Cutaneous Malignancies: Melanoma and Nonmelanoma Types

David T. Netscher, M.D.
Mimi Leong, M.D.
Ida Orengo, M.D.
Deborah Yang, M.D.
Carolyn Berg, M.D.
Bhuvaneswari Krishnan, M.D.
Houston, Texas

Learning Objectives: After reviewing this article, the participant should be able to: 1. Describe the epidemiology and etiology of skin cancers. 2. Understand the biology and predisposing conditions. 3. Understand tumor types and their clinical behavior. 4. Discuss the importance of diagnostic biopsy and various treatment options. 5. Understand the basis of surgical management and principles of reconstruction. 6. Review the most recently published literature and understand new concepts in tumor biology.

Summary: This article reviews melanoma and nonmelanoma cutaneous malignancies. (Plast. Reconstr. Surg. 127: 37e, 2011.)

This article covers basal cell carcinoma, squamous cell carcinoma, and cutaneous malignant melanoma. Over 1 million nonmelanoma skin cancers and over 56,000 cutaneous malignant melanomas occur in the United States each year. One in five Americans develops skin cancer in a lifetime; more than $1 billion was spent worldwide in 2004 to treat nonmelanoma skin cancer. Cutaneous malignant melanoma constitutes 4 to 11 percent of all skin cancers but is responsible for more than 75 percent of skin cancer–related deaths.1,5

Basal cell carcinoma is the most common skin cancer with no known precursor lesions, although the rare hamartoma or nevus sebaceus may transform into basal cell carcinoma. Eighty-six percent of basal cell carcinomas occur on the head and 7 percent on the trunk and extremities.7 Basal cell carcinoma is rare on the hand, penis, and lower lip; cutaneous malignancies at these sites are more likely squamous cell carcinoma. Cutaneous malignancies of the upper lip are almost always basal cell carcinoma, whereas those of the lower lip are usually squamous cell carcinoma. Basal cell carcinoma is the most common malignant eyelid tumor,8 with 67 percent on the lower lid and 10 percent at the inner canthus.

Squamous cell carcinoma most frequently occurs on the face, hands, and forearms. Actinic keratoses are squamous cell carcinoma “precursor” lesions.9 Squamous cell carcinoma rarely occurs on the eyelids; the ratio of basal cell carcinoma to squamous cell carcinoma on eyelids is 3:1. Squamous cell carcinoma accounts for 60 percent of tumors of the external ear.9 Skin cancers in the external auditory meatus are rare, but squamous cell carcinoma outnumbers basal cell carcinoma at this site.10

The distribution of basal cell carcinoma among African Americans is similar to that of Caucasians, although African Americans often develop cutaneous malignant melanoma in non–sun-exposed areas, such as the feet, subungually, and in the mucous membranes of the mouth, nasal passages, and genitals.11 Cutaneous malignant melanoma is twice as common in women, but the incidence is increasing rapidly in male subjects, having risen by 25 percent in men and 12 percent in women over the last 5 years.

Predisposing Factors

See Video 1, which reviews predisposing factors to skin cancers, inherited conditions, and...
basic genetics, available in the “Related Videos” section of the full-text article on PRSJournal.com. Video for Ovid users is available at http://links.lww.com/PRS/A299.

Clinical Risk Stratification of Basal Cell Carcinoma and Squamous Cell Carcinoma and Biopsy Techniques

See Video 2, which describes and demonstrates shave biopsy technique and also reviews Mohs surgery in depth available in the “Related Videos” section of the full-text article on PRSJournal.com. Video for Ovid users is available at http://links.lww.com/PRS/A300 (Tables 2 and 3).

DIAGNOSIS OF CUTANEOUS MALIGNANT MELANOMA AND NONMELANOMA SKIN CANCER

The clinician should follow the “ugly duckling” rule for melanomas. If an unusual-looking pigmented lesion stands out—an “ugly duckling”—biopsy is indicated. Adhere to the ABCDEs of melanoma for biopsy guidelines (Table 4).

Clinical experience and the naked eye provide the correct diagnosis in 65 percent of pigmented lesions.66 Accuracy is improved (80 to 85 percent) with imaging tools, such as epiluminescence microscopy and serial total body photography, but most clinicians prefer biopsy of suspicious lesions over reliance on clinical examination for decision making.67

BASAL CELL CARCINOMAS

Tumor Spread

Basal cell carcinomas rarely (<0.1 percent) metastasize. Experimentally transplanted basal cell carcinomas do not survive free of dermal tissue.71,72 Basal cell carcinomas spread along paths of least resistance (periostium, perichondrium, fascia, or tarsal plate8). Bone, cartilage, and muscle invasion are uncommon but can occur. A nasal tip basal cell carcinoma, for example, will grow along the perichondrium until it encounters articulating cartilages; it then extends into the soft-tissue plane separating the cartilages. Embryonic fusion planes are vulnerable to basal cell carcinoma penetration. Basal cell carcinoma recurrence in the inner canthus, the base of nostrils, and the preauricular and postauricular areas is higher than at other sites73,74 (Fig. 1).

