Reliability of Biopsy Margin Status for Basal Cell Carcinoma: A Retrospective Study

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PRACTICE POINTS
- Clinicians must recognize the limitations of margin assessment of biopsy specimens and not rely on margin status to dictate treatment.
- Dermatopathologists should consider modifying how margin status is reported, either by omitting it or clarifying its limitations on the pathology report.

The reporting of biopsy margin status for basal cell carcinoma (BCC) varies among dermatopathologists. For biopsy specimens with seemingly negative margins, the question arises if the tumor extends beyond the margin in unexamined sections. We sought to determine the reliability of negative margin status for BCC and identify if any factors were predictive of positive true margins. We examined BCC biopsy specimens initially determined to have negative margins after routine sectioning and re-evaluated the margin status after complete tissue block sectioning of the initial biopsy specimen was performed. Our findings remind clinicians of the limitations of margin assessment and provide impetus for dermatopathologists to consider modifying how margin status is reported.

Basal cell carcinoma (BCC) is the most common type of skin cancer frequently encountered in both dermatology and primary care settings. When biopsies of these neoplasms are performed to confirm the diagnosis, pathology reports may indicate positive or negative margin status. No guidelines exist for reporting biopsy margin status for BCC, resulting in varied reporting practices among dermatopathologists. Furthermore, the terminology used to describe margin status can be ambiguous and differs among pathologists; language such as “approaches the margin” or “margins appear free” may be used, with nonuniform interpretation between pathologists and providers, leading to variability in patient management.

When interpreting a negative margin status on a pathology report, one must question if the BCC extends beyond the margin in unexamined sections of the specimen, which could be the result of an irregular tumor growth pattern or tissue processing. It has been estimated that less than 2% of the peripheral surgical margin is ultimately examined when serial cross-sections are prepared histologically (the bread loaf technique). However, this estimation would depend on several variables, including the number and thickness of sections and the amount of tissue discarded during processing. Importantly, reports of a false-negative margin could lead both the clinician and patient to believe that the neoplasm has been completely removed, which could have serious consequences.

Our study sought to determine the reliability of negative biopsy margin status for BCC. We examined BCC biopsy specimens initially determined to have uninvolved margins on routine tissue processing and determined the proportion with truly negative margins after complete tissue block sectioning of the initial biopsy specimen. We felt this technique was a more accurate measurement of true margin status than examination of a re-excision specimen. We also identified any factors that were predictive of positive true margins.

Methods
We conducted a retrospective study evaluating tissue samples collected at Geisinger Health System (Danville, Pennsylvania)
## Basal Cell Carcinoma Biopsy Specimen True Margin Status and Patient/Tumor Characteristics

<table>
<thead>
<tr>
<th>Final Margin Status</th>
<th>All Specimens (N=122)</th>
<th>Positive (n=53)</th>
<th>Negative (n=69)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean patient age, y (SD)</td>
<td>66.0 (11.3)</td>
<td>67.0 (12.8)</td>
<td>65.2 (9.9)</td>
<td>.4018</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>.4733</td>
</tr>
<tr>
<td>Female</td>
<td>44 (36.1)</td>
<td>21 (39.6)</td>
<td>23 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>78 (63.9)</td>
<td>32 (60.4)</td>
<td>46 (66.7)</td>
<td></td>
</tr>
<tr>
<td>Final margin status (categorized), n (%)</td>
<td></td>
<td></td>
<td></td>
<td>.7849</td>
</tr>
<tr>
<td>Tumor</td>
<td>44 (36.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroma</td>
<td>9 (7.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clear</td>
<td>69 (56.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Final margin status (total), n (%)</td>
<td></td>
<td></td>
<td></td>
<td>.2548</td>
</tr>
<tr>
<td>Positive</td>
<td>53 (43.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>69 (56.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median clinical tumor size (range), mm</td>
<td>6 (5, 9)</td>
<td>6 (5, 10)</td>
<td>6 (5, 8)</td>
<td></td>
</tr>
<tr>
<td>Tumor location, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>.2921</td>
</tr>
<tr>
<td>Head and neck</td>
<td>14 (11.5)</td>
<td>8 (15.1)</td>
<td>6 (8.7)</td>
<td></td>
</tr>
<tr>
<td>Trunk and extremities</td>
<td>107 (87.7)</td>
<td>44 (83.0)</td>
<td>63 (91.3)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.8)</td>
<td>1 (1.9)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Tumor subtype, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>.4344</td>
</tr>
<tr>
<td>Aggressive</td>
<td>8 (6.6)</td>
<td>5 (9.4)</td>
<td>3 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Nonaggressive</td>
<td>114 (93.4)</td>
<td>48 (90.6)</td>
<td>66 (95.7)</td>
<td></td>
</tr>
<tr>
<td>Biopsy technique, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>.3350</td>
</tr>
<tr>
<td>Shave</td>
<td>121 (99.2)</td>
<td>52 (98.1)</td>
<td>69 (100)</td>
<td></td>
</tr>
<tr>
<td>Punch</td>
<td>1 (0.8)</td>
<td>1 (1.9)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>No. of gross specimen sections (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>41 (33.6)</td>
<td>22 (41.5)</td>
<td>19 (27.5)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>58 (47.5)</td>
<td>21 (39.6)</td>
<td>37 (53.6)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>15 (12.3)</td>
<td>6 (11.3)</td>
<td>9 (13.0)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>7 (5.7)</td>
<td>3 (5.7)</td>
<td>4 (5.8)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1 (0.8)</td>
<td>1 (1.9)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Provider specialty, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>.2269</td>
</tr>
<tr>
<td>Dermatology</td>
<td>117 (95.9)</td>
<td>49 (92.5)</td>
<td>68 (98.6)</td>
<td></td>
</tr>
<tr>
<td>Mohs micrographic surgery</td>
<td>3 (2.5)</td>
<td>2 (3.8)</td>
<td>1 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Primary care</td>
<td>2 (1.6)</td>
<td>2 (3.8)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Provider type, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>.1955</td>
</tr>
<tr>
<td>Physician</td>
<td>97 (79.5)</td>
<td>45 (84.9)</td>
<td>52 (75.4)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>25 (20.5)</td>
<td>8 (15.1)</td>
<td>17 (24.6)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: SD, standard deviation.

