ORIGINAL ARTICLE

Evaluation of the Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis (MPATH-Dx) classification scheme for diagnosis of cutaneous melanocytic neoplasms: Results from the International Melanoma Pathology Study Group

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Background: Pathologists use diverse terminology when interpreting melanocytic neoplasms, potentially compromising quality of care.

Objective: We sought to evaluate the Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis (MPATH-Dx) scheme, a 5-category classification system for melanocytic lesions.

Methods: Participants (n = 16) of the 2013 International Melanoma Pathology Study Group Workshop provided independent case-level diagnoses and treatment suggestions for 48 melanocytic lesions.

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Individual diagnoses (including, when necessary, least and most severe diagnoses) were mapped to corresponding MPATH-Dx classes. Interrater agreement and correlation between MPATH-Dx categorization and treatment suggestions were evaluated.

Results: Most participants were board-certified dermatopathologists (n = 15), age 50 years or older (n = 12), male (n = 9), based in the United States (n = 11), and primary academic faculty (n = 14). Overall, participants generated 634 case-level diagnoses with treatment suggestions. Mean weighted kappa coefficients for diagnostic agreement after MPATH-Dx mapping (assuming least and most severe diagnoses, when necessary) were 0.70 (95% confidence interval 0.68-0.71) and 0.72 (95% confidence interval 0.71-0.73), respectively, whereas correlation between MPATH-Dx categorization and treatment suggestions was 0.91.

Limitations: This was a small sample size of experienced pathologists in a testing situation.

Conclusion: Varying diagnostic nomenclature can be classified into a concise hierarchy using the MPATH-Dx scheme. Further research is needed to determine whether this classification system can facilitate diagnostic concordance in general pathology practice and improve patient care. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.04.052.)

Key words: classification; diagnosis; dysplastic nevus; melanoma; Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis; nevus; pathology; variability; variation.

CAPSULE SUMMARY

- Pathologists use diverse terminology to diagnose melanocytic lesions.
- The Melanocytic Pathology Asessment Tool and Hierarchy for Diagnosis—a novel classification system—simplifies diagnosis and yields high interrater agreement among pathologists skilled in diagnosis of melanocytic neoplasms, or among experienced pathologists.
- Implementation of the Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis system may aid in diagnostic consistency of melanocytic lesions.

Pathologists use highly varied terminology when interpreting melanocytic neoplasms. Substantial discordance from nomenclature variability may arise during evaluation of these lesions[1,2] consequent to provider-level characteristics (eg, training, clinical experience) and uncertainty regarding underlying biologic behavior associated with these neoplasms. The latter may reflect intrinsic "complexity in the histologic continuum from benign to unequivocally malignant melanocytic lesions,"[1] and subjectivity in application of diagnostic criteria.

A diagnostic label may not expressly convey when additional surgical treatment is needed, and nondermatologist clinicians performing biopsies may not accurately infer appropriate treatments from pathology reports, impacting patient-centered care.[1,3] Moreover, epidemiologic research regarding melanocytic lesions and associated outcomes has been limited by diagnostic inconsistency. Treatment suggestions in pathology reports may help resolve this ambiguity. The Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis (MPATH-Dx) classification system integrates diagnosis and treatment considerations for melanocytic lesions, but it is not known how practicing/experienced pathologists and clinicians receiving their reports might apply these guidelines.[1]

Accordingly, we evaluated variability in diagnostic terms applied to melanocytic lesions within a group of experienced pathologists. We tested use of the MPATH-Dx classification system[1] for categorizing diagnostic terms and hypothesized that: (1) numerous diagnostic terms exist for histologically identical melanocytic neoplasms, (2) these terms can be mapped to 1 of the 5 MPATH-Dx classes, (3) moderate to good interrater agreement can be achieved using MPATH-Dx diagnostic classifications, and (4) cases with myriad diagnoses can be consistently assigned to suggested treatment categories, potentially simplifying interpretation of pathology reports and aiding physician decision-making.

