit) if lead skin collimation is used. Bolus is necessary when using electron beam to achieve adequate surface dose. An electron beam energy should be chosen that which achieves adequate surface dose and encompasses the deep margin of the tumor by at least the distal 90% line. Appropriate medical physics support is essential.

[2] Electron beam doses are specified at 90% of the maximal depth dose (Dmax). Orthovoltage x-ray doses are specified at Dmax (skin surface) to account for the relative biologic difference between the 2 modalities of radiation.



[a] Including basosquamous carcinoma and squamous cell skin cancer in situ (showing full-thickness epidermal atypi, excluding actinic keratoses).
[b] See Risk Factors for Recurrence (page 848).
[c] Any high-risk factor places the patient in the high-risk category.
[d] Sentinel lymph node mapping should be considered in certain high-risk lesions, although the benefit of this technique has yet to be proven.
[e] For complicated cases, consider multidisciplinary tumor board consultation.

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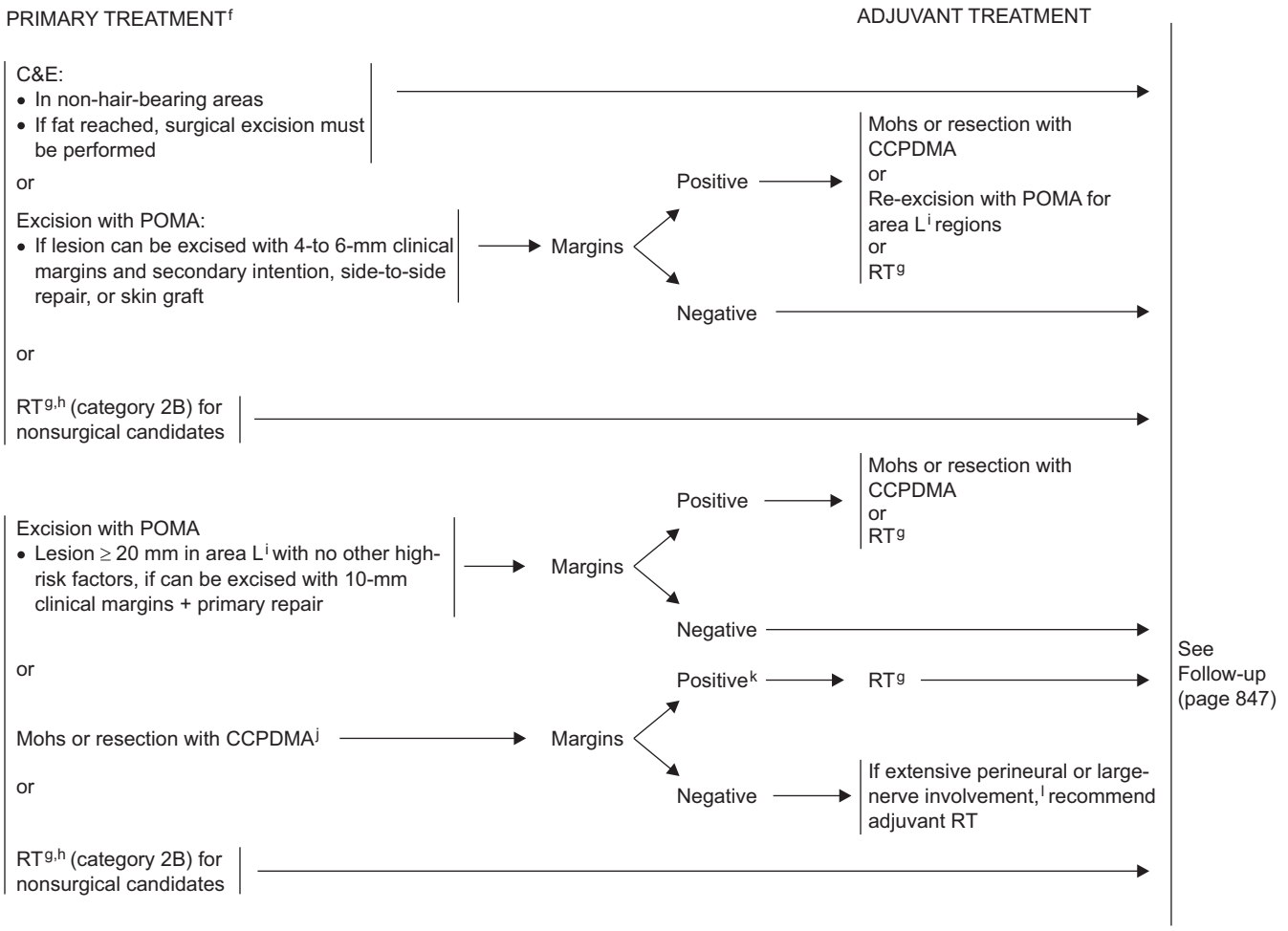
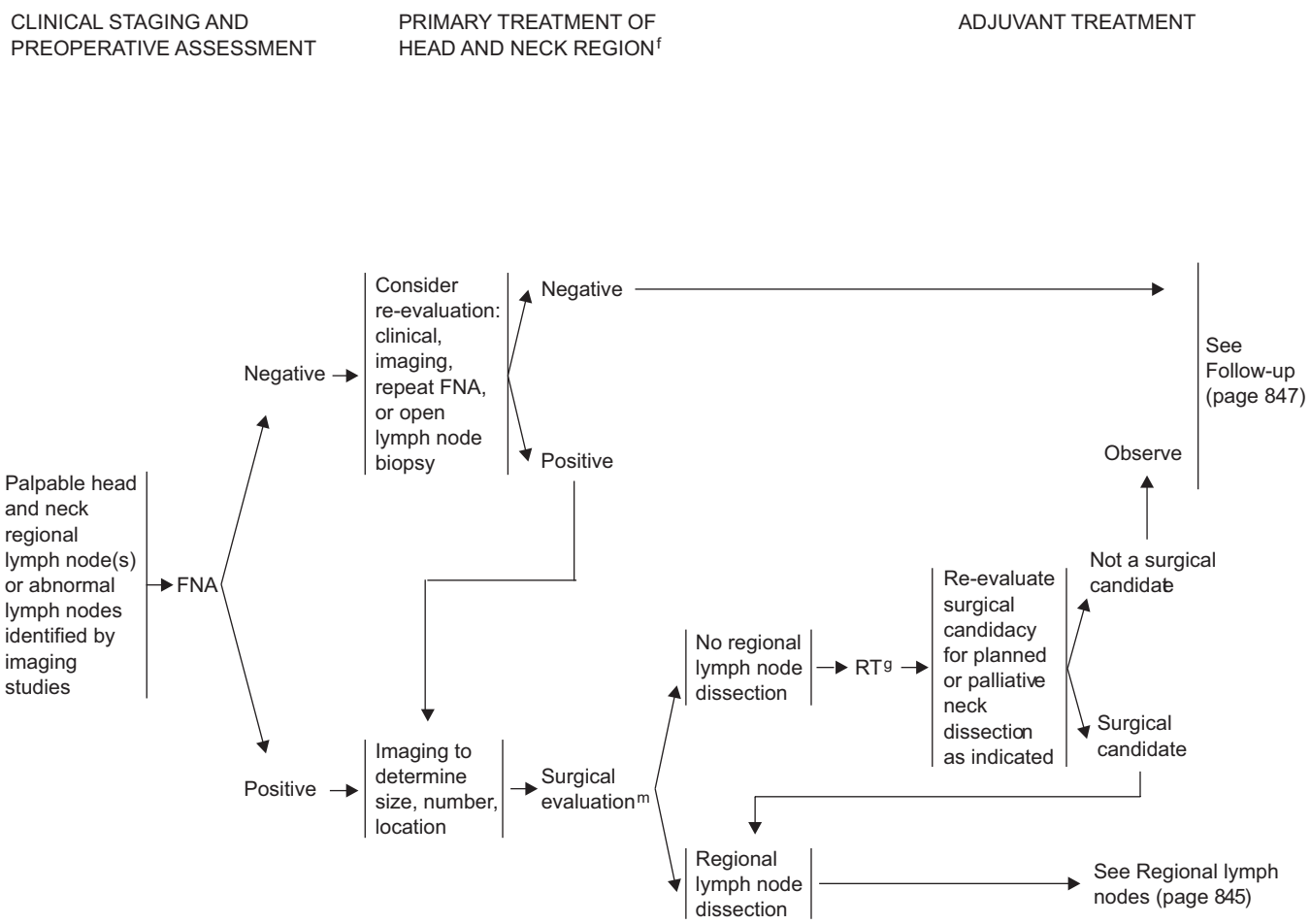


