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Pathologists' Agreement on Treatment Suggestions for Melanocytic Skin Lesions

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Abstract

BACKGROUND: While treatment guidelines exist for melanoma *in situ* and invasive melanoma, guidelines for other melanocytic skin lesions do not exist.

OBJECTIVE: To examine pathologists' treatment suggestions for a broad spectrum of melanocytic skin lesions and in comparison with existing guidelines.

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METHODS: Pathologists (N=187) completed a survey and then provided diagnoses and treatment suggestions for 240 melanocytic skin lesions. Physician characteristics associated with treatment suggestions were evaluated using multivariable modeling.

RESULTS: Treatment suggestions were concordant with National Comprehensive Cancer Network (NCCN) guidelines for the majority of cases interpreted as melanoma *in situ* (73%) and invasive melanoma (86%). Greater variability of treatment suggestions was seen for other lesion types without existing treatment guidelines. Characteristics associated with provision of treatment suggestions discordant with NCCN guidelines were: low caseloads (invasive melanoma), lack of fellowship training or board certification (melanoma *in situ*), and >10 years of experience (invasive melanoma and melanoma *in situ*).

LIMITATIONS: Pathologists could not perform immunohistochemical staining or other diagnostic tests; only one glass side provided per biopsy case.

CONCLUSIONS: Pathologists' treatment suggestions vary significantly for melanocytic lesions, with lower variability for lesion types with national guidelines. Results suggest the need for standardization of treatment guidelines for all melanocytic lesion types.

Introduction:

While clinicans ultimately determine patient treatment for melanocytic skin lesions (MSLs), factoring histopathology, dermoscopy, clinical suspicion, and clinical history, the pathologists may typically be the only provider examining a skin biopsy specimen and therefore can also serve as an important resource on guiding optimal treatment options. Our study follows-up on a national survey which found that a majority of skin pathologists reported providing treatment suggestions along with their biopsy interpretations of MSL on some of their reports. Although national guidelines exist for the management of melanoma, there is less agreement for the treatment of other types of MSL (e.g., atypical/dysplastic nevi)^{2–5}.

As a result of striking variability among pathologists in the diagnosis of melanocytic lesions. ^{6–10}, we hypothesized that there would also be extensive variation in treatment recommendations given for MSLs, even when controlling for the diagnosis provided by the pathologists. Since many patients undergoing skin biopsies have dysplasic nevi or borderline diagnoses where no treatment guidelines exist, or the patients are evaluated and treated by nonspecialized clinicians such as primary care physicians, we suspect that variation in pathologists' treatment suggestions could lead to extensive variation in clinical care. ^{11,12} About one in five skin biopsies obtained in the U.S. are of melanocytic lesions, highlighting the commonality of these lesions in clinical practice⁸ and thus the significance of this topic.

In this report, we examine the variability in treatment suggestions regarding reexcision and margin width for a given diagnosis, specifically looking at pathologists' treatment suggestions for melanoma *in situ* and invasive melanoma cases and concordance with national guidelines for treatment.¹³ In addition, we examine concordance of pathologists' treatment suggestions for other types of MSLs (e.g., dysplastic nevi, Spitz lesions) and concordance of treatment suggestions by pathologists and the MPATH-Dx treatment suggestions¹⁴. This study, which presents data on pathologists' treatment recommendations

during the actual interpretation of skin biopsies, follows up on our prior survey study of pathologists' views regarding appropriate treatments for differing types of MSLs.³

Methods:

Data derive from the M-Path study, a national project examining the accuracy and reproducibility of pathologists' interpretations of MSLs. IRB approval was acquired and informed consent was obtained from each participant. M-Path methods have been previously reported in detail. 9,14–16

Study Pathologists Identification, Recruitment, and Baseline Characteristics:

Pathologists from 10 U.S. states were identified using publicly available information from professional organizations and updated through internet searches and telephone calls. Pathologists were then invited by email, with postal and telephone follow-up. Pathologists were informed that they would receive a confidential, individualized report of their interpretive results alongside those of their peers and an expert panel, and free CME credit (up to 20 hours category 1). Eligibility criteria included self-reported interpretation of MSL over the past year, and an expectation to continue interpreting MSLs over the two subsequent years. The study excluded residents and fellows. Pathologists completed a baseline survey regarding demographics.