METHODS

Study overview and participants

Eligible pathologists included those attending the International Melanoma Pathology Study Group Workshop during the Society for Melanoma Research Congress in November 2013. Data collection included: (1) an online survey to ascertain participant characteristics and attitudes concerning

Abbreviations used:

BI-RADS:	Breast Imaging Reporting and Data System
CI:	confidence interval
MPATH-Dx:	Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis
SLN:	sentinel lymph node

interpretation of melanocytic lesions, and (2) glass slide microscopic review of a test set of melanocytic neoplasms. Participants provided their independent diagnosis and treatment suggestion for each specimen. Our study received institutional board review approval from the University of Washington.

Test set of cutaneous melanocytic neoplasms

Melanocytic skin lesions biopsied between January 1, 2010, and December 31, 2011, from patients ages 20 years or older were obtained from a private pathology practice (Dermatopathology Northwest, Bellevue, WA). Cases were selected to represent a broad range of melanocytic neoplasms, including benign nevi, atypical/dysplastic nevi, melanoma in situ, and invasive melanoma. Shave, punch, and excisional biopsy specimens were included, whereas consultative cases and re-excisions were excluded.

This sample of melanocytic lesions covered the full spectrum of the 5 MPATH-Dx[1] classes. Class I lesions, such as common and mildly dysplastic nevi, pose very low risk for adverse outcomes, and no further treatment is generally recommended; class II includes moderately dysplastic and spindle cell/epithelioid nevi without atypia that have low, but presently unquantifiable, risk of progression and may merit narrow excision (<5-mm margins); class III lesions, such as severely dysplastic nevi and melanoma in situ, have higher risk of progression and may require excision with larger margins (5 mm to <1 cm); class IV encompasses stage T1a invasive melanomas potentially warranting wide excision (≥1-cm margins); and class V includes stage T1b (or greater) invasive melanomas posing more significant risk of metastasis, which may require wide excision (≥1-cm margins) and additional diagnostic workup (sentinel lymph node [SLN] biopsy), adjuvant therapy (eg, interferon), or both.

The final test cases included 240 melanocytic neoplasms. Permuted block randomization (whereby cases are assigned to blocks of equal size for all possible permutations followed by random block selection) allocated the 240 cases into 5 test sets, each comprising 48 cases. One of the 5 test sets was randomly chosen for use in the current study. Detailed information regarding test set development is provided elsewhere.[1]

Test set interpretation

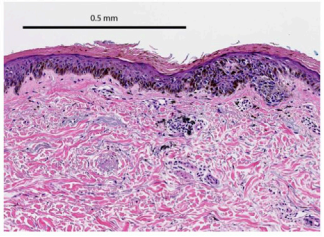
Participants were first provided an overview of the MPATH-Dx classification scheme, including a description of each MPATH-Dx class and associated treatment considerations. Participants then sequentially evaluated test cases (1 hematoxylin and eosin–stained glass slide per case) using a multiheaded microscope with a digital projector, driven by one of the authors (S. R. K.). The order of case presentation was randomly assigned before viewing. Participants offered their independent diagnostic assessments (entered into a blank write-in field) and treatment recommendations using 4 prespecified checkboxes: (1) no further treatment indicated, (2) re-excise less than 5-mm margins (narrow but complete), (3) re-excise greater than or equal to 5-mm margins (but <1 cm), and (4) re-excise greater than or equal to 1-cm margins (wide excision). In addition, participants could choose SLN biopsy, adjuvant therapy (eg, interferon), or both.

Participants were informed that these treatment options should be regarded as suggestions for consideration, as they were developed using US guidelines (when available) and may not reflect all practice patterns. Participants were instructed to assume that the biopsy specimen was representative of the entire lesion and that the lesion was present at the margin. Patient age, biopsy type, and anatomic site were also provided.

Data were independently transcribed into an electronic database by 2 authors (J. P. L. and G. A. Z.), and ambiguities in data entry as a result of handwriting were resolved by joint consensus review to ensure data fidelity.

