

# Excision of Periocular Basal Cell Carcinoma With Stereoscopic Microdissection of Surgical Margins for Frozen-Section Control

## Report of 200 Cases

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**Objective:** To report our experience with 200 cases of basal cell carcinoma (BCC) in 192 patients treated with an enhanced frozen-section control (FSC) technique using stereoscopic microdissection of surgical margins.

**Methods:** Retrospective series of 192 patients with 200 lesions diagnosed as BCC of the periocular region. All were excised en bloc with 1-mm margins beyond the clinically apparent tumor and examined using an enhanced FSC technique with stereoscopic microdissection of the surgical margins.

**Results:** Of 200 malignant BCCs, 93.0% represented primary tumors. The overall recurrence rate was 1.0%, with a mean follow-up of 4 years. In patients with primary le-

sions, the overall recurrence rate was 1.1%, with a mean follow-up of 3.9 years. There were no recurrences in the secondary tumor group after a mean follow-up of 4.8 years. Of the 200 lesions, 66.0% lesions required a single en bloc resection to achieve tumor-free margins.

**Conclusions:** An enhanced FSC technique using stereoscopic microdissection of the surgical margins permits greater conservation of healthy tissue and yields cure rates comparable to those of the standard FSC technique and Mohs micrographic surgery. We believe that this enhanced FSC technique is a highly effective method for resection of periocular BCC.

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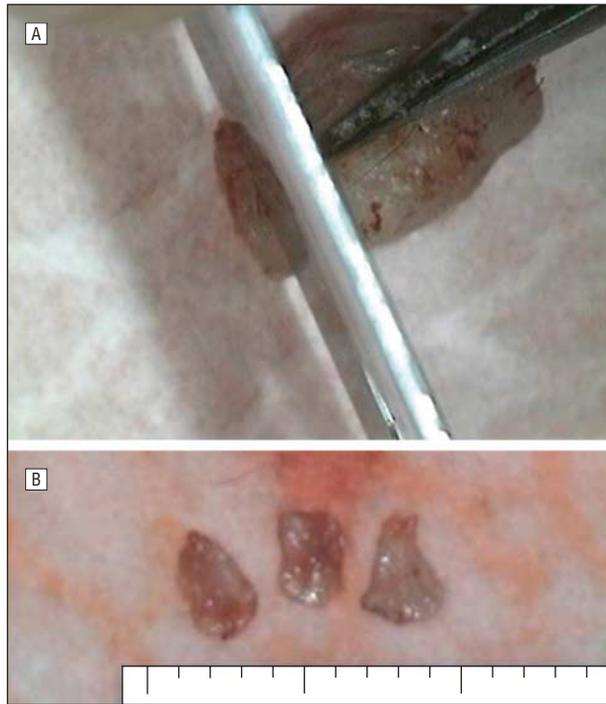
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**B**ASAL CELL CARCINOMA (BCC) is the most common malignant neoplasm of the eyelid, accounting for 90% of cases.<sup>1</sup> Tumors occur most frequently on the lower eyelid, followed in order of frequency by the medial canthus, upper eyelid, and lateral canthus. Although BCC is usually slow growing and metastases are rare, local invasion can cause significant morbidity if the tumor is not treated in a timely and appropriate manner. Aggressive types of BCC are occasionally observed, especially in young patients.<sup>2</sup> Compared with primary BCC, recurrent tumors can exhibit more aggressive behavior and are associated with poorer outcome.

Treatments described in the literature include surgical excision, cryotherapy, radiotherapy, laser surgery, and photodynamic therapy.<sup>2,3</sup> Complete surgical resection is generally regarded as the mainstay of treatment.<sup>3</sup> Recurrence of BCC after surgical excision generally results from inadequate excision of the tumor. Complete surgical resection can be ensured only by microscopic control of the surgical margins. Without such control, recurrence rates as high as 23% have been reported.<sup>4</sup>

Two techniques have been used for microscopic margin control: Mohs micrographic surgery and traditional frozen-section controlled (FSC) excision. Both techniques are associated with a low reported recurrence rate. Traditionally, BCCs have been excised with 3- to 4-mm margins combined with primary repair.<sup>5</sup> To achieve the best functional and cosmetic outcome, it is preferred to minimize the loss of normal tissue. Although the Mohs technique ideally achieves complete excision with minimal loss of normal tissue, it is costly and time-consuming, requiring multiple tissue excisions and histological examinations. The irregularly cut margins require refinements for optimal wound edge apposition, resulting in loss of normal tissue and making reconstruction of the tumor resection site more difficult.