Reticular dermis is a relative barrier to basal cell carcinoma penetration, which may explain why basal cell carcinomas on the posterior trunk remain superficial, although their lateral spread may be greater than suspected.75 Perineurial spread occurs only in highly invasive forms of basal cell carcinoma.75

Tumor Types

Basal cell carcinoma differential includes factitious ulceration, eczema, actinic keratosis, psoriasis, and fungal infections. Nevi may be maculopapular and resemble nodular, pigmented basal cell carcinoma. The latter are firm and cannot be indented by a blunt-tipped swab. Lesions that feel thickened and appear to have deep extension beneath a superficial abnormality likely need biopsy.

When predicting tumor behavior and hence optimizing treatment, histologic growth pattern is more relevant than type of differentiation.76 Jacobs et al.77 were the first to differentiate tumor types and tumor behavior, distinguishing among nodular, ulcerative, and infiltrative histologic types. We now distinguish primarily between circumscribed and diffuse lesions; secondarily, within these two large groups, we classify basal cell carcinoma according to type and degree of differentiation78–80 and depth of invasion (especially if affixed to deeper structures) (Table 5).

Pigmented basal cell carcinoma may be nodular, nodulo-ulcerative, micronodular, or superficial (Fig. 2). These are differentiated from nevi, melanoma, pigmented seborrheic keratosis, and pigmented Bowen’s disease.
1. Circumscribed types
   
   A. Solid (nodular) basal cell carcinoma (Fig. 3)
   - May ulcerate—nodulo-ulcerative
   - Most common form of basal cell carcinoma
   - Dome-shaped, well-defined borders, pink/red papule, “pearly” appearance, telangiectasias

   B. Adenoid basal cell carcinoma
   - Adenoid cystic basal cell carcinoma—both adenoid and cystic areas present (Fig. 4)

   C. Fibroepithelioma of Pinkus
   - Sometimes called fenestrated tricho-blastoma

---

Table 1. Risk Factors for Carcinogenesis

<table>
<thead>
<tr>
<th>Individual Risk Factors</th>
<th>BCC</th>
<th>SCC</th>
<th>CMM</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fair skin</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Blond hair/red hair</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Freckling</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Personal or family histories of skin cancer</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>50% of patients treated for NMSC at risk of another NMSC in 5 yr Risk of second primary CMM increases 11–24% after first CMM</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Environmental Risk Factors</th>
<th>BCC</th>
<th>SCC</th>
<th>CMM</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>UVR</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>UV exposure associated with 90% of NMSC and 65% of CMM</td>
</tr>
<tr>
<td>Other exposure to UV light</td>
<td>±</td>
<td>+</td>
<td>±</td>
<td>Risk not increased among dark-skinned patients receiving PUVA</td>
</tr>
<tr>
<td>(PUVA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arsenic</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Polycyclic aromatic hydrocarbons</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>3.3 times increased risk of SCC development</td>
</tr>
<tr>
<td>Smoking</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Ionizing radiation</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genetic syndromes</th>
<th>BCC</th>
<th>SCC</th>
<th>CMM</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>XP</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>UVR induces dimerization between thymine nucleotides → normal cells would excise UV-induced thymine dimers</td>
</tr>
<tr>
<td>Gorlin syndrome</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Repair process deficient in XP excision</td>
</tr>
<tr>
<td>Albinism</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>AD disorder with mutation in patched gene</td>
</tr>
<tr>
<td>Epidermodysplasia verruciformis</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>AR disorder with defective cell-mediated immune response to HPV</td>
</tr>
<tr>
<td>Familial atypical multiple mole melanoma syndrome</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>AD disease with following diagnostic criteria: (1) one or more first or second-degree relative with CMM; (2) many nevi—some irregular in color, shape, size; (3) melanoma development at a younger age (usually by 33 yr) Lifetime risk of CMM is 100% CDKN2A mutation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical situations</th>
<th>BCC</th>
<th>SCC</th>
<th>CMM</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevus sebaceus</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>10–20% evolve into BCC</td>
</tr>
<tr>
<td>Porokeratosis</td>
<td></td>
<td></td>
<td></td>
<td>Most commonly seen in porokeratosis of Mibelli or disseminated superficial actinic porokeratosis</td>
</tr>
<tr>
<td>Bowenoid papulosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DLE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic inflammation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunosuppression</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BCC, basal cell carcinoma; SCC, squamous cell carcinoma; CMM, cutaneous malignant melanoma; NMSC, nonmelanoma skin cancer; UVR: ultraviolet radiation; UV, ultraviolet; PUVA, psoralen and ultraviolet A therapy; HPV, human papilloma virus; XP, xeroderma pigmentosum; AD, autosomal dominant; AR, autosomal recessive; DLE, discoid lupus erythematosus; AIDS, autoimmune deficiency syndrome.
Pedunculated skin-colored nodules
May be mistaken for melanoma

D. Basosquamous (metatypical) carcinoma
Controversial term
Basal cell carcinomas with squamous differentiation behave like pure basal cell carcinoma

2. Diffuse types: plaque-like with horizontal spread and poorly defined margins
A. Superficial basal cell carcinoma (Fig. 5)
Superficial “multicentric” basal cell carcinoma is misnomer; three-dimensional histologic reconstructions reveal interconnections among apparent multiple foci
Second most common type of basal cell carcinoma
Trunk and extremities
Flat, pink, scaly patches with ulcerations and crusting
Horizontal growth extends beyond clinically defined borders
Seldom invade deep dermis
Confused with eczema, actinic keratosis, psoriasis, fungal infection