Primary outcomes

Case-level diagnoses and treatment suggestions constituted the primary outcomes. Write-in diagnoses were mapped to corresponding MPATH-Dx classes, with the following modifications. First, write-in diagnoses indicating "invasive melanoma" (or variants therein) could not be definitively mapped to MPATH-Dx classes IV or V as participants were not asked depth of invasion, mitotic rate, or presence/absence of ulceration, and thus were grouped a priori into a combined MPATH-Dx category (MPATH-Dx class IV/V). Second, write-in diagnoses for which a differential diagnosis was provided by participants (eg, "moderate vs severe dysplastic nevus") were classified in 2 ways for analytic purposes: (1) according to the least severe



Verbatim Write-in Diagnosis[a]	Treatment (tx) Consideration	MPATH-Dx Class (mapped directly)	MPATH-Dx Class (presuming least severe diagnosis)[b]	MPATH-Dx Class (presuming most severe diagnosis)[b]
Solar lentigo/lentiginous junctional nevus with mild focal dysplasia	No further tx	I	NA	NA
Junctional nevus - lentiginous	No further tx	I	NA	NA
Lentiginous nevus	No further tx	I	NA	NA
Junctional nevus, mild AD, mod cyt. atypia (also component of solar lentigo) Note: rec re-excise because lesion is non-uniform--only focal nesting	Re-excise <5mm margins	NA	I	II
Lentiginous junctional dysplastic nevus (LJDN) with moderate atypia	Re-excise <5mm margins	II	NA	NA
Lentiginous nevus with moderate atypia	Re-excise <5mm margins	II	NA	NA
Irritated atypical lentiginous junctional nevus with atypical junctional melanocytic hyperplasia slight-moderate atypia	Re-excise <5mm margins	NA	I	II
Lentiginous nevus w/ moderate atyp. DD melanoma in situ	Re-excise ≥5mm to <1cm margins	NA	II	III
Lentig compd dysplastic nevus w/ ??? Severe atypia (2) solar lentigo (3) solar elastosis	Re-excise <5mm margins	NA	I	III
Lentigo maligna	Re-excise ≥5mm to <1cm margins	III	NA	NA
Intraepidermal melanocytic prolif w/ severe atypia bordering on MIS--solar elastosis	Re-excise ≥5mm to <1cm margins	III	NA	NA
Junctional nevus w/ severe dysplasia	Re-excise ≥5mm to <1cm margins	III	NA	NA
Melanoma in situ	Re-excise ≥5mm to <1cm margins	III	NA	NA
MIS	Re-excise ≥5mm to <1cm margins	III	NA	NA
Melanoma in situ	Re-excise ≥5mm to 1<cm margins	III	NA	NA

Fig 1. The photomicrograph depicts a broad lesion with irregular epidermal thinning and thickening. Note verbatim write-ins are ordered by increasing treatment (*tx*) severity and do not reflect the actual order of case presentation to participants. Widely varying terminology was used by pathologists for its histopathologic interpretation and diagnosis. [a]Missing data from 1 participant not shown. [b]Mapping of write-in diagnoses to least and most severe Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis (*MPATH-Dx*) categories performed only when needed. *NA*, Not applicable.

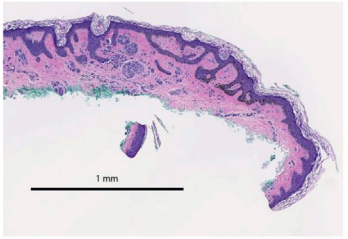
corresponding MPATH-Dx class, and (2) according to the most severe corresponding MPATH-Dx class. This was only performed when diagnoses provided in the histologic differential corresponded to different MPATH-Dx classes. Illegible write-in diagnoses were treated as missing data.