The purpose of this study was to report our experience with 200 cases of BCC in 192 patients treated with an enhanced FSC technique. Recurrence rates of primary and secondary tumors were calculated and compared with those previously reported in the literature.



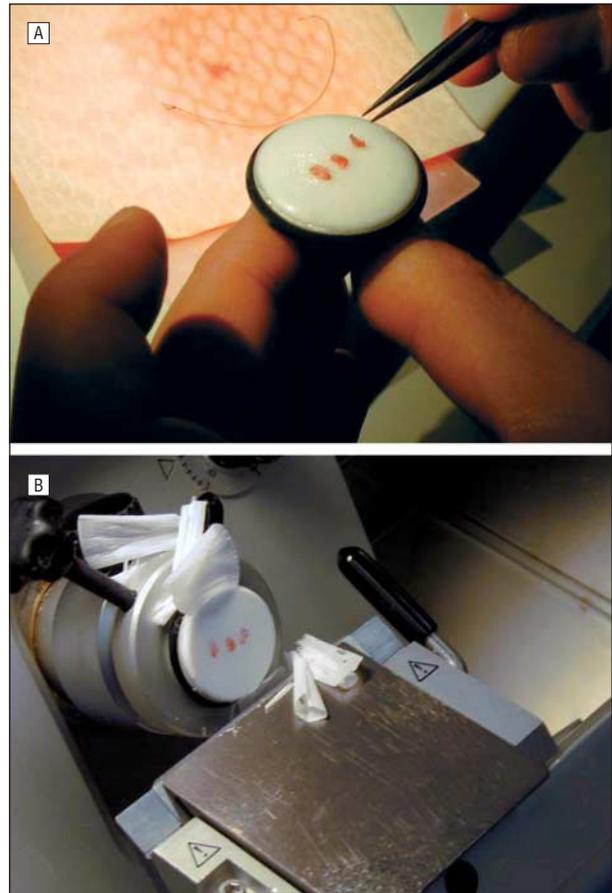
**Figure 1.** Preparation of en face margins of resection from the en bloc resection specimen. En face margins are prepared by cutting less than 0.5 mm of the marginal tissue with a single-edged razor blade while the tissue is stabilized with a forceps (A). These are laid out in order to correspond with the labeling recorded as “medial,” “lateral,” and so forth (B). They are examined to ensure that the tissue represents the entire margin in question. All of these steps are done using a stereomicroscope. Each small tick on the scale in B represents 1 mm.

## METHODS

A retrospective medical record review of 192 patients with 200 lesions diagnosed as BCC of the periocular region and requiring surgical excision was performed in a tertiary oculoplastics referral practice between January 1, 1993, and December 31, 2006. The criteria for selection were all cases of periocular BCC referred to the private practice of two of us (E.M. and R.C.D.) for the evaluation of suspected or biopsy-proved BCC. The following data were selected for analysis: age at first examination, sex, history of BCC, anatomical location, lesion size, reconstructive repair technique, recurrence after treatment, and duration of follow-up. The in-laboratory turnaround time for the enhanced FSC technique and the additional time for reexcision and histopathological evaluation of additional resections were assessed. All data collection was in compliance with the regulations of the Health Insurance Portability and Accountability Act and was approved by the institutional review board.

Primary lesions were new BCCs, and secondary lesions were those that had been previously removed by other surgeons and had recurred, requiring a second excision. Exclusion criteria consisted of lesions less than 5 mm long at the eyelid margin, patients in whom palliative debulking procedures were performed, patients who refused further treatment, and patients with less than 3 months of follow-up.

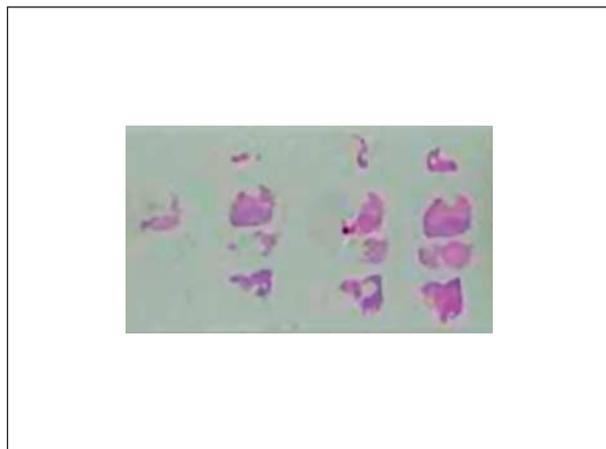
Informed consent was obtained for excision of all BCCs. Excision was performed with the patient under monitored local anesthesia or general anesthesia, depending on the size of the lesion and the anticipated repair procedure. The slitlamp microscope and/or the surgical microscope was used to define and mark a 1-mm margin beyond the clinically apparent tumor. Surgery was performed by one of us (E.M. or R.C.D.) at The New York Eye and Ear Infirmary.