B. Morpheaform (sclerosing or fibrosing) basal cell carcinoma (Fig. 6)
Most aggressive subtype
Firm, depressed plaque surrounded by “scar”
Margin definition by inspection or palpation impossible
Spread extends 7 mm beyond apparent tumor border

Table 2. Risk of Recurrence of Nonmelanoma Skin Cancer Based on Location

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Trunk (extremities)</td>
</tr>
<tr>
<td>Medium</td>
<td>Cheeks, forehead, neck, scalp</td>
</tr>
<tr>
<td>High</td>
<td>Central face, eyelids, eyebrows, peri orbital area, lips, chin, mandible, preauricular and postauricular areas, genitalia, hands, feet</td>
</tr>
</tbody>
</table>

Table 3. Clinical and Pathologic Risk Factors for Recurrence of Nonmelanoma Skin Cancer

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Low Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical risk factors</td>
<td>Low &lt;20 mm</td>
<td>Low &gt;20 mm</td>
</tr>
<tr>
<td>Location—diameter</td>
<td>Medium &lt;10 mm</td>
<td>Medium &gt;10 mm</td>
</tr>
<tr>
<td></td>
<td>High &lt;6 mm</td>
<td>High &gt;6 mm</td>
</tr>
<tr>
<td></td>
<td>Well-defined</td>
<td>Poorly defined</td>
</tr>
<tr>
<td></td>
<td>Primary</td>
<td>Recurrent</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Border</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary or recurrent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunosuppression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor at site of prior radiotherapy or chronic inflammatory process</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapidly growing tumor</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Neurologic symptoms, pain, paresthesia, paralysis (SCC only)</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Pathologic risk factors</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Perineurial or vascular involvement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtype (BCC only)</td>
<td>Nodular, superficial</td>
<td>Morpheaform, micronodular, metatypical</td>
</tr>
<tr>
<td>Degree of differentiation (SCC only)</td>
<td>Well-differentiated</td>
<td>Moderately or poorly differentiated</td>
</tr>
<tr>
<td>Depth, Clark level or thickness (SCC only)</td>
<td>I, II, and III are &lt;4 mm</td>
<td>IV and V are &gt;4 mm</td>
</tr>
</tbody>
</table>

BCC, basal cell carcinoma; SCC, squamous cell carcinoma.

Deep infiltration of dermis
- Dense stroma precludes curettage

C. Infiltrative basal cell carcinoma\(^8\) (Fig. 7)
- Opaque yellow-white color
- Blends with surrounding skin, no raised border
- Occurs along embryonic fusion lines, such as inner canthus

D. Micronodular\(^8\)
- Deceptive histologic subtype
- Clinically undetected extension

**SQUAMOUS CELL CARCINOMAS**
Squamous cell carcinomas, unlike basal cell carcinomas, have premalignant precursors and an in situ variant. They may occur in mucous membranes and genitalia, and they metastasize to lymph nodes and hematogenously.

**Prognosticators**
Although tumor type is the principal prognosticator in the treatment of basal cell carcinoma, the following are more important factors influencing prognosis of squamous cell carcinoma:

**Broder grades of differentiation.**\(^8\) There are four grades: grade 1 has a 3:1 ratio of differentiated to undifferentiated cells, with the ratio declining through grade 4, which has no differentiation. Grades 3 and 4 are twice as likely to recur and three times more likely to metastasize than grades 1 and 2.

**Location.** External ear, lips, nose, scalp, and genitals are high-risk locations.\(^8,8\) Periungual squamous cell carcinoma has a high incidence of local recurrence but a low metastatic rate.\(^8\)

**Tumor size.** \(T_1\) indicates lesion size less than 2 cm, \(T_2\) is 2 to 4 cm, and \(T_3\) is more than 4 cm. Squamous cell carcinomas larger than 2 cm are twice as likely to recur and three times more likely to metastasize than tumors less than 2 cm.

**Tumor depth.** Some believe tumor depth to be the most important factor determining whether cutaneous squamous cell carcinoma will metastasize.\(^47\) Squamous cell carcinomas more than 4 mm deep or extending into subcutaneous tissue (Clark level V) are more likely to recur and metastasize.\(^8\)

**Perineurial invasion.** Perineurial invasion is a poor prognostic sign for both recurrence and metastasis and an indication for postexcision radiation therapy. It is associated with 47 percent local

---

**Table 4. “ABCDEs” of Melanoma**

<table>
<thead>
<tr>
<th>A</th>
<th>Asymmetry of lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Border irregularity</td>
</tr>
<tr>
<td>C</td>
<td>Color variegation</td>
</tr>
<tr>
<td>D</td>
<td>Diameter &gt;6 mm</td>
</tr>
<tr>
<td>E</td>
<td>Evolution (changing lesion)</td>
</tr>
</tbody>
</table>