Suggestions of wide re-excisions (≥1 cm), SLN mapping, adjuvant therapy, or a combination of these were collapsed into 1 treatment category (participants who chose either SLN or adjuvant therapy alone or in combination were assumed to have recommended wide re-excision, even if not selected). Choice of mutually exclusive treatment options (eg, boxes checked for both "re-excise <5-mm margins [narrow but complete]" and "re-excise ≥5-mm margins [but <1 cm]") were considered ineligible responses, as were surgical re-excisions less than 1 cm combined with SLN or adjuvant therapy.

Statistical analysis

Correlation between MPATH-Dx diagnostic classes and treatment considerations was assessed using Spearman rank correlation coefficient (rho). We assessed interobserver variability of MPATH-Dx diagnostic classes by calculating means of unweighted and weighted kappa coefficients for each pairwise combination of participants' ratings across all 48 cases, again calculated separately presuming the least and most severe diagnosis when needed. Weights for kappa coefficients were calculated using the Cicchetti-Allison method, given this analytic approach assigns a weight of 2/3 to adjacent diagnoses and 1/3 to diagnoses that are 2 categories removed (based on a 4-category classification scheme). By assigning greater weights to diagnostic classifications that are "closer" to each other, this weighting scheme reflects variation in agreement that may differ according to diagnostic severity.

The associated percentile 95% confidence interval (CI) for each mean kappa coefficient was estimated using cluster bootstrapping with 2000 resamples.[4] Likewise, mean kappa coefficients were independently calculated for case-level treatment recommendations. Strength of agreement



Verbatim Write-in Diagnosis[a]	Treatment (tx) Consideration	MPATH-Dx Class (mapped directly)	MPATH-Dx Class (presuming least severe diagnosis)[b]	MPATH-Dx Class (presuming most severe diagnosis)[b]
Nevus compound dysplastic mild	No further tx	I	NA	NA
Compound nevus maybe mild dysplasia at most	No further tx	I	NA	NA
LCDN w/ mild atyp	No further tx	I	NA	NA
DN mild	No further tx	I	NA	NA
LCN	No further tx	I	NA	NA
Compound lentiginous nevus slight atypia	No further tx	I	NA	NA
Compound nevus, special site	No further tx	I	NA	NA
CDN mild	No further tx	I	NA	NA
Cpnd nevus with mild junctional dysplasia	Re-excise <5mm margins	I	NA	NA
Cmpd nevus w/ lentiginous prolif at periphery	Re-excise <5mm margins	I	NA	NA
Atypical CN w/ sl-mod junctional atypia	Re-excise <5mm margins	NA	I	II
Dys, comp	Re-excise <5mm margins	NA	I	III
Atypical nevus	Re-excise <5mm margins	NA	I	III
CND mod	Re-excise <5mm margins	II	NA	NA
LCDN with focal severe	Re-excise ≥5mm to <1cm margins	III	NA	NA

Fig 2. The photomicrograph depicts a broad lesion composed mainly of nevoid melanocytes in the dermis. Note verbatim write-ins are ordered by increasing treatment (*tx*) severity. Widely varying terminology was used by pathologists for its histopathologic interpretation and diagnosis. [a]Missing data from 1 participant not shown. [b]Mapping of write-in diagnoses to least and most severe Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis (*MPATH-Dx*) categories performed only when needed. *NA*, Not applicable.

for kappa coefficients was assessed according to Fleiss benchmark scale (poor agreement <0.40; intermediate to good agreement 0.40 to <0.75; excellent agreement ≥0.75).[5] Analyses were performed using SAS, Version 9.4 (SAS Institute Inc, Cary, NC) and Stata, SE 13.1 (StataCorp, College Station, TX), and all statistical tests were 2-tailed with alpha equal to 0.05.

RESULTS

Participants consisted of 16 pathologists, the majority of whom were board-certified dermatopathologists (n = 15; 93.8%). Most were age 50 years or older (n = 12; 75%), male (n = 9; 56%), practicing within the United States (n = 11; 69%), and held a primary academic appointment (n = 14; 88%). All reported being regarded as melanocytic lesion experts by their colleagues, with 13 pathologists reporting 10 or more years of experience in this area. Three pathologists reported being "extremely confident" in their interpretation of melanocytic skin lesions, whereas 11 reported being "very confident." The majority (n = 9; 56%) agreed that melanocytic lesion diagnosis was "challenging" or "very challenging," whereas none rated diagnosis of these lesions as "very easy," "easy," or "somewhat easy."