See Primary Treatment for Head and Neck Disease (pages 844 and 845)
or
See Primary Treatment for Trunk or Extremity Disease (page 846)

C&E = curettage and electrodesiccation
POMA = postoperative margin assessment
CCPDMA = complete circumferential peripheral and deep margin assessment with frozen or permanent section

[f] See Principles of Treatment for Squamous Cell Skin Cancer (page 848).
[g] See Principles of Radiation Therapy for Squamous Cell Skin Cancer (page 849).
[h] RT generally reserved for patients older than 60 y because of concerns about long-term sequellae.
[i] Area L = trunk and extremities (see page 848).
[j] If invasion to parotid fascia, superficial parotidectomy.
[k] Negative margins unachievable by Mohs surgery or more extensive surgical procedures.
[l] If large-nerve involvement is suspected, consider MRI to evaluate extent and rule out skull involvement.



[f] See Principles of Treatment for Squamous Cell Skin Cancer (page 848).
[g] See Principles of Radiation Therapy for Squamous Cell Skin Cancer (page 849).
[m] Regional lymph node dissection is preferred, unless the patient is not a surgical candidate.

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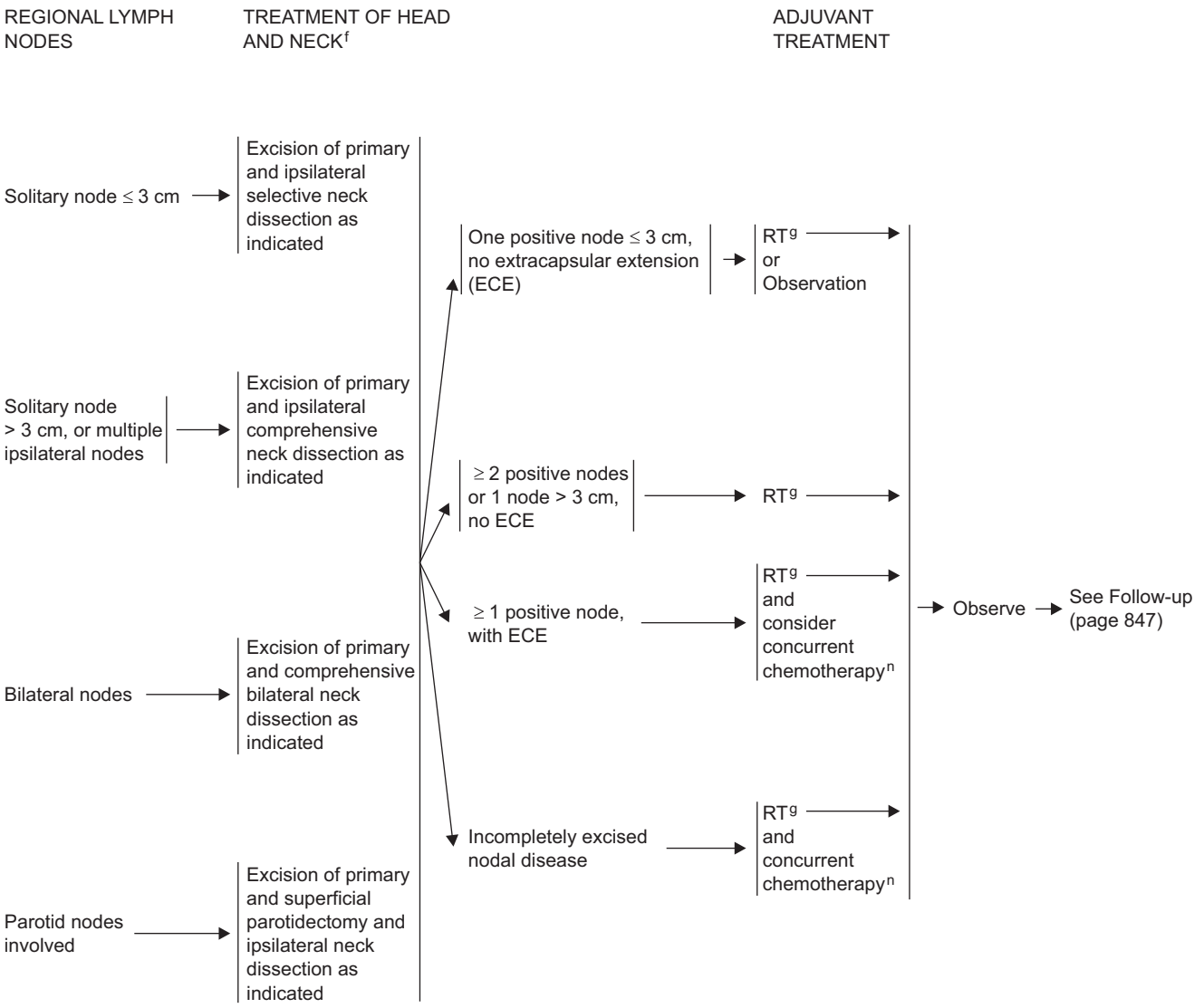
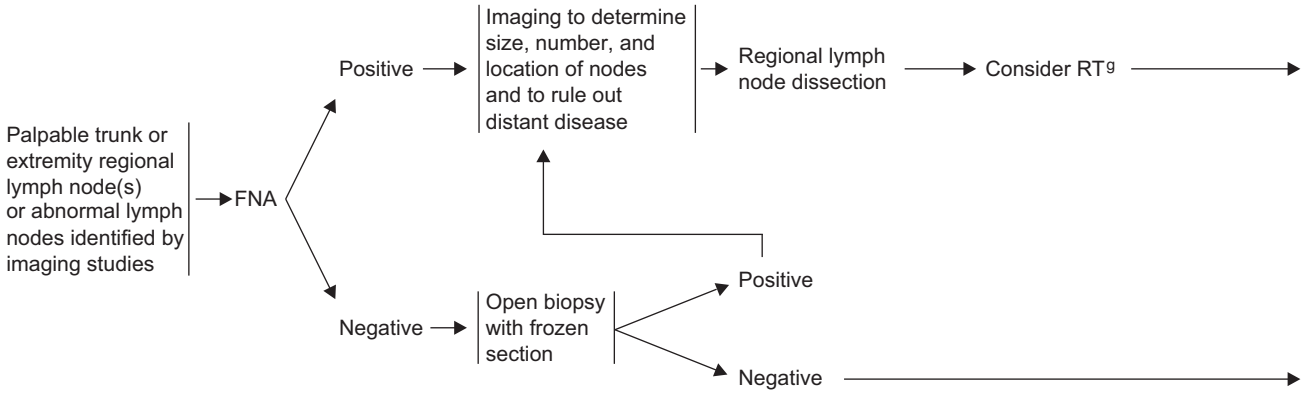


[f]See Principles of Treatment for Squamous Cell Skin Cancer (page 848).
[g]See Principles of Radiation Therapy for Squamous Cell Skin Cancer (page 849).
[n]Concurrent chemotherapy: cisplatin 100 mg/m^2 every 3 weeks or cisplatin weekly at 30 mg/m^2.