**Fig. 1.** Basal cell carcinomas at embryonic fusion lines (such as retroauricular) have higher recurrence rates.

**Fig. 2.** Pigmented nodular basal cell carcinoma of the nose.

---

**Table 5. Classification of Basal Cell Carcinoma**

<table>
<thead>
<tr>
<th>Circumscribed BCC</th>
<th>Diffuse BCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodular, solid</td>
<td>Superficial</td>
</tr>
<tr>
<td>Nodular, ulcerative</td>
<td>Morpheaform (sclerosing)</td>
</tr>
<tr>
<td>Adenoid</td>
<td>Infiltrating</td>
</tr>
<tr>
<td>Cystic</td>
<td>Micronodular</td>
</tr>
<tr>
<td>Keratotic (cornifying)</td>
<td>Eccrine and apocrine epitheliomas</td>
</tr>
<tr>
<td>Fibroepithelioma of Pinkus</td>
<td></td>
</tr>
</tbody>
</table>

BCC, basal cell carcinoma.
recurrence, 35 percent metastasis to regional nodes, and 15 percent distant metastasis. Most patients are asymptomatic with perineural involvement but may have pain or motor symptoms, especially if the second division of the trigeminal nerve or the facial nerve branches are involved.

**Rapid growth and recurrence.** Rapid growth and recurrence are both high risk factors for tumor recurrence and metastasis.

---

**Fig. 3.** (Above) Nodular and nodulo-ulcerative basal cell carcinomas (as in this case with a nasal lesion) have clinically well-defined margins. (Below) Histologic analysis of nodular basal cell carcinoma shows a well-circumscribed tumor, and nodules demonstrate peripheral palisading (hematoxylin and eosin, ×100).

**Fig. 4.** Adenoid cystic basal cell carcinoma may be quite large but will have well-defined clinical borders. Large lacunae rupture onto the skin surface.
When developing a surgical management plan, one must understand the meaning of "high risk." Recommended surgical margins for excision of low-risk squamous cell carcinoma are 4 mm and for high-risk tumors, 6 mm, including underlying fat.

**Squamous Cell Carcinoma Tumor Subtypes**

The characteristic clinical appearance of squamous cell carcinoma is a raised pink papule or plaque, often scaly and sometimes ulcerated. Tumor appearance varies from lesions with ill-defined borders, such as actinic keratosis, to large ulcerated invasive lesions. Because squamous cell carcinoma may appear quite similar to actinic keratosis, only biopsy accurately identifies significant cytologic atypia and invasion of squamous cell carcinoma.

1. Squamous cell carcinoma in situ: confined to epidermis
   A. Actinic keratosis
      • Most common premalignant cutaneous lesion

   B. Bowen disease
      • Dysplasia at all epidermal levels
      • Controversial association with extracutaneous malignancy
      • Called erythroplasia of Queyrat on glans penis
      • 10 percent become invasive after many years
      • Invasive squamous cell carcinoma is more virulent than squamous cell carcinoma arising de novo; metastases develop in one-third of cases

- Rough, scaly, discrete epidermal lesions (Fig. 8)
- Predominant on sun-exposed areas
- Bleeding surface remains when scales are removed
- Invasive squamous cell carcinoma develops in approximately 20 percent of actinic keratoses
- Squamous cell carcinomas may arise de novo but more commonly develop from precursors; these are less virulent than squamous cell carcinomas arising in normal skin

---

Fig. 5. (Above) Spreading superficial basal cell carcinoma of the leg was initially mistakenly treated as a venous ulcer. (Below) Superficial multifocal basal cell carcinoma shows basoloid cell proliferation with peripheral palisading (arrow) from the base of the epidermis. The deeper dermis shows lymphocytic infiltrates (hematoxylin and eosin, ×100).
• Invasive squamous cell carcinoma occurs in higher percentage of erythroplasia of Queyrat (30 percent) than Bowen disease occurring elsewhere.\textsuperscript{95}
• Clinical appearance is erythematous, scaly, macular patch with sharply defined enlarging borders; occasional fissuring or pigmentation; nail bed with periungual scaling and nail discoloration (Fig. 9)
• Ulceration usually a sign of invasive squamous cell carcinoma

2. Invasive squamous cell carcinoma, common subtypes: invasion through basement membrane into dermis
   A. Invasive squamous cell carcinoma associated with actinic keratosis
   • Most usual form of invasive squamous cell carcinoma
   • Always located in sun-damaged and sun-exposed skin
   • Low metastatic risk and favorable prognosis
   B. De novo invasive squamous cell carcinoma
   • Not preceded by in situ component (Fig. 10)
   • High-risk squamous cell carcinoma variant with metastatic rate as high as 14 percent.\textsuperscript{96}
   • Occurs in organ transplant and immunocompromised patients and in areas of chronic irritation (e.g., burn scars)

C. Keratoacanthoma
   • Rapidly growing firm nodule with central keratin plug;\textsuperscript{97} may spontaneously regress with considerable scarring (Fig. 11)
   • Most feel it should be called squamous cell carcinoma keratoacanthoma type
   • Clinical and histological difficulty in differentiating solitary keratoacanthoma from more aggressive invasive squamous cell carcinoma.\textsuperscript{98}
   • Complete surgical removal recommended

D. Adenoid (acantholytic) squamous cell carcinoma
   • Uncommon; overwhelming male predominance
   • Sun-exposed areas in elderly
   • Clinical appearance of eroded nodules, especially on face and ears, with rapid local growth rivaling keratoacanthoma.\textsuperscript{99}
   • Three to 19 percent metastasize