Of 768 potential write-in responses (16 pathologists each interpreting 48 cases), 101 (13.2%) were missing a diagnosis, usually because the participant was temporarily absent during case presentation, whereas 21 diagnoses (2.7%) were illegible and 12 lacked suggested treatments. A total of 634 test case interpretations had completely mapped MPATH-Dx diagnoses with treatment responses and were analyzed.

Although some cases were uniformly interpreted with the same diagnostic term (eg, all pathologists diagnosed "invasive melanoma," with minor qualification), other cases showed substantial variability in diagnostic labeling. For example, Fig 1 shows a slide image with diagnoses ranging from benign (eg, "lentiginous junctional nevus") to malignant (eg, "melanoma in situ"), with 7 distinct diagnostic terms given for this case. Of note, this case would be mapped to MPATH-Dx class III by 7 of the participants. Fig 2 shows a similar spectrum of diagnostic terms applied to another case.

The distribution of diagnoses and treatment considerations are shown in Fig 3 and Table I.

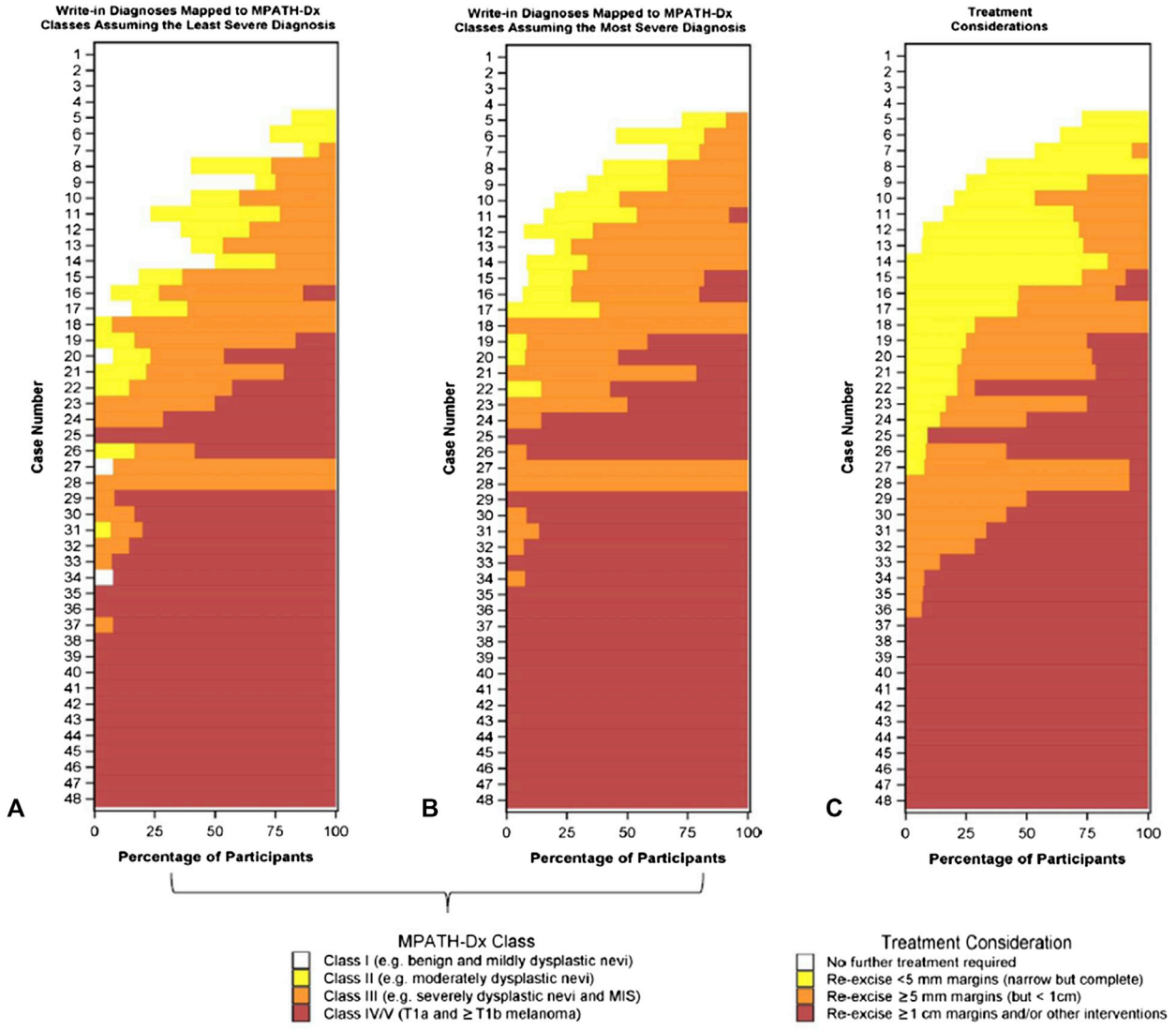


Fig 3. Distribution of Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis (*MPATH-Dx*) diagnostic classes (**A** and **B**) and treatment considerations (**C**) are shown per case. Note cases are ordered by increasing treatment severity and do not reflect the actual order of case presentation to participants.

Mean unweighted and weighted kappa coefficients for MPATH-Dx classes (assuming the least severe write-in diagnoses) were 0.57 (95% CI 0.56-0.59) and 0.70 (95% CI 0.68-0.71), respectively, demonstrating intermediate to good agreement. A comparable magnitude of interrater agreement was observed when assuming the most severe write-in diagnosis, with mean unweighted and weighted kappa coefficients of 0.62 (95% CI 0.60-0.63) and 0.72 (95% CI 0.71-0.73), respectively. Mean unweighted interrater kappa coefficient for agreement regarding treatment was 0.54 (95% CI 0.52-0.56), whereas the mean weighted estimate was 0.69 (95% CI 0.68-0.71).