Case Selection and Composition

The skin biopsy cases were of cutaneous melanocytic lesions from shave, punch, and excisional specimens. Cases were initially selected using stratification on patient age (20–49 years, 50–64 years, 65 years) and medical chart documentation of the original diagnosis in order to achieve the desired target distribution of cases across MPATH-Dx diagnostic categories and an even distribution of cases across these three age groups within each diagnostic category. One single slide for each case was used. Three expert dermatopathologists (RB, DE, MP) independently reviewed the new H&E stained glass slides for each case, followed by a consensus review using a modified Delphi Approach¹⁷. The final 240 cases were then selected with the desired distribution across MPATH-Dx categories for this consensus diagnosis and with an even distribution across age categories. The final 240 cases had intentionally higher proportions in MPATH-Dx Classes II-V than typically found in clinical practice with distribution as follows: 10.4% (n=25) in class I, 15% (n=36) in class II, 25% (n=60) in class III, 22.9%(n=55) in class IV, and 25.4% (n=61) in class V. The final 240 cases were assembled into five sets of 48 cases.

Case Interpretation by Pathologists:

After completing the survey, pathologists were randomized to receive one of five sets of 48 MSL glass slides developed for the M-Path study. A permutated block randomization with stratification on pathologists' clinical expertise was used. Expertise was dichotomized based on possession of one or more of the following self-reported characteristics on the baseline survey: fellowship trained or board certified in dermatopathology; considered by colleagues to be an expert in melanocytic lesions; or 10% or more of usual caseload included cutaneous melanocytic lesions. Slides were presented in a random order to each participant.

Using the online MPATH-Dx form, pathologists reported their diagnoses and treatment suggestions for each case. ¹⁴ Participants were provided with the patient's age, sex, biopsy type, and anatomic location of the biopsy site on each online histology form for a case. Standardized diagnostic definitions or educational materials were not provided for participants. Participants were also asked to assume that the single glass slide was representative of the entire lesion and that the margin was positive.

Participants could provide their treatment recommendation for a case at any time during their review of the slide. The pathologists were asked "Although final treatment decisions may rest with the clinician and the patient, what clinical course would you suggest for consideration?" and were given four possible options: a. No further treatment; b. Excision <0.5cm; c. Excision 0.5cm to <1cm; d. Excision 1 cm. Pathologists were told to assume the glass slide was representative of the lesion as a whole, and that the lesion extended all the way to the edge of the sample (i.e., if there were any residual lesion beyond the edge of the specimen it would not be different from what was already on the slide). These assumptions were stipulated so as to obligate participants to consider the four MPATH-Dx treatment options for every lesion, because otherwise they would not recommend re-excision for completely excised lesions, except for melanomas.

Statistical Analysis:

A classification scheme for melanocytic lesions, the Melanoma Pathology Assessment Tool and Hierarchy for Diagnosis (MPATH-Dx) tool¹⁴, was used in this study.^{10,14} The MPATH-Dx tool moves beyond National Comprehensive Cancer Network (NCCN) guidelines by providing treatment suggestions for the full spectrum of MSLs. The MPATH-Dx classification tool categorizes interpretations into five overarching diagnostic classes, ¹⁴ with example diagnoses and corresponding treatment suggestions as follows: I) nevus/mild dysplastic nevi (no further treatment required); II) moderate dysplastic nevi (narrow but complete re-excision <0.5 cm); III) severe dysplastic nevi/melanoma *in situ* (repeat excision with 0.5 cm but < 1cm margins); IV) T1a invasive melanoma (wide excision 1cm) and V) >= T1b invasive melanoma (wide excision 1cm, and consideration of sentinel lymph node staging or adjuvant therapy).

A wide spectrum of diagnostic terms are used in clinical practice for melanocytic lesions⁹. The MPATH-Dx system classifies some diagnostic terms on the basis of the treatment suggested by the pathologists (e.g., MELUMP, Melanocytic Lesion of Uncertain Malignant Potential might be classified as an MPATH-Dx class II, III,IV or V based on the suggested treatment indicated by the interpreting pathologist). As this is a study of suggested treatment for more clearly specified diagnostic terms, 477 interpretations receiving variable diagnostic designations such as the latter were excluded.