Considerations for management of nonmelanoma skin cancers are as follows.\textsuperscript{100–107}
Tumor type. Well-demarcated, exophytic basal cell carcinomas have circumscribed nodular histology and can be managed by curettage, electrodesiccation and curettage, cryosurgery, radiation, or surgical excision, all with an expected high cure rate. Lesions with ill-defined edges have more extensive subclinical spread and higher recurrence rate, and are best managed with Mohs micrographic surgery. Electrodesiccation and curettage or cryosurgery may be the treatment of choice for large superficial basal cell carcinomas of the back, as excision and skin grafting may produce suboptimal cosmetic results. Lesions less than 2 cm in diameter, other than superficial basal cell carcinoma, are best treated with surgical excision and Mohs micrographic surgery. Irradiation may be suitable. Tumor recurrence increases significantly with other forms of treatment.

Patient age. Physicians often assume that the elderly are not surgical candidates and should be treated with radiation. Elderly patients should not be denied curative surgery; they often tolerate even a difficult Mohs resection under local anesthesia. Because aged skin is more forgiving than young

Fig. 7. (Above) Infiltrative basal cell carcinoma, medial canthus. An indistinct tumor border blends with the surrounding skin. (Below) Ulcerated skin with loss of the epidermis in the midportion and infiltrating basal cell carcinoma in the dermis. Irregular islands of neoplastic cells are infiltrating into the deep dermis. A small portion of the intact epidermis is seen on the left (hematoxylin and eosin, ×40).

Fig. 8. Classic clinical appearance of multiple actinic keratoses on the forehead.

Fig. 9. Bowen disease may present a variety of clinical appearances. This clinical example shows diffuse finger involvement with hyperkeratosis and fissuring.
skin, electrodesiccation and curettage of a lesion yields a good cosmetic result in an older patient when the same treatment might produce hypertrophic scarring in a younger person.

**Number of lesions.** Excision of multiple lesions may be difficult. Cryosurgery or electrodesiccation and curettage may be the most realistic treatment approach for a patient with multiple superficial basal cell carcinomas of the trunk.

**Anatomic location.** Nonmelanoma skin cancers in high-risk areas, such as nasal ala, preauricular and postauricular areas, and medial canthus, may be best managed by frozen-section margin determination. Aside from mode of tumor spread, anatomic location may have particular unsuitable characteristics; for example, mobility of eyelid or lip tissue may make for effective curettage in these areas difficult. Basal cell carcinomas in areas rich in pilosebaceous units, such as the scalp and nasal tip, may bud off hair follicles and escape the curette. The deep dermis on the distal nose is so dense that tumor invaginations may not be adequately removed by curettage. Invasive basal cell carcinomas of the scalp are usually not treated cryosurgically because the scalp’s vascularity makes obtaining an adequate freeze difficult.

**Primary versus recurrent tumor.** Mohs surgery may be the best approach, since recurrent tumors are usually clinically ill-defined and embedded in a sclerotic matrix.

### Types of Treatment

**Cryotherapy**

See Video 2, available in the “Related Videos” section of the full-text article on PRSJournal.com. Video for Ovid users is available at [http://links.lww.com/PRS/A300](http://links.lww.com/PRS/A300). This video describes and demonstrates shave biopsy technique and also reviews Mohs surgery in depth.

**Electrodesiccation and Curettage**

Five-year electrodesiccation and curettage recurrence rates for small basal cell carcinoma, squamous cell carcinoma, and squamous cell carcinoma in situ are comparable to rates for surgical excision, with 5-year recurrence for primary basal cell carcinoma less than 1 cm being 3.3 to 5.7 percent and with similar rates for treatment of squamous cell carcinoma. Most studies exclude high-risk nonmelanoma skin cancer. Diagnosis may be obtained from curetted material, but curettage has no submission of tissue to confirm margins. A study showed 5-year basal cell carci-
noma recurrence rates of 1.2 percent even in medium-risk and high-risk facial sites. In some situations, electrodesiccation and curettage may be an option for high-risk areas, although it is generally reserved only for low-risk lesions. The cosmetic result for electrodesiccation and curettage is usually inferior to that for surgical excision, often yielding a round, hypopigmented, and possibly hypertrophic scar.

**Topical Therapies**

Topical therapies offer at-home treatment convenience, the ability to treat large surface areas with multiple lesions, and good cosmesis. Disadvantages include longer treatment time and the need for excellent patient compliance. Imiquimod (Aldara; Graceway Pharmaceuticals, Bristol, Tenn.) is U.S. Food and Drug Administration–approved for treatment of superficial basal cell carcinomas; over 90 percent clearance of superficial basal cell carcinomas with the use of imiquimod five to seven times per week for 6 to 16 weeks has been reported. Nodular basal cell carcinomas had a 70 to 100 percent clearance rate when imiquimod was used nightly three to seven times a week, with best results attained with treatment carried out for 6 to 12 weeks. Reports describe the efficacy of imiquimod for treatment carried out for 6 to 12 weeks.112,113 Reports describe the efficacy of imiquimod 5% cream in Bowen disease,114 invasive squamous cell carcinoma,115 and lentigo maligna melanoma.116 In these circumstances, given limited data, imiquimod should be used only if a patient cannot undergo other treatments.