PRIMARY TREATMENT OF TRUNK OR EXTREMITY REGION[f]

ADJUVANT TREATMENT



[f] See Principles of Treatment for Squamous Cell Skin Cancer (page 848).
[g] See Principles of Radiation Therapy for Squamous Cell Skin Cancer (page 849).

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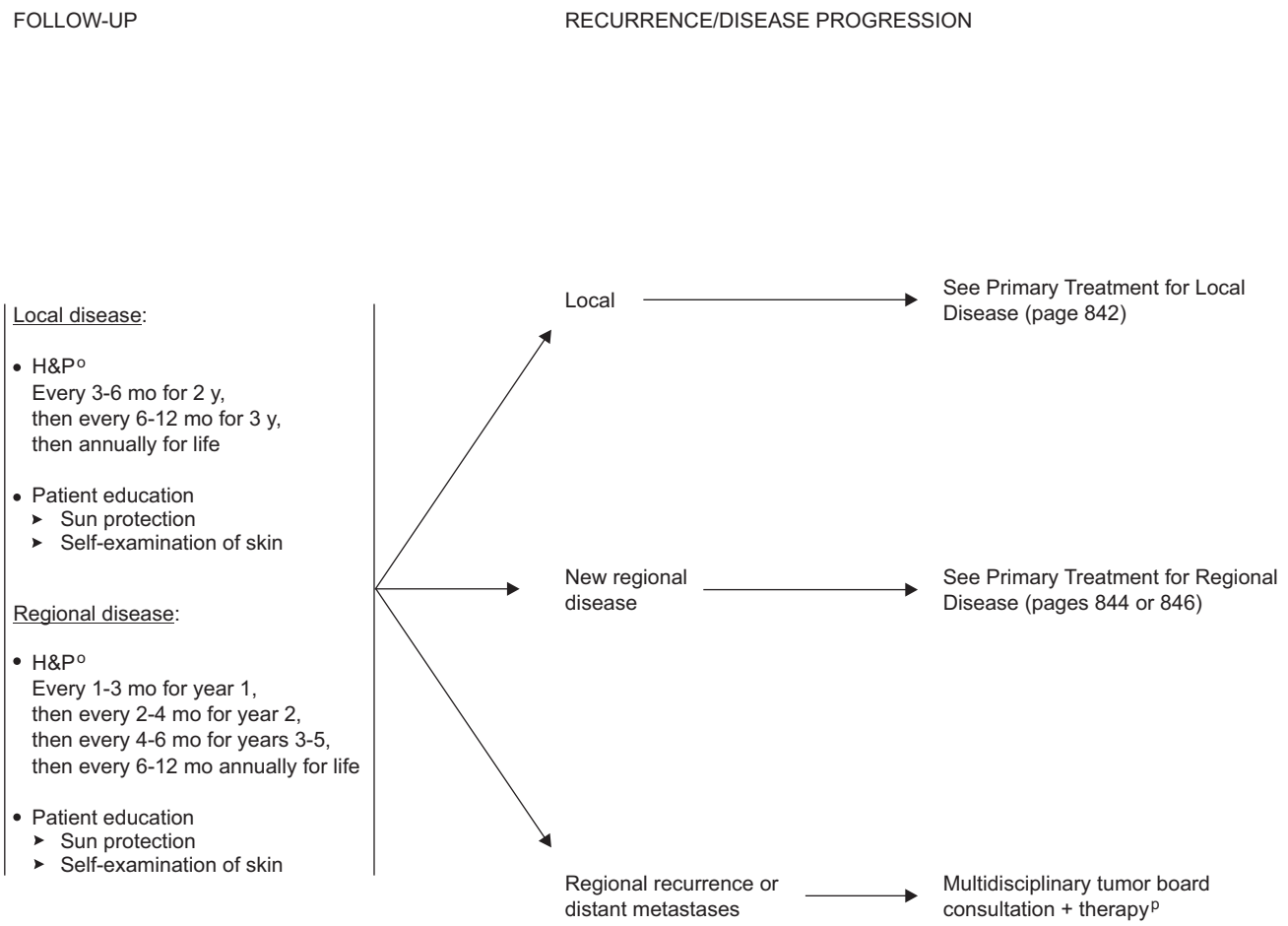

[o]Including complete skin and regional lymph node exam.
[p]Clinical trials are recommended for metastatic cutaneous squamous cell carcinoma. If the patient is a solid organ transplant recipient undergoing immunosuppressive therapy, consider dose reduction of the immunosuppressive agents and/or minimizing the doses of calcineurin inhibitors and/or antimetabolites in favor of mTOR inhibitors where appropriate. Cisplatin, either as a single agent or combined with 5FU, doxorubicin, or bleomycin, has occasionally produced useful responses, but data supporting efficacy are limited.

RISK FACTORS FOR RECURRENCE

H&P	Low Risk	High Risk
Location/size[1]	Area L < 20 mm	Area L ≥ 20 mm
	Area M < 10 mm	Area M ≥ 10 mm
	Area H < 6 mm[3]	Area H ≥ 6 mm[3]
Borders	Well-defined	Poorly defined
Primary vs. recurrent	Primary	Recurrent
Immunosuppression	(-)	(+)
Site of prior RT or chronic inflammatory process	(-)	(+)
Rapidly growing tumor	(-)	(+)
Neurologic symptoms	(-)	(+)
Pathology		
Degree of differentiation	Well-differentiated	Moderately or poorly differentiated
Adenoid (acantholytic), adenosquamous (showing mucin production), or desmoplastic subtypes	(-)	(+)
Depth: Clark level or thickness[2]	I, II, III, or < 4 mm	IV, V, or ≥ 4 mm
Perineural or vascular involvement	(-)	(+)

Area H = "mask areas" of face (central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermillion], chin, mandible, preauricular and postauricular skin/sulci, temple, ear), genitalia, hands, and feet.
Area M = cheeks, forehead, scalp, and neck.
Area L = trunk and extremities.

PRINCIPLES OF TREATMENT FOR SQUAMOUS CELL SKIN CANCER

- The goals of primary treatment of squamous cell skin cancer are the cure of the tumor and the maximal preservation of function and cosmesis. All treatment decisions should be customized to account for the particular factors present in the individual case and for the patient's preference. Customary age and size parameters may have to be modified.
- Surgical approaches often offer the most effective and efficient means for accomplishing cure, but considerations of function, cosmesis, and patient preference may lead to choosing radiation therapy as primary treatment in order to achieve optimal overall results.
- In certain patients at high risk for multiple primary tumors, increased surveillance and consideration of prophylactic measures may be indicated. (See Identification and Management of High-Risk Patients, pages 850 and 851.)
- In patients with low-risk squamous cell carcinoma in situ (Bowen's disease), in whom surgery or radiation is contraindicated or impractical, topical therapies such as 5-fluorouracil, imiquimod, photodynamic therapy (e.g., porfimer sodium, topical amino levulinic acid [ALA], or vigorous cryotherapy) may be considered even though cure rate may be lower.

[1]Must include peripheral rim of erythema.
[2]A modified Breslow measurement should exclude parakeratosis or scale/crust, and should be made from base of ulcer if present.
[3]Location independent of size may constitute high risk in certain clinical settings.