*Not documented by clinician in 15 of 122 specimens.
BIOPSY MARGIN STATUS FOR BCC

from January to December 2016. Specimens were qu-
ri
ered via the electronic database system at our institution
(CoPath). We included BCC biopsy specimens with nega-
thistologic margins on initial assessment that subse-
quently had block exhaust levels routinely ordered. These
levels are cut every 100 to 150 µm, generating approxi-
mately 8 glass slides. We excluded all tumors that did not
fit these criteria as well as those in patients younger than
18 years. Data collection was performed utilizing speci-
men pathology reports in addition to the note from the
 corresponding clinician office visit from the institution’s
electronic medical record (Epic). Appropriate statistical
calculations were performed. This study was approved by
an institutional review board at our institution, which is
required for all research involving human participants. This
served to ensure the proper review and storage of patients’
protected health information.

Results
The search yielded a total of 122 specimens from
104 patients after appropriate exclusions. We examined a
total of 122 BCC biopsy specimens with negative initial
margins: 121 (99.2%) shave biopsies and 1 (0.8%) punch
biopsy. Of 122 specimens with negative initial margins,
53 (43.4%) were found to have a truly positive mar-
gin based on the presence of either tumor or stroma
at the lateral or deep tissue edge after complete tissue
block sectioning. Sixty-nine (56.6%) specimens had
clear margins and were categorized as truly negative
after complete tissue block sectioning. Specimens with
positive and negative final margin status did not differ
significantly with respect to patient age; gender; biopsy
technique; number of gross specimen sections; or tumor
characteristics, including location, size, and subtype
(Table) (P > .05).

We also examined the type of treatment performed,
which varied and included curettage, electrodesic-
cation and curettage, excision, and Mohs micrographic surgery.
Clinicians, who were not made aware of the exhaust
level protocol, chose not to pursue further treatment in
6 (4.9%) of the cases because of negative biopsy margins.
Four (66.7%) of the 6 providers were physicians, and
2 (33.3%) were advanced practitioners. All of the provid-
ers practiced within the Department of Dermatology.

Comment
Our findings support prior smaller studies investigat-
ing this topic. A prospective study by Schnebelen et al4
examined 27 BCC biopsy specimens and found that
8 (30%) were erroneously classified as negative on rou-
tine examination. This study similarly determined true
margin status by assessing the margins at complete tissue
block exhaustion. Willardson et al5 also demonstrated
the poor predictive value of margin status based on
the presence of residual BCC in subsequent excisions.
They found that 34 (24%) of 143 cases with negative
biopsy margins contained residual tumor in the corre-
sponding excision.

Our study revealed that almost half of BCC biopsy
specimens that had negative histologic margins with
routine sectioning had truly positive margins on com-
plete block exhaustion. This finding was independent of
multiple factors, including tumor subtype, indicating that
even nonaggressive tumors are prone to false-negative
margin reports. We also found that reports of negative
margins persuaded some clinicians to forgo definitive
treatment. This study serves to remind clinicians of the
limitations of margin assessment and provides impetus
for dermatopathologists to consider modifying how mar-
gin status is reported.

Limitations of this study include a small number of
cases and limited generalizability. Institutions that rou-
tinely examine more levels of each biopsy specimen may
be less likely to erroneously categorize a positive margin
as negative. Furthermore, despite exhausting the tissue
block, we still may have underestimated the number of
cases with truly positive margins, as this method inher-
ently does not allow for complete margin examination.

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of Dermatopathology and the Geisinger Biostatistics &
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assistance with our project.

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