Topical 5-fluorouracil has a role, especially in the treatment of diffuse actinic keratoses of the face. Application of a 1% or 2% solution twice a day for 4 weeks is used (a 5% solution may be required for scalp). Lesions resistant to treatment may contain foci of squamous cell carcinoma.117

**Surgical Excision**

Surgical excision is subdivided into excision with standard margins, excision with frozen-section margin evaluation, and Mohs micrographic surgery. For low-risk nonmelanoma skin cancers extending into the dermis only, excision with standard margins (4 mm for basal cell carcinoma) is the usual treatment. Adequate margins of 4 mm for low-risk squamous cell carcinoma and 6 mm for high-risk squamous cell carcinoma have been demonstrated by direct tumor extension from the clinical margin but are not necessarily an estimate of cure rate but rather of contiguous tumor excision. Because of superior cosmesis, some prefer excision to superficial ablative techniques; excision also provides pathologic specimens for histologic examination.

Surgical excision offers overall cure rates greater than 90 percent.118 Loupe magnification for tumor excision allows more accurate visual assessment of tumor borders. A 2-mm margin yields a cure rate of 94 percent in small (<1 cm) nodular basal cell carcinomas.119 Margins of 3 to 5 mm around a tumor and extending into subcutaneous fat are recommended for primary basal cell carcinomas less than 2 cm in diameter. Basal cell carcinomas more than 2 cm may require margins as wide as 10 mm, as do tumors with aggressive histologic growth patterns, such as superficial basal cell carcinoma of the trunk and morpheaform lesions.120,121

Frozen sections of tumor margins are expensive and not recommended for every suspected nonmelanoma skin cancer. They are unnecessary for well-circumscribed lesions less than 1 cm in diameter, for lesions in noncritical areas in locations where wide surgical margins can be taken, for lesions where repair requires only direct suture closure, and for low-risk patients. One can safely excise the lesion and await the pathologist’s permanent section report. If microscopic margins are found to be involved, subsequent excision does not adversely affect cure.

To evaluate completeness of excision, frozen sections of margins are recommended for high-risk squamous cell carcinoma and basal cell carcinoma in high-risk areas, lesions more than 2 cm, and any morpheaform basal cell carcinoma. Bread-loafing and cross-section methods of tissue examination evaluate a small percentage of the tissue margin. Comparison of several methods for checking surgical margins revealed that only peripheral sectioning combined with bread-loafing/cross-sectioning examined almost 100 percent of the surgical margin.122

Mohs micrographic surgery is an increasingly popular treatment. (See Video 2, available in the “Related Videos” section of the Full-Text article on PRSJournal.com. Video for Ovid users is available at http://links.lww.com/PRS/A300.) Indications for Mohs surgery include tumors greater than 2 cm, recurrent tumors, tumors in high-risk areas, tumors with indistinct clinical margins, and tumors in cosmetically sensitive regions. Contraindicated for this technique are tumors with pathology that may be difficult to assess on frozen section. Caution must be exercised in multifocal tumors, such as recurrent tumors within a surgical scar; it is better in such cases to excise the entire scar and evaluate the margins surrounding this tissue. Mohs micrographic surgery has an advantage over conventional excision for squamous cell carci-
noma with lower recurrence rates in the following situations: lip, 3.1 percent versus 10.9 percent; ear, 5.3 percent versus 18.7 percent; recurrent tumors, 10 percent versus 23.3 percent; perineurial invasion, 0 percent versus 25.2 percent; tumors more than 2 cm, 25.2 percent versus 41.7; and poorly differentiated squamous cell carcinomas, 32.6 percent versus 53.6 percent.125

Radiotherapy
Radiotherapy is an option for patients when excision is not possible, for instance, in the elderly, patients with large lesions, and patients with concomitant medical comorbidities that might complicate surgery. Five-year recurrence for primary basal cell carcinoma treated with radiotherapy is 8 to 15.8 percent,126 and that for squamous cell carcinoma is similar at 5 to 10 percent.127 Radiotherapy can be used for adjuvant treatment of nonmelanoma skin cancers, such as incompletely excised large tumors, or tumors at high-risk for metastasis, such as large or deep squamous cell carcinomas or those with perineurial invasion.128

Sentinel Lymph Node Biopsy
Squamous cell carcinomas are slower to invade deeper tissue than are cutaneous malignant melanomas. Superficial dermis and epidermis are devoid of lymphatic drainage, making squamous cell carcinoma less likely to spread via lymphatics. Sentinel lymph node biopsy of high-risk squamous cell carcinomas is currently under investigation.129

CUTANEOUS MALIGNANT MELANOMA

Morphologic Subtypes
Several cutaneous malignant melanoma morphologic subtypes occur (Figs. 12 through 16); these do not directly influence survival but may affect ultimate prognosis. Cutaneous malignant melanoma classification subdivides those lesions with rapid radial growth (superficial spreading, lentigo maligna, acral lentiginous, and other unclassified lesions) and those with relative absence of radial growth (nodular melanoma). Vertical growth determines tumor depth and ultimate prognosis. Breslow thickness is measured from epidermal basement membrane to deepest melanoma tumor cells.13,14