PRINCIPLES OF RADIATION THERAPY FOR SQUAMOUS CELL SKIN CANCER

Primary Tumor[1]	Dose Time Fractionation Schedule
Tumor Size	Dose Fractionation and Treatment Duration
< 2 cm	64 Gy in 32 fractions over 6-6.4 wk 55 Gy in 20 fractions over 4 wk 50 Gy in 15 fractions over 3 wk 35 Gy in 5 fractions over 5 d
≥ 2 cm	66 Gy in 33 fractions over 6-6.6 wk 55 Gy in 20 fractions over 4 wk
Postoperative adjuvant	50 Gy in 20 fractions over 4 wk 60 Gy in 30 fractions over 6 wk
Regional Disease—all doses at 2 Gy per fraction using shrinking field technique	
• After Lymph node dissection	
▸ Head and neck; with ECE	60-66 Gy over 6-6.6 wk
▸ Head and neck; without ECE	56 Gy over 5.6 wk
▸ Axilla, groin; with ECE	60 Gy over 6 wk
▸ Axilla, groin; without ECE	54 Gy over 5.4 wk
• No lymph node dissection	
▸ Clinically (-) but at risk for subclinical disease	50 Gy over 5 wk
▸ Clinically evident adenopathy: head and neck	66-70 Gy over 6.6-7 wk
▸ Clinically evident adenopathy: axilla, groin	66 Gy over 6.6 wk

ECE = Extracapsular extension

- Protracted fractionation is associated with improved cosmetic results.
- Radiation therapy is contraindicated in genetic conditions predisposing to skin cancer (e.g., basal cell nevus syndrome, xeroderma pigmentosum) and connective tissue diseases (e.g., scleroderma).

[1] Field margins for < 2 cm primary tumors should be 1-1.5 cm; for tumors > 2 cm, field margins should be 1.5-2 cm. Tighter field margins can be used with electron beam adjacent to critical structures (e.g., the orbit) if lead skin collimation is used. Bolus is necessary when using electron beam to achieve adequate surface dose. An electron beam energy should be chosen which achieves adequate surface dose and encompasses the deep margin of the tumor by at least the distal 90% line. Electron beam doses are specified at 90% of the maximal depth dose (Dmax). Orthovoltage x-ray doses are specified at Dmax (skin surface) to account for the relative biologic difference between the 2 modalities of radiation. If intensity-modulated radiation therapy is used to treat primary tumors, appropriate focus must be directed at assuring that adequate surface dose is present. Appropriate medical physics support is essential.

IDENTIFICATION AND MANAGEMENT OF HIGH-RISK PATIENTS

DEFINITION

- Certain patient groups are at high risk for developing multiple squamous cell skin cancers and tumors that can behave aggressively, including:
  - Organ transplant recipients
  - Those with immunosuppression from other causes (e.g., lymphoma, drug-induced, HIV)
  - Those with xeroderma pigmentosum
- Within these high-risk groups, individual high-risk patients should be identified for closer follow-up.
- Important individual risk factors include:
  - Total number of tumors
  - Frequency of development
  - Occurrence of aggressive tumors (e.g., extension beyond cutaneous structures, perineural involvement, large and poorly differentiated, having ≥ 3 risk factors for recurrence; see Risk Factors for Recurrence, page 848)
- In these patients, urgent diagnosis and treatment of lesions are important.

DIAGNOSIS

- Skin lesions in these high-risk populations may be difficult to assess clinically. Therefore, a low threshold for performing skin biopsies of suspect lesions is necessary.

TREATMENT OF PRECANCERS

- Actinic keratoses should be treated aggressively at first development.
  - Accepted treatment modalities include cryosurgery, topical 5-fluorouracil, topical imiquimod, photodynamic therapy (e.g., methyl aminolevulinate, porfimer sodium, topical ALA), and curettage & electrodessication.
  - Other modalities that may be considered include chemical peel (trichloroacetic acid) and ablative skin resurfacing (laser, dermabrasion).
- Actinic keratoses that have an atypical clinical appearance or do not respond to appropriate therapy should be biopsied for histologic evaluation.
- Ablative laser vermilionectomy may be of value in the treatment of extensive actinic cheilitis.

TREATMENT OF SKIN CANCERS

- Because patients in high-risk groups may develop multiple lesions in short periods, destructive therapies (curettage & electrodessication, cryotherapy) may be preferred for clinically low-risk tumors because of the ability to treat multiple lesions at a single patient visit. If curettage has been performed based solely on the clinical appearance of a low-risk tumor, the pathology from the biopsy taken at curettage should be reviewed to ensure no high-risk pathologic features are present that would suggest the need for further therapy beyond curettage.
- In patients who develop multiple adjacent tumors in proximity, surgical excision of invasive disease sometimes does not include surrounding in situ disease, and tissue rearrangement is minimized. In situ disease may then be treated with secondary approaches.
- In patients with multiple adjacent tumors of the dorsal hands and forearms, en bloc excision and split thickness skin grafting have been used with efficacy. However, healing is prolonged and morbidity is significant.
- Compared with the normal population, RT is used more frequently as an adjuvant therapy and for perineural disease, and less frequently for the treatment of primary tumors.
- Satellite lesions (in-transit cutaneous metastases) may occur more frequently in this population. They must be treated aggressively, with strong consideration of RT as the primary therapy.
- In organ transplant recipients, decreasing the level of immunosuppressive therapy may be considered in cases of life-threatening skin cancer or the rapid development of multiple tumors.

FOLLOW-UP

- Follow-up schedules should be titrated to the frequency of tumor development, and in rare cases may be as frequently as weekly.

IDENTIFICATION AND MANAGEMENT OF HIGH-RISK PATIENTS (cont.)

PATIENT EDUCATION

- Individual risk assessment is necessary and should be discussed.
- Both extensive and repetitive patient education regarding sun avoidance and protection are required.
- Sun avoidance and protection methods must be stringent.
- Monthly self-examination of all skin surfaces is recommended. With a history of invasive skin cancer, self-examination of the lymph nodes should be taught and performed.
- Rapid entrance into the health care delivery system at the onset of tumor development is critical.
- Patient education should begin at transplantation for organ transplant recipients, and at birth or diagnosis for patients with xeroderma pigmentosum.

PREVENTION

- Use of oral retinoids (acitretin, isotretinoin) has been effective in reducing the development of precancers and skin cancers in some high-risk patients. Side effects may be significant. Therapeutic effects disappear shortly after cessation of the drug. Oral retinoids are teratogenic and must be used with extreme caution in women with child-bearing potential.
- Aggressive treatment of precancers can prevent the development of subsequent invasive tumors.

Text continued from p. 837

- American Academy of Family Physicians. "Safe-Sun" Guidelines. American Academy of Family Physicians, 2000 (http://www.aafp.org/afp/20000715/375ph.html).
- Skin protection from ultraviolet light exposure: American College of Preventive Medicine Practice Policy Statement. Washington, DC: American College of Preventive Medicine (http://www.acpm.org/skinprot.htm).
- Centers for Disease Control and Prevention. Preventing skin cancer: findings of the Task Force on Community Preventive Services on reducing exposure to ultraviolet light (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5215a1.htm).