Increasing severity of diagnoses after mapping into MPATH-Dx classes was associated with increasing intensity of suggested treatment considerations (Table I). Correlation between MPATH-Dx diagnostic classification (assuming the least severe write-in diagnosis, when necessary) and treatment was 0.91 (95% CI 0.90-0.92) ($P < .001$). Similarly, correlation between MPATH-Dx classes, assuming the most severe write-in diagnosis when necessary, and treatment was 0.91 (95% CI 0.90-0.93) ($P < .001$).

DISCUSSION

Achieving diagnostic agreement for melanocytic skin lesions remains challenging. In the absence of substantial technologic advances enabling precise classification of these neoplasms, complete elimination of disagreement is overly ambitious. For example, although improvements in adjunctive molecular testing for melanoma appear promising,

Table I. Distribution of participant responses by Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis class and treatment consideration

	Suggested treatment consideration made by participant for the case				
	I: No further treatment	II: Re-excise <5-mm margins	III: Re-excise ≥5-mm to <1-cm margins	IV/V: Re-excise ≥1-cm margins*	Total
MPATH-Dx classification based on participants' write-in diagnosis					
Presuming least severe diagnosis (when needed)†					
Class I: No apparent risk for continued local proliferation and adverse outcome	89 (67.9)	40 (30.5)	2 (1.5)	0 (0.0)	**131**
Class II: Low-level risk for local proliferation of remaining cells	2 (3.8)	41 (78.8)	9 (17.3)	0 (0.0)	**52**
Class III: Higher likelihood of local tumor progression and greater need for intervention	0 (0.0)	30 (21.1)	96 (67.6)	16 (11.3)	**142**
Class IV/V: Invasive melanoma stage T1a or ≥T1b	0 (0.0)	3 (1.0)	29 (9.4)	277 (89.6)	**309**
Total	**91**	**114**	**136**	**293**	**634**
Presuming most severe diagnosis (when needed)†					
Class I: No apparent risk for continued local proliferation and adverse outcome	86 (87.8)	12 (12.2)	0 (0.0)	0 (0.0)	**98**
Class II: Low-level risk for local proliferation of remaining cells	3 (6.4)	43 (91.5)	1 (2.1)	0 (0.0)	**47**
Class III: Higher likelihood of local tumor progression and greater need for intervention	2 (1.3)	55 (34.8)	96 (60.8)	5 (3.2)	**158**
Class IV/V: Invasive melanoma stage T1a or ≥T1b	0 (0.0)	4 (1.2)	39 (11.8)	288 (87.0)	**331**
Total	**91**	**114**	**136**	**293**	**634**