**Figure 2.** Stereoscopic microdissection of surgical margins for frozen-section control. The tissue margins are carefully transferred to a previously prepared foundation of frozen-section mounting medium (Tissue-Tek optimum cutting temperature [OCT] Compound; Sakura Finetek USA, Inc; Torrance, California) that is parallel to the plane of the frozen tissue specimen stage (“chuck”) (A). They are then covered with additional mounting media and frozen. The chuck is faced until the first tissue is seen and then step-sectioned at approximately 50- to 60- $\mu$ m intervals (B). Three or 4 levels are placed on each slide. Because of the fastidious preparation of the tissue, the plane of sectioning complete tissue outlines is generally reached within 150  $\mu$ m.

All BCCs were excised and examined using an enhanced FSC technique. The excised specimen was then immediately transported to the pathology laboratory for examination. In all cases, the pathologist (S.A.M.) used a stereomicroscope (model SZH or SZX9; Olympus Corporation, Tokyo, Japan) at 30 $\times$  to 100 $\times$  magnification to microdissect 0.3- to 0.5-mm en face margins of resection from the en bloc resection specimen (**Figure 1**). This procedure mimics the Mohs micrographic technique, except that the margin tissue is removed in a controlled in vitro fashion from the specimen rather than from the patient.<sup>6</sup> This results in smaller surgical defects and greater tissue conservation. Each of the surgical margins was labeled for orientation purposes with ink when necessary and placed in an oriented fashion on a single frozen-section specimen platform for simultaneous cryosectioning, thus reducing the processing time required when sectioning each margin separately.

Rigid technical procedures must be followed to obtain consistent results. For example, the “shaved” margins must be of a nearly identical thickness, and the frozen-section specimen platform (in our case, standard “chucks” are used) must have a level layer of previously frozen embedding medium (Tissue-Tek optimum cutting temperature [OCT] Compound; Sakura Finetek USA, Inc, Torrance, California) on which to orient the margin specimens (**Figure 2**). Conventions must be used consistently to ensure main-



**Figure 3.** Orientation is carefully maintained by placing the cryosections neatly on the glass slide. Initial sections shown here are incomplete (bottom of slide [left]) but are complete by the fourth level (top of slide [right]).

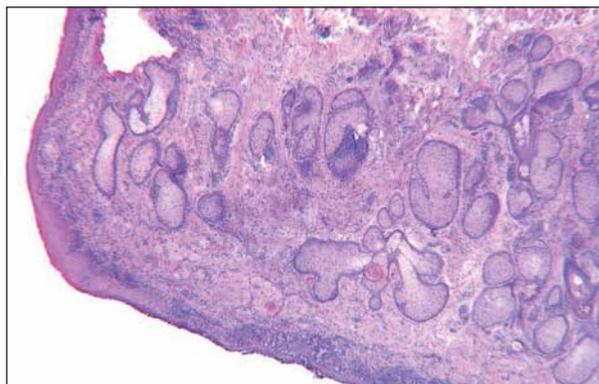
tenance of the orientation and identification of the site of origin (eg, margins are lettered consecutively and noted; the requisitional tissue is laid out from left to right as A, B, C, and so forth; and the left side of the chuck is marked with a felt-tip pen). Sections are placed on the glass slide so that their orientation is maintained (**Figure 3**). In our laboratory, 4 pathologists (including S.A.M.) and 1 histotechnologist are involved in these cases, and all follow the same conventions for microdissection, specimen preparation and freezing, and slide preparation (**Figure 4**). It is also important that the cryostat be maintained properly. The traveling head of the cryotome must be aligned so that the plane of cutting is parallel to the plane of the chuck. This allows the initial sections of the margins to be fully displayed on the slide within 100  $\mu$ m after facing the frozen block. We check this alignment monthly.

The pathologist communicated his findings by speaker-telephone to the surgeon in the operating room. If a margin of the specimen was positive for tumor cells, the clinical margin was reevaluated with the use of a surgical microscope. The precise anatomic location of the positivity was determined from the microscopic examination and was communicated to the surgeon. An additional 1-mm block of tissue was excised from the area that showed histopathological evidence of residual tumor and was submitted for pathological examination. In the meantime, reconstruction was undertaken in the region distant to the positive margin's site. Frozen-section diagnoses were subsequently confirmed in permanent sections of routinely processed paraffin-embedded, previously frozen tissue in all patients.