Genetics

The genetics of basal and squamous cell cancers are still being determined. Mutations in the tumor-suppressor PTCH (patched) gene system found on chromosome 9q are frequently present in basal cell cancers.[13] Mutations in the tumor suppressor gene *p53* seem to be an early common event in cutaneous squamous cell cancer development.[14,15] Mutations in several oncogenes (e.g., *ras* and *fos*) have also been identified. However, in NMSC development, the role any specific oncogene plays is unclear.[16,17]

Finally, certain genetic syndromes greatly predispose affected individuals to NMSC formation, such as albinism (in which skin pigment is absent), xeroderma pigmentosum (in which defects exist in ultraviolet light-induced unscheduled DNA repair), and nevoid basal cell carcinoma syndrome. Certain settings of immunosuppression (most notably, organ transplantation) also predispose affected individuals.[18,19]

Steps in Developing the Guidelines

In developing the practice guidelines for the treatment of NMSC, the NCCN panel initially limited the algorithms to basal and squamous cell cancers, which account for most of the NMSC.[20] Algorithms for rare forms of NMSC, Merkel cell carcinoma and dermatofibrosarcoma protuberans, were later developed as a supplement (see NCCN Clinical Practice Guidelines in Oncology [NCCN Guidelines] on Merkel Cell Carcinoma and Dermatofibrosarcoma Protuberans [to view the most recent version of these guidelines, visit the NCCN Web site at www.NCCN.org]). The panel decided to expand the American Joint Committee on Cancer (AJCC) staging system (see the staging table, available online, in these guidelines, at www.NCCN.org [ST-1]),[21] because more than 95% of basal and squamous cell cancers only involve local disease. Thus, the panel sought to develop a more comprehensive stratification system. This stratification system would reflect clinically relevant "levels" or "tiers of difficulty" involved in treating primary tumors.

The panel examined risk factors for basal and squamous cell cancers associated with inadequate treatment of primary tumors (i.e., risk factors associated with recurrence and metastasis). For each parameter, the group agreed on specific criteria to indicate when a given tumor is at a high risk for recurrence or metastasis. If a tumor has any parameter indicating high-risk behavior, then that tumor enters the high-risk category. In this way, the panel produced specific risk factors for recurrence for basal cell cancer (see page 840) and for squamous cell cancer (see page 848).

Clinical Risk Factors

Several clinical risk factors apply to both basal and squamous cell cancers (see pages 840 and 848). These risk factors include tumor location and size, the status of tumor borders, whether the tumor is primary or recurrent, certain settings of immunosuppression, and tumors developing in previously irradiated sites.

Location and Size

The panel elected to group together 2 separate risk factors: location and size. The science of dividing these factors into low- and high-risk categories is somewhat arbitrary because, to a certain extent, both factors, especially size, involve a continuous spectrum of risk.

For many years, location has been known to be a risk factor for NMSC recurrence and metastasis.[22,23] Stated in general terms, both basal and squamous cell cancers that develop in the head and neck area are more likely to recur than carcinomas developing on the trunk and extremities. Squamous cell carcinomas that develop on the genitalia, mucosal surfaces, and ear are also at greater risk of metastasizing. The concept of a so-called high-risk "mask area of the face" dates back to at least 1983 (Figure 1).[24,25] Size has also been shown to be a risk factor for NMSC

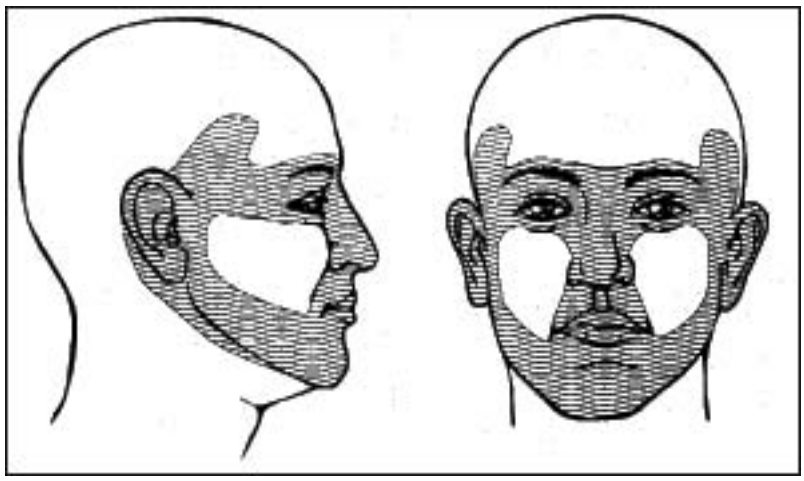

Figure 1 High-risk mask area of the face.
Basal cell and squamous cell carcinomas that develop in the high-risk mask area of the face are more likely to recur and metastasize than those that develop on the trunk and extremities.
Adapted with permission from Swanson NA. Mohs surgery: technique, indications, applications, and the future. Arch Dermatol 1983;119:761–773. Copyright 1983, American Medical Association. All rights reserved.

recurrence.[26–28] Various different divisions have been used; probably the most common has been "greater than (or less than) 2 cm in diameter."

The panel ultimately elected to base the location and size criteria mostly on a 27-year retrospective review of the experience of the Skin and Cancer Unit of the New York University (NYU) School of Medicine. This review, published in 1991, evaluated a database containing information on 5755 basal cell cancers.[29,30] Of the 5755 basal cell cancers evaluated, 2314 primary tumors were treated by curettage and electrodesiccation. Based on modified life-table 5-year recurrence rates generated in this study, anatomic sites were divided into high-, middle-, and low-risk sites for recurrence. The high-risk sites correspond roughly to the mask areas of the face (Figure 1). The middle- and low-risk sites correspond roughly to the middle- and low-risk divisions listed in the algorithms (see pages 840 and 848). In addition, recurrences in the NYU study were significantly more common when tumors in high-risk locations were 6 mm or more in diameter and when tumors in middle-risk locations were 10 mm or more in diameter.

These criteria based on size and locations are also more or less in agreement with similar work performed at the national level for the Health Care Financing Administration, which defined what constitutes high-risk tumors appropriate for Mohs micrographic surgery.[31]

Clinical Borders and Primary Versus Recurrent Disease

The risk factors of well- versus ill-defined clinical tumor borders and primary versus recurrent disease have been documented extensively in the biomedical literature.[25,27,28,32]

Immunosuppression

Settings of immunosuppression, such as organ transplantation[33,34] and long-term use of psoralen and ultraviolet A light (PUVA),[35,36] significantly increase the incidence of squamous cell cancer development. Basal cell carcinoma incidence also increases slightly in these settings.

Although several small anecdotal reports describe aggressive tumor behavior in patients with underlying malignancies or those taking immunosuppressive medications for non-oncologic diseases, the best data are from the organ transplant literature. The incidence of metastatic squamous cell cancer is significantly greater in this population than in individuals who have not undergone transplantation.[37] Uncertainty remains whether this is simply because of a greater number of tumors per patient or actually reflects more aggressive tumor behavior at the biologic level. Because organ transplant recipients collectively have worse outcomes, these patients (see pages 850 and 851) and their neoplasms are designated as high risk.

Actually, few published data suggest that basal cell cancers are more likely to recur or metastasize when they develop in immunosuppressed individu-

als.[38,39] The only evidence supporting this concept includes a few anecdotal clinical reports and several studies documenting laboratory evidence of immunosuppression in these patients. Nevertheless, because of this evidence and their own anecdotal experiences, the panel decided to classify both basal and squamous cell cancers that develop in settings of immunosuppression as potentially high-risk tumors.

Site of Prior Radiotherapy

"Tumors developing in sites of prior radiotherapy" refer to primary NMSCs arising in areas within radiation fields where radiation was administered previously for benign conditions. All recurrent tumors, irrespective of prior therapy, have already been defined as high-risk. Again, only a few articles in the biomedical literature support prior radiotherapy for benign conditions as a risk factor for NMSC recurrence or metastasis.[40–42] However, the panel consensus was that this is a valid risk factor.