Values expressed as count (row percent). Bold used for emphasis.
MPATH-Dx, Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis.
*Includes sentinel lymph node sampling, adjuvant therapy (eg, interferon), or both as additional treatment responses.
†Write-in responses that included differential diagnoses were classified using 2 scenarios, one presuming the least severe diagnosis and the other presuming the most severe diagnosis.

ambiguous results still occur, and it remains unclear whether sufficiently "black or white" results are possible in the near future. We believe that the litany of diagnostic terms is and will remain a substantive contributor to diagnostic discordance for melanocytic lesions. To our knowledge, this is the largest study describing the variability in diagnostic terms applied to melanocytic neoplasms.

Our results highlight the diverse diagnostic terminology used by pathologists and illustrate concise mapping of these terms into MPATH-Dx. We found that write-in diagnoses mapped to MPATH-Dx classes were significantly correlated with treatment suggestions, providing further validation of this integrated approach.[1] Recognizing, however, that more diverse and complex terminology may provide valuable information for patient care, we do not envisage replacing current real-world practice. Rather, potential inclusion of MPATH-Dx categories (after future research to optimize this classification scheme) in pathology reports may be useful as an added feature to clarify reporting. This will likely be valuable when reports are circulated outside of pathology practice groups to local networks of referring physicians that may be less familiar with potential nuances of dermatopathology terminology and treatment implications.

Our results should be considered in context of the known complexities in interpretation of dermatopathology reports. A recent study indicated that surgeons may misinterpret pathology reports up to 30% of the time.[6] The risk of misinterpretation of dermatopathology reports is likely to be clinically significant given the lack of standardized diagnostic terminology for melanocytic neoplasms.[1] In addition, recent regulatory changes to Clinical Laboratory Improvement Amendments of 1988 enable direct patient access to pathology reports from Clinical Laboratory Improvement Amendments–certified dermatopathology laboratories.[7] Although increasing medical record transparency will undoubtedly increase patient engagement in health care, many patients may be confused by the diagnostic terms they encounter, raising risks of psychological harm and increased demands for subsequent and potentially unnecessary procedures.[8] Communication problems

might be mitigated and pathology reporting improved through use of classification schemes such as MPATH-Dx. Our results show that varied histopathologic assessments can be simplified into a manageable number of categories using this scheme.

Comparable efforts have been successfully pursued in the radiographic interpretation of mammograms by the American College of Radiology through the development of the Breast Imaging Reporting and Data System (BI-RADS).[9] Like MPATH-Dx, BI-RADS categorizes mammographic lesions into categories with associated clinical management recommendations. Not only has BI-RADS improved quality of care for women with abnormal mammogram findings—reducing both underuse and overuse of follow-up procedure services[10]—it has also standardized breast cancer research by providing a coherent, universal framework interpreting mammograms.[11]

The MPATH-Dx system is promising for dermatopathology and the histopathologic interpretation of melanocytic neoplasms. Simplified classification is both timely and requisite for longer-term efforts to advance care delivery for patients undergoing biopsies of pigmented lesions. By reducing diagnostic confusion and establishing a reference framework for diagnosis and treatment of melanocytic proliferations, use of the MPATH-Dx system may also help reduce exposure to medicolegal liability. Future research is needed to determine whether MPATH-Dx improves concordance of diagnostic interpretation among community pathologists. Broader implementation of this system will likely require additional piloting and revision by professional societies in dermatopathology and dermatology.