Superficial spreading melanoma
- 50 to 70 percent of melanoma types
- Long horizontal growth phase (6 months to 6 years) before vertical growth phase; therefore, better prognosis

Lentigo maligna (solar) melanoma
- Strong correlation with sunlight exposure
- Older persons (30 to 50 percent become lentigo maligna melanoma)
- Remains the in situ lesion of lentigo maligna for years before becoming invasive
Acral lentiginous melanoma
- 2 to 8 percent of cutaneous malignant melanoma
- Protracted radial growth phase
- Late observation because of location (subungual, soles, palms)
- Develops in relatively or completely sun-protected sites
- Most frequent in ethnic groups of color
- Subungual melanoma is a distinctive variant often involving the nail bed of the great toe or thumb (Fig. 17)

Nodular melanoma
- 10 to 20 percent of cutaneous malignant melanomas
- Frequently thick at time of diagnosis
- Increased metastatic potential

Amelanotic melanoma
- Diagnostic challenge
- Can be mistaken for intradermal nevus, nodular basal cell carcinoma

Prognosis
The American Joint Commission on Cancer staging system is based on independent prognostic indicators for survival: Breslow thickness, macroscopic or microscopic ulceration, and lymph node involvement as determined by sentinel lymph node biopsy, all of which upstage disease.130,131

Fig. 15. Acral lentiginous melanoma, sole of the foot.

Fig. 16. (Above) Melanoma in situ showing the melanocytic proliferation confined to the epidermis. The basal lamina is intact (hematoxylin and eosin stain, x400). (Below) Melanoma with both radial and vertical growth phase showing melanocytic proliferation at the dermoepidermal junction and in the dermis. There is also some lymphocytic reaction (hematoxylin and eosin, ×100).

Fig. 17. Subungual melanoma of the great toe demonstrates Hutchinson’s sign with pigmentation of the eponychium together with hyponychial pigmentation. Hutchinson’s sign is not necessarily pathognomonic for nail unit melanoma.
logic type, corrected for thickness, does not influence survival. Additional correlations exist between survival and gender, mitotic rate, and truncal versus limb location.132–137

Cutaneous Malignant Melanoma Staging

A new cutaneous malignant melanoma staging system was published in 2001 (Tables 6 through 8).138

Lymph node metastases are staged by the presence of micrometastases and macrometastases and by the number of positive nodes. Staging is complicated by the presence of primary tumor ulceration.138,139 Three subgroups of distant metastases are distinguished: skin and soft-tissue metastases (best prognosis), lung metastases, and other visceral metastases (worst prognosis). Elevated lactate dehydrogenase in either of the first subgroups up-stages to the last subgroup.139

Staging examinations in surveillance and follow-up of cutaneous malignant melanoma patients are controversial. The National Institutes of Health consensus of 1992 recommended that laboratory investigation was unnecessary for early cutaneous malignant melanoma (<1-mm thickness) in the absence of signs or symptoms that might suggest metastatic disease. Although little supports routine blood studies and/or imaging for such patients or that such detailed examinations would influence prognosis, many perform these investigations with newly diagnosed cutaneous malignant melanoma as an initial staging process.140 No uniform recommendations exist regarding the type of staging examination at initial diagnosis and during follow-up, but chest radiographs, blood counts, liver function tests, tumor marker serum levels, and computed tomography scans are frequently ordered.138,139 These modalities can be combined and can be helpful in determining whether patients who have developed distant metastases are eligible for surgical excision. Positron emission tomography–computed tomography helps identify developing metastases and facilitates decision for surgical resection.141

Local Treatment

In the 1970s and 1980s, safety margins of 5 cm, independent of tumor thickness, were the surgical standard.134 Current excision guidelines have been inferred from the results of a number of trials142–146 (Tables 7 and 8).

Locally recurrent disease should be excised with narrow margins. No improvement in local control or survival is achieved with wider excision of secondary local disease. Patients without evidence of distant secondary disease in these situations may be considered for isolated limb perfusion.

Evaluation of Lymphatic Basins

Sentinel lymph node biopsy is used to stage melanoma patients who are clinically node-negative. Lymph node staging to detect micrometastasis is routine in the surgical management of cutaneous malignant melanoma with Breslow’s tumor thickness of more than 1 mm or for tumors of less than 1 mm and Clark’s level IV or V. Thin melanomas (<1 mm Breslow thickness) account for approximately 70 percent of new cases. Some suggest that there may be a role for sentinel lymph node biopsy with thin melanomas; four studies show sentinel lymph node biopsy positivity rates of 3 to 10.8 per-

---

Table 6. Primary Tumor*

<table>
<thead>
<tr>
<th>Tumor Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>xT</td>
<td>Primary tumor cannot be assessed (e.g., shave biopsy or regressed melanoma)</td>
</tr>
<tr>
<td>T0</td>
<td>Primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Melanoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Melanoma ≤1.0 mm</td>
</tr>
<tr>
<td>T2</td>
<td>1.01–2.0 mm</td>
</tr>
<tr>
<td>T3</td>
<td>2.01–4.0 mm</td>
</tr>
<tr>
<td>T4</td>
<td>&gt;4.0 mm</td>
</tr>
</tbody>
</table>