Follow-up data were obtained by reviewing the patients' medical records or via communication with the referring physician if recent follow-up data were not available. Communication was based on a questionnaire documenting the last visit and on the presence or absence of recurrence. The main outcome measure was tumor recurrence.

## RESULTS

Between January 1, 1993, and December 31, 2006, 200 malignant BCCs were identified in 192 patients who met the study inclusion criteria. Thirty-five patients had a history of BCC outside the periocular area. The right side was involved in 51.5% of the 200 cases of BCC. Of the tumors excised, 186 (93.0%) represented primary and 14 (7.0%) represented secondary tumors. In all, 40.6% of the patients (78) were men and 59.4% (114) were women, with an average age of 77 years (range, 31-95



**Figure 4.** Photomicrograph demonstrating the quality that can be achieved in cryosections when fastidious attention is paid to each detailed step in the process (hematoxylin-eosin, original magnification  $\times 20$ ).

years). The lower eyelid was most commonly involved, as shown in the following tabulation:

Tumor Location	No. (%)
Lower eyelid	139 (69.5)
Medial canthus	27 (13.5)
Upper eyelid	16 (8.0)
Lateral canthus	8 (4.0)
Cheek	4 (2.0)
Forehead	3 (1.5)
Nose	3 (1.5)

Twenty-seven lesions (13.5%) had a diameter of 15 mm or larger, 51 (25.5%) were between 10 and 14.9 mm, and 121 (60.5%) were between 5 and 9.9 mm. (The size of 1 lesion was not recorded.) The size of the defects associated with tumor resection required various reconstruction techniques, as given in the following tabulation:

Reconstruction Method	No. (%)
Hughes procedure	60 (30.0)
Skin graft	36 (18.0)
Tenzel flap	28 (14.0)
Primary repair	25 (12.5)
Canthoplasty	22 (11.0)
Myocutaneous advancement flap	18 (9.0)
Glabellar flap	2 (1.0)
Cutler-Beard flap	1 (0.5)
Not recorded	8 (4.0)

Clinical BCC variant was described in 86 lesions, with the nodular type seen in 52 lesions (60%), sclerosing type in 30 (35%), and superficial type in 4 (5%).

The overall recurrence rate for FSC excision was 1.0%, with a mean follow-up of 4 years (range, 3-145 months). In patients with primary lesions, the overall recurrence rate was 1.1% (2 of 186 lesions), with a mean follow-up of 47 months (3.9 years). One hundred ten primary lesions were followed up for at least 3 years, with a recurrence rate of 0.9% in that group. Sixty-seven primary lesions were followed up for at least 5 years, with no documented recurrences. In the 2 patients who had recurring tumors, the original tumor size was 15 mm and 6 mm, with time to recurrence of 1.8 and 3.9 years, respectively. Both tumors were originally removed with a single en bloc excision and showed no evidence of malignant cells on histopathological examination of the tumor margins. One patient has been followed up for 15 months since the reexcision and showed no signs of re-

currence at the last examination. The second patient has had no evidence of recurrence after 47 months of close observation.

Of the 14 secondary tumors, 10 have been followed up for more than 3 years and 8 for at least 5 years. Of the 8 lesions with known pathological variant, 6 were the sclerosing type. There were no recurrences among the 14 secondary tumors after a mean follow-up of 4.8 years.

Of the 200 lesions, 66.0% were removed with a single en bloc resection to achieve tumor-free margins. The in-laboratory turnaround time (from receipt of the specimen to reporting of the results) averaged 11 minutes. Of the 65 lesions with positive margins, 57 (88%) required a single additional 1-mm en bloc resection for complete histological removal. (The margin status of 3 lesions was not recorded.) The time for reexcision and histopathological evaluation of second-level tissue averaged 20 minutes. None of the recurrences were in patients who required more than the initial excision to achieve tumor-free margins.

#### COMMENT

Basal cell carcinoma is a common periocular tumor. The primary goals of treatment are complete resection of the tumor followed by optimal restoration of the function and aesthetics of the involved area. Complete microscopic eradication of the neoplasm and maximal sparing of the normal tissues are the paramount goals for successful management.