Perineural Involvement

Perineural involvement poses a greatly increased risk of recurrence, whether the tumor is a basal or squamous cell cancer, and an increased risk of metastasis for squamous cell cancer.[22,23,27] Although perineural involvement is uncommon in any NMSC, it develops much more frequently in squamous cell cancer. In a prospective study, lesion size of 4 cm or more and perineural and deep invasion were identified as the pathologic factors associated with disease-specific mortality in squamous cell cancer.[26] If large nerve involvement is suspected, MRI should be considered to evaluate extent and rule out skull involvement.[43]

Degree of Differentiation

In their extensive meta-analysis of risk factors for local recurrence and metastasis of squamous cell cancer, Rowe et al.[27] found that patients with well-differentiated tumors fared significantly better than those with poorly differentiated lesions. Although Broders[44] originally divided squamous cell cancers histologically into 4 groups or grades, the modern trend has been to reduce the divisions to 2 groups: 1) well-differentiated and 2) moderately differentiated, poorly differentiated, or undifferentiated.[45] The panel adopted this modern approach.

Young Age Is Not a Clinical Risk Factor

Although young age (typically < 40 years) is generally viewed as a clinical risk factor for aggressive NMSC behavior, after much deliberation the panel decided it is not. The published biomedical literature does not strongly support "young age," per se, as a risk factor. Leffell et al.[46] documented an increased percentage of basal cell cancer with aggressive histologic growth patterns in young persons, but this histologic feature is already a separate risk factor in the algorithm.

When the features of 54 basal cell cancers in young patients referred for Mohs surgery were compared with similar tumors in older patients,[47] tumor location, histology, and clinical morphology did not differ appreciably between the groups. In fact, initial lesion and final defect sizes were statistically smaller in the younger group. In a study from the United Kingdom in which 39 young patients with basal cell cancer were followed up for a minimum of 5 years,[48] 4 tumors were incompletely excised, 2 recurred, and 1 metastasized. Another study observed a higher number of recurrent tumors in younger women referred for Mohs surgery than in other demographic groups.[49] Finally, 2 more recent studies found no difference in either recurrence rates or presence of aggressive histologic subtypes in younger versus older patients with basal cell skin cancer.[50,51]

The panel decided that, taken together, these studies do not support the suggestion that young age alone is a high-risk factor for NMSC behavior. Any tumor showing an aggressive histologic growth pattern, regardless of patient age, becomes a high-risk tumor.

Pathologic Risk Factors for NMSC

Histologic Subtypes

Basal Cell Skin Cancer: Histologic subtyping of basal cell cancer as a predictor of recurrence risk is a well-established concept.[52,53] The subtypes encompassed by the term *aggressive growth pattern*, including the micronodular, infiltrative, sclerosing, and morpheaform (or desmoplastic) patterns, are more likely to recur than the nodular and superficial basal cell cancers.

Squamous Cell Skin Cancer: The panel elected to include the entity basosquamous carcinoma under the category of squamous cell cancer rather than basal cell cancer. Basosquamous carcinomas are tumors, of which one part has the histologic appearance of a basal cell carcinoma and another that of a squa-

mous cell carcinoma. Some basosquamous tumors are the result of a basal cell cancer colliding with an adjacent squamous cell cancer. Others represent truly biphenotypic tumors, many of which may have started as basal cell cancer but subsequently have undergone prominent partial squamous metaplasia.[54] The risk for metastasis of these tumors seems to be determined by the squamous component. Several studies suggest that basosquamous carcinomas have metastatic capacity more like squamous cell cancer than basal cell cancer.[55–57] For this reason, the panel felt these tumors are best conceptualized as squamous cell cancers until other more instructive data become available.

Additional Clinical Risk Factors for Squamous Cell Carcinoma

The panel identified a few additional clinical parameters that increase the risk of squamous cell cancer only (see page 848), which are discussed in this section.

Site of a Chronic Inflammatory Process

A substantial body of biomedical literature has documented increased rates of metastasis for cutaneous squamous cell cancers arising in the setting of chronic scarring.[42]

Rapidly Growing Tumor

Only one article in the biomedical literature documents rapid growth of a cutaneous squamous cell cancer as a risk factor for increased metastasis and even death.[58] Nevertheless, the panel members unanimously agreed this is a rare, albeit definite, clinical setting indicative of high-risk behavior.

Neurologic Symptoms

In tumors with perineural involvement, clinical symptoms suggesting possible involvement of sensory or motor nerves may occur in up to 40% of cases. Symptoms may include pain, burning, stinging, anesthesia, paresthesia, facial paralysis, diplopia, and blurred vision.[59] Any suggestion of neurologic involvement in the region of a squamous cell cancer should place that tumor in a high-risk category.

Other Histologic Parameters

The panel members discussed whether any other histologic parameters should be included as risk factors for squamous cell cancer (see page 848) besides the degree of differentiation and perineural involvement.

Included Parameters: After some discussion, the panel elected to maintain the histologic subtypes of adenoid (or acantholytic) and adenosquamous (or mucin-producing) squamous cell cancer as markers for an increased risk of recurrence or metastasis. Again, few studies document the prognostic significance of these subtypes.[60–62] However, because these tumors probably would not be included in the high-risk category based on their degree of differentiation, the panel decided to list them as separate risk factors.

One histologic feature reported in the biomedical literature is the presence of desmoplasia. In studies from Germany, desmoplastic cutaneous squamous cell cancer was shown to pose a greatly increased risk of both recurrence and metastasis.[63,64] After some discussion, this histologic subtype was included in the guidelines as a risk factor for aggressive squamous cell cancer behavior.

Finally, a small, somewhat older body of biomedical literature found an association between invasion of squamous cell cancer into the deep reticular dermis or subcutaneous fat (corresponding to a Clark level IV or V melanoma) and aggressive behavior.[45] Several more studies suggest that squamous cell tumor depth, as measured in millimeters (similar to Breslow's original work with melanoma), may also have prognostic value.[45,63] After some discussion, and based on a meta-analysis of squamous cell cancer risk factors for recurrence and metastasis that found both types of depth measurements to have prognostic value,[27] the panel decided to include these 2 risk factors and used the division points determined by Rowe et al.[27] in the algorithm (see page 848).

One final note should be made regarding squamous cell cancer histology. The panel elected to include full-thickness atypia, or *squamous cell cancer in situ*, in the algorithm. Although the risk of metastasis from in situ disease is negligible, the risk of recurrence, as with the superficial form of basal cell cancer, depends on the presence or absence of any of the risk factors listed on page 848.

Excluded Parameter: The presence or absence of an infiltrative component at the advancing border of a squamous cell tumor was discussed. Some authors have advocated this parameter as a risk factor.[45] However, the pathologists on the panel believe this feature usually correlates well with the degree of differentiation, and that it is a description not routinely applied to squamous cell cancer. Consequently, this

parameter was excluded.

Similarly, the histologic subtype termed *spindle cell squamous cell cancer* has been associated with perineural invasion, which by itself is a risk factor for aggressive squamous cell cancer behavior.[65] However, the panel decided this indirect association did not warrant listing this subtype as a separate risk factor.

Identification and Management of Patients at High Risk for Squamous Cell Skin Cancer

The panel developed recommendations for the identification and management of patients at high risk for squamous cell skin cancer (see pages 850 and 851). Two members of the International Transplantation Skin Cancer Collective assisted the panel in this process and provided expert input. Certain populations of individuals, chiefly those with the nevoid basal cell carcinoma syndrome, are at risk for the development of multiple basal cell cancers; however, the panel believed that the existing basal cell cancer algorithm provides reasonably adequate guidance for care of these patients.

Oral retinoids have been found to be effective in reducing the development of precancers and skin cancers in some high-risk patients.[66–68] Side effects may be significant. Oral retinoids are teratogenic and must be used with extreme caution in women of child-bearing age.