This study has limitations. Pathologists interpreted a single slide per case in an artificial setting characterized by time constraints and inability to "drive" the microscope or consult colleagues, and thus these results may differ from actual practice. Our analysis did not consider diagnostic or therapeutic disagreement for invasive melanoma cases that were, by necessity, collapsed into a combined category (MPATH-Dx class IV/V), thereby obscuring potential additional variation in agreement. In addition, our study only included a self-selected group of pathologists skilled in diagnosis of melanocytic neoplasms, and therefore these results may not be generalizable to the broader community of pathologists.

The test set of melanocytic lesions also excluded consultative cases, which may have resulted in inclusion of "easier" cases and inflated estimates of interrater agreement. Finally, the MPATH-Dx scheme also assumes that each biopsy specimen represented the entire lesion and that the lesion was present at the margin. The utility of this classification scheme may be limited for biopsy specimens that do not represent the entire lesion or have negative margins. Such scenarios may warrant pursuit of different/alternative treatments to ensure appropriate management.

We understand that agreement concerning treatment recommendations does not necessarily imply complete diagnostic agreement or consensus regarding the ultimate biologic behavior of melanocytic neoplasms. It is unlikely that uncertainty surrounding some of these lesions can be completely eliminated, no matter what the approach. Nonetheless, our findings highlight that many different diagnostic terms are applied to the same skin biopsy specimens, even by expert dermatopathologists, and underscore the need for development and implementation of novel interventions, such as the MPATH-Dx system, to improve diagnostic agreement and simplify treatments for melanocytic neoplasms.

REFERENCES

1. Piepkorn MW, Barnhill RL, Elder DE, et al. The MPATH-Dx reporting schema for melanocytic proliferations and melanoma. *J Am Acad Dermatol*. 2014;70:131-141.
2. Corona R, Mele A, Amini M, et al. Interobserver variability on the histopathologic diagnosis of cutaneous melanoma and other pigmented skin lesions. *J Clin Oncol*. 1996;14:1218-1223.
3. Niebling MG, Haydu LE, Karim RZ, et al. Pathology review significantly affects diagnosis and treatment of melanoma patients: an analysis of 5011 patients treated at a melanoma treatment center. *Ann Surg Oncol*. 2014;21:2245-2251.
4. Davison AC, Hinkley DV. *Bootstrap methods and their application (Cambridge series in statistical and probabilistic mathematics)*. 1st ed. Cambridge (United Kingdom): Cambridge University Press; 1997.
5. Fleiss JL, Levin B, Paik MC. *The measurement of interrater agreement. Statistical methods for rates and proportions*. 3rd ed. Hoboken (NJ): John Wiley and Sons; 2003.
6. Powsner SM, Costa J, Homer RJ. Clinicians are from Mars and pathologists are from Venus. *Arch Pathol Lab Med*. 2000;124:1040-1046.
7. Young MJ, Scheinberg E, Bursztajn H. Direct-to-patient laboratory test reporting: balancing access with effective clinical communication. *JAMA*. 2014;312:127-128.
8. Lott JP, Piepkorn MW, Elmore JG. Dermatology in an age of fully transparent electronic medical records. *JAMA Dermatol*. 2015;151:477-478.
9. American College of Radiology. *Breast Imaging Reporting and Data System (BI-RADS)*. 3rd ed. Reston (VA): American College of Radiology; 1998.
10. Eberl MM, Fox CH, Edge SB, Carter CA, Mahoney MC. BI-RADS classification for management of abnormal mammograms. *J Am Board Fam Med*. 2006;19:161-164.
11. Burnside ES, Sickles EA, Bassett LW, et al. The ACR BI-RADS experience: learning From history. *J Am Coll Radiol*. 2009;6:851-860.