Historically, Mohs micrographic surgery and Mohs micrographic surgery and FSC excision have yielded the highest cure rates and lowest frequency of recurrence. Mohs<sup>7</sup> reported a 0.7% recurrence rate in patients with BCC of the skin and a 2% recurrence rate in patients with periocular BCC at 5 years of follow-up. Other studies using the Mohs technique cited similar results.<sup>3,8,9</sup>

A number of large retrospective studies described similar success rates with FSC excision of periocular BCCs.<sup>3,4,10-15</sup> Most agreed on the need for FSC in the removal of such lesions. According to Doxanas et al,<sup>15</sup> even with 4-mm margins, 64% of tumors would have been incompletely excised histologically, resulting in a recurrence rate as high as 23%. Others<sup>11,16</sup> have reported varying rates of incomplete histological excision (5%-54%) and recurrences (10%-75%) when customary 3- to 4-mm margins were used without histopathological control prior to repair. Conway et al<sup>10</sup> performed a comparative analysis that demonstrated significantly reduced long-term recurrence when using FSC in the excision of primary periocular BCC. They concluded that FSC is reliable for ensuring complete tumor removal and that the low recurrence rate is comparable to that of Mohs micrographic surgery.

Our overall recurrence rate for primary BCC when using an en bloc FSC excision technique was 1.0%. Notable are the narrow margins that were excised in these patients. Our low recurrence rate when using the tissue-conservative approach demonstrates the utility of stereoscopic microdissection of margins in the laboratory. This permits greater sparing of healthy tissue while yielding cure rates that are comparable to those obtained using the FSC technique and Mohs micrographic surgery.

Wong et al<sup>3</sup> followed up 423 primary BCC lesions and reported an overall 0.71% recurrence rate. Ninety-seven of those lesions were followed up for at least 5 years and yielded a 2.2% recurrence rate. Secondary recurrences treated with FSC excision resulted in a 3.8% recurrence rate. Glatt et al<sup>13</sup> reported a 99.2% overall and a 97.5% 5-year success rate in a similarly large population study. Other authors<sup>4,11,12,15</sup> have reported 0% to 2.19% recurrence rates with less than 5 years of follow-up. Of the 110 primary lesions followed up for at least 3 years in our study, there was 1 recurrence, yielding a 0.9% recurrence rate. There were no recurrences among the 67 primary lesions followed up for at least 5 years. Excision of the 14 secondary tumors resulted in a 100% cure rate in our patients. The low number of secondary cases is one possible limitation of our study.

Basal cell carcinomas treated with FSC excision have traditionally been excised with 3- to 4-mm margins.<sup>5,11,16</sup> The 3- to 4-mm margin has evolved because it achieves an acceptable cure rate irrespective of the type of tumor. More recently, 2-mm margins have been used in the excision of nodular adnexal BCC, with no documented recurrences after 5 years of follow-up.<sup>5,6</sup>

Our patients underwent enhanced en bloc FSC excision with 1-mm margins after careful evaluation of the tumor preoperatively with a slitlamp and intraoperatively with a surgical microscope. At our institution, the pathologists are equipped to microdissect very small (0.3- to 0.5-mm) margins from the submitted specimen. This allows the surgeon to remove a minimal amount of normal tissue while permitting histopathological control. Most of the lesions excised (66.0%) had negative histological margins after a single en bloc excision. Of those with positive histological margins, 88.0% required a single additional 1-mm en bloc excision. There was no positive correlation between the number of excisions needed and the morpheiform tumor type or recurrence. Given the large size of most lesions, 1-mm margins allowed greater sparing of healthy tissue and resulted in better functional and cosmetic outcomes without compromising treatment for cure. Because reconstruction was undertaken away from the positive margins site, the need for additional excision did not significantly prolong the intraoperative time.

One of the limitations of our study was the inability to follow up all patients by direct observation, resulting in our reliance on questionnaires completed by the referring physicians. Ideally, all patients would have been followed up for at least 5 years. We recommend that all patients with BCCs—especially those with previous recurrences—undergo lifelong follow-up.

Although our study did not directly compare cure rates and cosmetic outcomes between Mohs micrographic surgery and FSC excision, our data support the previously reported similarities in the outcomes of these techniques. We believe that the enhanced en bloc FSC excision technique is a highly effective method for the resection of periocular BCC. It effectively defines tumor margins and allows for greater sparing of normal tissue, which, in our opinion, allows easier reconstruction with less complicated wound healing. Another advantage of this technique is the immediate reconstruction

of the defect following tumor resection. This eliminates potential morbidity associated with a repair delay and makes it more cost-effective. Our study not only focuses on recurrence rates of BCC with the margin-sparing technique but also provides information on tumor size and the reconstruction method used. These data will allow future comparison between various treatment methods for BCC, which eventually will optimize the management of this common malignant neoplasm of the eyelid.

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