Clinical Presentation and Workup

On clinical presentation of the patient with a suspicious lesion, workup of both basal and squamous cell cancers begins with a history and physical examination (see page 838). For basal cell cancer, the emphasis is on a complete skin examination. For squamous cell cancer, the emphasis is on a complete skin and regional lymph node examination. A full skin examination is recommended, because those with skin cancer often have additional, concurrent precancers or cancers located at other, usually sun-exposed, skin sites. These individuals are also at increased risk of developing cutaneous melanoma.[69,70] A skin biopsy is then performed on any suspicious lesion. The biopsy should include deep reticular dermis if the lesion is suspected to be more than a superficial process. This procedure is preferred, because an infiltrative histology may sometimes be present only at the deeper, advancing margins of a tumor, and superficial biopsies will frequently miss this component.[45,53] Because skin lesions in high-risk populations (see pages 850 and 851) may be difficult to assess clinically, a low threshold for performing skin biopsies in these patients is necessary. Imaging studies can be performed in all patients as clinically indicated for extensive disease.

In patients with squamous cell cancer, the presence of a palpable regional lymph node or abnormal lymph nodes identified by imaging studies should prompt a fine-needle aspiration (FNA) for diagnosis (see pages 844 and 846). When aspiration of lymph nodes in the head and neck region (see page 844) is negative, clinicians should consider reevaluation with imaging, repeat FNA, or open lymph node biopsy. Any positive findings should be followed by imaging to determine the size, number, and location of abnormal lymph nodes. When aspiration of lymph nodes in the trunk or extremity region (page 846) is positive, imaging should be performed as clinically indicated. If the aspiration is negative, an open biopsy should be performed.

Although uncommon, skin cancers may present with the appearance of deep extension, such as into bone or the orbit, for which preoperative imaging studies may be useful to help assess the extent of soft tissue or bony involvement.

Selection of Primary Therapy

Basal and squamous cell carcinoma are most commonly treated with surgery or radiation therapy (RT). In an evidence-based review of the literature, the best results were obtained with surgery.[71] However, consideration of function, cosmetic outcome, and patient preference may cause RT to be chosen as primary treatment to achieve optimal overall results. The algorithms list all of the therapies currently used to treat localized NMSC, including surgical techniques (i.e., curettage and electrodesiccation, excision with postoperative margin assessment [POMA], Mohs surgery or excision with "complete circumferential peripheral and deep-margin assessment" [CCPDMA]), RT, and superficial therapies.[72,73]

To assist users of the guidelines, the panel arrived at several principles of primary treatment for both basal and squamous cell cancer (see pages 841 and 848, respectively). These principles were developed

to suggest the importance of customizing any and all therapeutic approaches to the particular factors and individual needs of each patient. In certain high-risk patients, increased surveillance and prophylactic measures may be warranted (see pages 850 and 851). Specifics about the application of RT, including caveats regarding different types of therapeutic radiation and total doses and fractionation ranges, are described on pages 841 and 849.

Curettage and Electrodesiccation

The curettage and electrodesiccation technique is deemed effective for low-risk tumors with 3 caveats.[30] The first caveat states that this technique should not be used to treat hair-bearing sites because of the risk that a tumor, which extends down follicular structures, might not be adequately removed.

The second caveat states that if the subcutaneous layer is reached during the course of surgery, then surgical excision must be performed instead of curettage and electrodesiccation. This change in therapy is necessary, because the effectiveness of the curettage and electrodesiccation technique rests on the ability of the clinician to distinguish between firm, normal dermis and soft tumor tissue when using a sharp curette. Because subcutaneous fat is even softer than tumor tissue, the ability of the curette to distinguish and therefore selectively and completely remove tumor cells disappears.

The third caveat states that if curettage has been performed based only on the appearance of a low-risk tumor, biopsy results of the tissue taken at curettage should be reviewed to ensure that no high-risk pathologic features are present that would require additional therapy.

Excision With Postoperative Margin Assessment

Another therapeutic option for both basal cell and squamous cell cancers is excision with POMA, consisting of standard surgical excision followed by postoperative pathologic assessment of margins. The clinical margins chosen by the panel for low-risk tumors are based on the work of Brodland and Zitelli[74] and Wolf and Zitelli.[75] Their analysis indicated that excision of basal or squamous cell tumors smaller than 2 cm in diameter and clinically well circumscribed should result in complete removal (with a 95% CI) if 4-mm clinical margins are taken. Any peripheral rim of erythema around a squamous cell cancer must be included in what is assumed to be the tumor. The panel expanded the clinical margins for squamous cell cancers to 4 to 6 mm because of this issue and concerns about achieving complete removal. The indications for this approach were also expanded to include 1) reexcision of low-risk primary basal cell and squamous cell cancers located on the trunk and extremities (area L regions), if positive margins are obtained after an initial excision with POMA, and 2) primary excision of larger tumors located in L regions, deemed high-risk because of their size, if 10-mm margins can be taken.

If lesions can be excised with the recommended margins, then side-to-side closure, skin grafting, or secondary intention healing (i.e., all closures do not rotate tissue around and alter where residual "seeds" of tumor might be sitting) are all appropriate reconstructive approaches. However, if tissue rearrangement or skin graft placement is necessary to close the defect, the group believes intraoperative surgical margin assessment is necessary.

Mohs Surgery or Excision with Intraoperative Frozen Section Assessment

Either Mohs surgery or excision with CCPDMA using intraoperative frozen section (IOFS) assessment is the recommended therapeutic approach for all high-risk tumors. IOFS is not acceptable as an alternative to Mohs surgery unless it includes a complete assessment of all deep and peripheral margins. The descriptive term *CCPDMA* underscores the panel's belief that intraoperative assessment of all tissue margins is the key to complete tumor removal. Mohs surgery is preferred because of its documented efficacy.[27,76,77] If Mohs surgery is unavailable, complete tissue margin assessment must still be performed in another fashion. Consequently, the emphasis is placed on CCPDMA. For certain high-risk squamous cell lesions, sentinal lymph node mapping may be considered, although the benefit of this technique has not been proven.

Radiation Therapy

The role of RT was probably the single largest area of disagreement among the panel. Initially, the radiation oncologists wanted to use this therapy for almost all tumors, whereas the surgeons did not.

A large biomedical literature review was performed and circulated among the participants, followed by a panel discussion of the evidence.[27,29,32,40,59,78–102] A reasonable consensus was achieved after the surgeons realized that, when properly applied, RT can result in very good cure rates and excellent cosmesis, and the

radiation oncologists agreed that RT must be properly applied to achieve those cure rates and cosmesis. In other words, the details of RT are important and must be included in the algorithms.

The panel consensus is that adequate training in the techniques of Mohs micrographic surgery and RT are essential to achieve high cure rates when treating NMSCs. If either approach is inappropriately or inadequately applied and performed, less-than-optimal cure rates will result.

The panel also included RT as an option for nonsurgical candidates, but it is generally reserved for patients older than 60 years because of concerns about long-term sequelae.[73] RT is delivered in fractional doses involving orthovoltage x-ray or electron beam. Protracted fractionation is associated with improved cosmetic results (see pages 841 and 849). Electron beam therapy requires wider field margins than orthovoltage x-rays. Tighter field margins are possible when using electron beam therapy adjacent to critical structures. The size and location criteria for RT were expanded to include tumors in high-risk locations up to 15 mm in diameter, and tumors in middle-risk locations up to 20 mm in diameter. The low-risk regions of the trunk and extremities are not usually treated with RT; the genitalia, hands, and feet are also excluded. Verrucous carcinoma is excluded, because several reports in the biomedical literature document an increased metastatic risk after RT in patients with this generally low-grade malignancy. RT is also contraindicated in genetic conditions predisposing to skin cancer (e.g., basal cell nevus syndrome, xeroderma pigmentosum) and connective tissue diseases (e.g., lupus, scleroderma). Radiation is an effective treatment option for selected patients with Bowen's disease who have large or multiple lesions and those who refuse surgery.[103]

Intensity-modulated RT recently has become more widely used. The panel emphasized the importance of proper support and training for medical physicists using this new technology as primary treatment. Special attention is warranted to ensure adequate surface dose to the target area.

