### Title

Comparison of community pathologists with expert dermatopathologists evaluating Breslow thickness and histopathologic subtype in a large international population-based study of melanoma




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## RESEARCH LETTER

### Comparison of community pathologists with expert dermatopathologists evaluating Breslow thickness and histopathologic subtype in a large international population-based study of melanoma

*To the Editor:* As of 2019 National Cancer Institute data show that melanoma is the fifth most common cancer in the United States.[1] There has been a recent push to include the histopathologic subtype of nodular melanoma as an independent prognostic classifier due to the identification of associated aggressive histopathologic characteristics and shorter recurrence-free times.[2,3]

We used the population-based, Genes, Environment, and Melanoma (GEM) study,[4] to assess the levels of agreement between community pathologists, those who originally diagnosed the melanoma, and expert study dermatopathologists, who reviewed the lesion for complete histology, histopathologic subtype, and Breslow thickness. The salient components of the GEM study were that it was population-based, multi-country size, and included disease-specific mortality data and re-review of hematoxylin-eosin–stained tissues by dermatopathologists. We evaluated how histopathologic subtype misclassification might impact the reported disease-specific mortality.

Our study included 1957 individuals with a first primary melanoma diagnosed in the year 2000, at centers of the GEM study in Australia, Canada, Italy, and the United States. The Institutional Review Board approval was obtained, and the subjects signed written consent. Each patient had their hematoxylin-eosin–stained slides read initially by a community pathologist, who reported Breslow thickness and histopathologic subtype followed by an independent review by a dermatopathologist, blinded to the community pathologist report. The vital status was obtained at an average of 7.4 years.

Within the study population and lethal melanoma cases, descriptive statistics were calculated and the frequency tables that compared the kappa value for the readings of community pathologists and dermatopathologists were created for Breslow thickness and histopathologic subtype. All the tests were two-sided and $P < .05$ was considered significant. The data were analyzed using SAS 9.4 software and the interobserver variability was calculated with Fleiss' method.[5]

The mean age of the subjects at diagnosis was 55 years and 48.5% of them were women. The kappa for Breslow thickness was 0.72 (95% CI, 0.69-0.75), demonstrating a "substantial agreement." The kappa within lethal cases was 0.56 (95% CI, 0.45-0.66), suggesting a "moderate agreement."

The overall kappa for the histopathologic subtype of 0.27 demonstrates only a "fair agreement" (Table I), whereas that for the reviewing dermatopathologists was 0.68, indicating a "substantial agreement." The kappa for nodular subtype had only 51.3% agreement. Within the lethal cases, the kappa value was "fair," 0.30 (Table II).

Our study illustrated a moderate-to-substantial agreement on Breslow thickness between the community pathologists and dermatopathologists. The decrease in Breslow-related kappa in fatal cases may represent less precision in measuring thicker tumors as lethal tumors tended to be deeper. We also observed higher rates of disagreement among pathologists for the histopathologic subtype. Considering that the subtype can indicate tumor characteristics, any misclassification might influence patients' counseling, treatment options, and their disease perception.

The limitations of our study were that only the Breslow thickness and histopathologic subtype were measured due to the limited initial reporting by community pathologists and that the slide reviewed by the community pathologist may differ from the same slide reviewed by the dermatopathologist.

Based on these results, we propose the judicious interpretation of nodular melanoma as a prognostic factor. The data on subtype without expert dermatopathology review should be used with caution until the interrater concordance improves. The patient prognosis should continue to be based on more reproducible characteristics such as Breslow thickness, ulceration, mitotic index, and metastasis.

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**Table I.** Concordance of histopathologic subtype between community pathologists and dermatopathologists

| | Dermatopathologists | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Community pathologists** | **SSM** | **NM** | **LMM** | **ALM** | **SC** | **NOS** | **Other** | **Total** |
| SSM | **919**† | 33 | 70 | 3 | 3 | 52 | 3 | |
| NM | 55 | **96**† | 7 | 1 | 2 | 18 | 3 | |
| LMM | 55 | 4 | **72**† | 1 | 0 | 4 | 4 | |
| ALM | 3 | 1 | 1 | **3**† | 1 | 0 | 0 | |
| SC | 8 | 2 | 0 | 0 | **1**† | 2 | 3 | |
| NOS | 354 | 50 | 46 | 2 | 2 | **49**† | 15 | |
| Other | 1 | 1 | 0 | 0 | 1 | 0 | **0**† | |
| Total (percent agreement) | 1395 (65.8) | 187 (51.3) | 196 (36.7) | 10 (0.30) | 10 (0.10) | 125 (39.2) | 28 (0.0) | **1951***† |

Overall Correlation = 0.27 (95% CI, 0.24-0.30).
*ALM*, Acral lentiginous melanoma; *LMM*, lentigo maligna melanoma; *NM*, nodular melanoma; *NOS*, not otherwise specified; *SC*, spindle cell; *SSM*, superficial spreading melanoma.
*6 missing values.
†Numbers in bold represent the number of subjects for which community pathologists and dermatopathologists agreed.

**Table II.** Deaths per histopathologic subtype

| | Dermatopathologists | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Community pathologists** | **SSM** | **NM** | **LMM** | **ALM** | **SC** | **NOS** | **Other** | **Total** |
| SSM | **34*** | 7 | 0 | 2 | 1 | 3 | 0 | |
| NM | 12 | **22*** | 2 | 1 | 0 | 5 | 1 | |
| LMM | 4 | 2 | **2*** | 0 | 0 | 0 | 1 | |
| ALM | 1 | 0 | 0 | **0*** | 0 | 0 | 0 | |
| SC | 0 | 1 | 0 | 0 | **0*** | 0 | 2 | |
| NOS | 9 | 8 | 2 | 1 | 0 | **9*** | 1 | |
| Other | 0 | 1 | 0 | 0 | 1 | 0 | **0*** | |
| Total (percent agreement) | 60 (56.7) | 41 (53.7) | 6 (33.3) | 4 (0.0) | 2 (0.0) | 17 (52.9) | 5 (0.0) | **135*** |

Overall Correlation = 0.30, (95% CI, 0.19-0.40).
*ALM*, Acral lentiginous melanoma; *LMM*, lentigo maligna melanoma; *NM*, nodular melanoma; *NOS*, not otherwise specified; *SC*, spindle cell; *SSM*, superficial spreading melanoma.
*Numbers in bold represent the number of cases where community pathologists and dermatopathologists agreed.

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**Conflicts of interest**

None disclosed.

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