Table 7. Regional Lymph Nodes

<table>
<thead>
<tr>
<th>Node Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No regional metastases</td>
</tr>
<tr>
<td>NX</td>
<td>Patients in whom regional nodes cannot be assessed (previously removed)</td>
</tr>
<tr>
<td>N1</td>
<td>One metastatic node: (1) micrometastasis, (2) macrometastasis</td>
</tr>
<tr>
<td>N2</td>
<td>Two to three metastatic nodes: (1) micrometastasis, (2) macrometastasis, and (3) satellites and in-transit metastases without metastatic nodes</td>
</tr>
<tr>
<td>N3</td>
<td>Four or more metastatic nodes, or matted nodes, or satellites/in-transit metastases with metastatic node(s)</td>
</tr>
</tbody>
</table>

Table 8. Distant Metastatic Melanoma

<table>
<thead>
<tr>
<th>Metastasis Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No detectable evidence of metastases</td>
</tr>
<tr>
<td>Mx</td>
<td>Presence or absence of metastases cannot be assessed</td>
</tr>
<tr>
<td>M1a</td>
<td>Metastases to skin, subcutaneous tissue, or distant lymph nodes</td>
</tr>
<tr>
<td>M1b</td>
<td>Metastases to lung</td>
</tr>
<tr>
<td>M1c</td>
<td>Metastases to all other visceral sites</td>
</tr>
</tbody>
</table>
percent for lesions of 0.75 to 1.0 mm in depth.\textsuperscript{148–151} Below this thickness, rates of histologic lymph node involvement is less than 2 percent. Melanoma regression does not appear to be a significant predictor of sentinel lymph node involvement\textsuperscript{149} (Fig. 18).

False-negative sentinel lymph node biopsy may occur, possibly due to surgeon inexperience. A significant learning curve exists for up to 50 cases.\textsuperscript{152}

Detection of micrometastasis by sentinel lymph node biopsy is the most important prognostic factor; if positive, the prognosis is significantly worse.\textsuperscript{139} It is unclear whether sentinel lymph node biopsy and subsequent radical lymphadenectomy for positive nodes prolong survival. Microscopic sentinel lymph node involvement is likely an indicator of systemic spread rather than a precondition for the future development of systemic spread.\textsuperscript{139} A prolongation of overall survival by sentinel lymph node biopsy and subsequent radical lymphadenectomy therefore remains unlikely.\textsuperscript{139}

Technique for intraoperative lymph node mapping has been standardized (Figs. 19 through 21).\textsuperscript{153–155} Sentinel lymph node biopsy should not be performed in patients with prior complex reconstructions that might distort lymphatic flow.\textsuperscript{156}

While the morbidity of sentinel lymph node biopsy is far less than total nodal clearance, complications may occur. Lymphedema rates following axillary and groin sentinel lymph node biopsies are 0.3 and 1.5 percent, respectively, compared with 4.6 and 31.5 percent, respectively, when complete node dissections are done at these sites.\textsuperscript{157}

**Subungual and Periungual Melanoma**

Nail unit melanoma commonly affects the thumb and great toe and is characterized by a brown-black band more than 3 mm in width with variegated borders. Newly pigmented atraumatic streaks of the nail should always be biopsied. Treatment for melanoma in situ or lesions of significant atypia is ablation of the nail bed with skin grafting. Treatment for invasive melanoma is amputation of the digit at the nearest involved interphalangeal

![Fig. 18. Melanoma showing surrounding regression or halo.](image)

![Fig. 19. Lymphoscintigram. The patient receives a four-point intradermal radiocolloid injection on the day of surgery.](image)

![Fig. 20. Isosulfan blue dye injection. A vital blue dye is injected 10 minutes before surgical preparation of the patient. The use of both radiocolloid and blue dye increases sentinel lymph node detection rates to more than 99 percent, compared with 87 percent when only blue dye is used.](image)
Adjuvant Therapy

Most patients in adjuvant melanoma trials have stage III (local regional metastases) or stage II (primary melanomas >1.5 mm thick) disease.139 None of the chemotherapeutic agent trials has shown any benefit.159,160 Beneficial results have been reported only for interferon-alpha, and even these studies have yielded conflicting results.139 Once distant metastases (stage IV) have developed, only palliative treatment modalities apply.139

The utility of sentinel lymph node biopsy is unclear as the effect on survival is unknown.158

Principles and Pearls for Reconstruction

See Video 3, which describes principles of reconstructive treatment and also describes the utility of local flaps in different anatomic sites, is available in the “Related Videos” section of the full-text article on PRSJournal.com. Video for Ovid users is available at http://links.lww.com/PRS/A301.

Fig. 21. (Above) Gamma probe identification of the sentinel lymph node. A handheld gamma probe intraoperatively identifies the hot spot in the regional nodal basin. Absolute radioactivity count is less important than activity ratio, as both time after injection and distance from primary lesion to lymphatic nodes are variable. Background radioactivity is measured. A sentinel lymph node is a node with an activity ratio of 3:1 or higher in vivo, or 10:1 or higher ex vivo. (Below) Sentinel lymph node identification. An incision is made over the hot spot, and small flaps are created to allow identification of the blue-stained afferent lymphatic vessels (forceps pointing). Dissection is guided by identification of the blue-stained node and by use of the gamma probe.
Volume 127, Number 3 • Cutaneous Malignancies