Superficial Therapies

Since cure rates may be lower, superficial therapies should be reserved for those patients where surgery or radiation is contraindicated or impractical.[104–106] Superficial therapies include topical treatment with 5-fluorouracil or imiquimod, photodynamic therapy (PDT), and cryotherapy. PDT involves the application of a photosensitizing agent on the skin followed by irradiation with a light source. In one randomized study with long-term follow-up, more patients with nodular basal cell carcinoma treated with methyl aminolevulinate (MAL) PDT had an excellent or good cosmetic outcome compared with those treated with surgery, even though surgery had superior efficacy.[107] In randomized studies, imiquimod was found to be effective for treating multiple, superficial basal cell skin cancers and squamous cell carcinoma in situ.[108,109]

In patients with low-risk shallow cancers, such as squamous cell carcinoma in situ (Bowen's disease)[48] or low-risk superficial basal cell carcinoma, topical therapies such as 5-fluorouracil, imiquimod, PDT (porfirmer sodium or topical amino levulinic acid), or vigorous cryotherapy may be considered even though the cure rate may be lower (see pages 841 and 848, respectively).

Actinic keratoses are most commonly treated with cryotherapy, or topical treatment with 5-fluorouracil or imiquimod.[8,110–112] PDT is a promising new treatment option for actinic keratoses. Randomized clinical trials showed that MAL PDT was as effective as cryotherapy for the treatment of actinic keratoses and squamous cell carcinoma in situ.[113–115]

Regional Lymph Node Dissection

For patients with squamous cell carcinoma, regional nodal involvement significantly increases the risk of recurrence and mortality.[116] If there are positive findings on either FNA or open biopsy of a lymph node, the preferred treatment is regional lymph node dissection following the corresponding pathway for the head and neck region (see page 845) or the trunk and extremity region (see page 846). Radiation alone is an alternative when surgery is not initially feasible; however, after radiation, patients should be reevaluated for neck dissection candidacy.

Parotid involvement is a poor prognostic factor for squamous cell carcinoma.[117,118] If the cancer extends down into the parotid fascia (i.e., into the parenchyma), a superficial parotidectomy must be performed because disease-specific survival is inferior with radiation alone.[119]

Adjuvant radiation with or without concurrent chemotherapy is often required after lymph node dissection.

Adjuvant Treatment

The value of postoperative radiation in reducing the rate of recurrence in high-risk patients has been widely accepted. The panel recommends adjuvant RT for any NMSC that shows evidence of substantial perineural involvement (i.e., involvement of more than just a few small sensory nerve branches or large nerve involvement). In select patients, local control approaches 100% with postoperative RT.[120] Adjuvant RT should also be considered if tissue margins are positive after Mohs surgery or a CCPDMA equivalent of a skin cancer (see pages 839 and 843).

Adjuvant RT should be considered for all patients with regional disease of the trunk and extremities who have undergone lymph node dissection. Postoperative radiation is recommended for all patients with nodal involvement in the head and neck region,[121,122] although observation is a reasonable alternative for those with only 1 small node and no extracapsular spread. Dosage information can be found on page 849.

Despite resection followed by RT, high-risk patients experience locoregional recurrence, distant metastasis, and 5-year survival rates of 30%, 25%, and 40%, respectively.[123] Two randomized trials on mucosal squamous cell tumors showed superior locoregional control and progression-free survival when combining postoperative radiation with concurrent cisplatin compared with radiation alone, although adverse events also increased.[124,125] These results support chemoradiation for squamous carcinomas of the skin. An analysis of the trials showed microscopically involved surgical margins and extracapsular extension as the only risk factors for which additional chemotherapy is beneficial.[126] Because margin assessment is not typically performed for neck dissections, concurrent chemotherapy should be considered in patients with extracapsular extension. All patients with incompletely excised nodes have a high risk of recurrence and should undergo chemoradiation.

Follow-Up and Recurrence

Two well-established points about patients with NMSC underlie the follow-up schedules. One point is that 30% to 50% of these patients will develop another NMSC during a 5-year follow-up period.[127] They are also at increased risk of developing cutaneous melanoma.[69,70] Therefore, continued long-term surveillance of these patients is essential, as is patient education about the values of sun protection and regular self-examination of the skin. A second point is that 70% to 80% of all cutaneous squamous cell cancer recurrences develop within 2 years of the initial therapy.[128] Therefore, close follow-up of these patients during this period is critical. Two phase II studies are underway to study the efficacy of gefitinib in the treatment of recurrent and metastatic squamous cell carcinoma of the skin.

Finally, for the management of local tumor recurrence, the algorithm directs clinicians to follow the appropriate pathways for primary treatment (see pages 839 and 847). Complicated high-risk tumors, regional recurrence, or the development of distant disease should be managed by a multidisciplinary tumor board, and clinical trials should be considered.

Metastatic Disease

Basal Cell Carcinoma

Although the behavior of cutaneous basal cell carcinoma is characteristically indolent, the disease rarely metastasizes to distant sites. In that instance, systemic therapy is indicated. No randomized prospective phase III trials for this situation are available, but published experiences report that responses to cytotoxic agents are not unusual, and occasional complete responses have been observed. In addition, a phase I clinical trial of an investigational inhibitor of the hedgehog signaling pathway has shown antitumor activity in 7 of 15 patients with metastatic basal cell carcinoma.[129]

Clinical trials of chemotherapy or biologic modifiers are recommended for metastatic basal cell carcinoma. Platinum-based combination chemotherapy has produced useful responses, including cisplatin and cyclophosphamide,[130] cisplatin and vinblastine,[131] cisplatin and doxorubicin,[132] and cisplatin and paclitaxel.[133,134]

Squamous Cell Carcinoma

Cutaneous squamous cell cancer with distant metastases, although rare, is more common than metastatic basal cell carcinoma, but less information is available regarding systemic therapy for the condition. No prospective phase III studies are available, and only one prospective phase II study is available. The preference is, again, participation in a clinical trial, although these trials are scarce. Often even large

centers do not open trials for rare diseases because of the costs involved.

If the patient has undergone solid organ transplantation and is taking immunosuppressive therapy, reducting the doses of the immunosuppressive agents or minimizing the doses of calcineurin inhibitors and/or antimetabolites in favor of mTOR inhibitors should be considered when appropriate.[135]

Cisplatin either as a single agent or combined with 5-fluorouracil, doxorubicin, or bleomycin has occasionally produced useful responses, but data supporting efficacy are limited. In the only phase II study of biochemotherapy with interferon-α, cis-retinoic acid, and cisplatin, 35 patients were assessed for response. Of these patients, 11 had distant metastases,[136] 1 of whom experienced a complete response; 12 patients with only regional lymph node metastases were treated, 3 of whom experienced either a partial (n = 2) or complete (n = 1) response, lending some credence to an effect of a cisplatin-based regimen. All other studies, reviewed by Weinberg et al.,[137] are retrospective and most are anecdotal.

Neoadjuvant systemic therapy in preparation for subsequent surgery and/or radiation is generally not considered useful for metastatic disease, with the possible exception of a few regional nodes.[132,138,139] Finally, some experts have advocated using therapies useful in treating metastatic squamous cell head and neck cancer for treating patients with metastatic cutaneous squamous cell cancer.[140] This strategy seems to have some merit, and has been used previously by the panel for treating metastatic Merkel cell tumor with therapies useful in treating small cell lung cancer.

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Individual Disclosures for the NCCN Basal Cell and Squamous Cell Skin Cancers Panel

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