In the analyses, cases given a Class III diagnosis were divided into two separate sub-groups; to wit, melanoma *in situ* and all other Class III cases (e.g. severely dysplastic nevus, atypical Spitz tumor, atypical nevus, lentiginous melanocytic proliferation with severe atypia), to allow comparison of treatment suggestions for cases interpreted as melanoma *in situ* per NCCN guidelines. ¹⁸ Invasive melanoma cases categorized into MPATH-Dx class IV and V were combined because we limited our study to recommendations on local excision

procedures and did not consider additional details such as sentinel lymph node staging or adjuvant therapy.

We placed greater emphasis on treatment suggestions for melanoma *in situ* and invasive melanoma because national guidelines provide precedent for these diagnoses. Treatment suggestions for melanoma *in situ* were parsed as a 3-category ordinal variable: suggested re-excision less than 0.5cm, suggested re-excision between 0.5cm and <1cm, and suggested re-excision >=1 cm. Treatment suggestions for invasive melanoma were dichotomized as suggested re-excision less than 1cm versus suggested re-excision 1cm or greater. Multivariable modeling to examine associations between physician characteristics and treatment suggestions employed generalized estimating equations accounting for repeated measures. SAS version 9.4 (SAS Institute Inc, Cary, NC) was used to conduct all analyses.

Results:

Of the 207 pathologists who completed the baseline survey, 187 (90.3%) completed the diagnostic interpretations. The average pathologist was 51 years old (range: 33–79). Most pathologists were not affiliated with a medical center (72%), did not hold fellowship or board-certification in dermatopathology (60%), had greater than ten years of experience interpreting MSL (60%), and reported high confidence in their own abilities to assess MSL (86%). The 187 pathologists, blinded to each others' interpretations, provided a total of 8,499 interpretations used in this analysis.

The majority of treatment suggestions by these pathologists aligned with the original published MPATH-Dx suggested management for each Class. Pathologists had highest agreement between treatment suggestions for cases they diagnosed as Class I (interpreted as benign cases with 81.6% suggesting no further treatment) and Class IV/V (interpreted as invasive melanoma with 86.1% suggesting margins of 1cm). While cases diagnosed as Class II and Class III lesions exhibited greater variability in the participants' corresponding treatment suggestions, the majority of the participants' treatment suggestions were aligned with the MPATH-Dx class suggested treatment: 65.8% (Class II); 50.9% (Class III, Other); 72.8% (Class III, Melanoma in situ).

The pathologists' treatment suggestions for diagnoses of dysplastic nevi (mild, moderate or severe) and Spitz nevus (conventional or atypical) are illustrated in Figure 1. The majority of pathologists suggested no treatment for mildly dysplastic nevi (64%), <0.5cm excision for moderately dysplastic nevi (70%), and 0.5 to <1cm excision for severely dysplastic nevi (55%). There was less agreement for treatment suggestions for both conventional and atypical Spitz tumors.

Figure 2 provides images and participants' treatment suggestions for two melanoma *in situ* study cases (reference diagnosis of melanoma *in situ* defined by a panel of three highly experienced dermatopathologists; MIS diagnosis agreed upon by 17 out of 18 participants). For Case A, 29% of participating pathologists suggested a lower treatment (<0.5cm) and 18% suggested a higher treatment (1cm margin) than NCCN guidelines, showing relatively large variability in treatment suggestions. In contrast, Case B had more consistent

treatment suggestions. For Case A, the pathological changes were subtle and required examination at higher magnification to notice pagetoid scatter and the poor circumscription. Case B, however, was a more circumscribed, larger lesion with easily identified nested growth at low magnification.

Table 1 displays the variation in treatment suggestions for melanoma *in situ* and invasive melanoma by pathologist characteristics. All characteristics in Table 1 are significantly associated (p<0.01) with variation in treatment suggestions for invasive melanoma. Three characteristics (board-certification and/or fellowship-training in dermatopathology, fewer years of experience, and greater caseload of MSLs) associate with higher agreement with NCCN guidelines for melanoma *in situ*.

Multivariable analysis of the pathologist characteristics data assessed the concordance/discordance parameter by reference to NCCN guidelines (Table 2). Pathologists with a greater number of years interpreting MSL (10+ years) are significantly less likely to provide treatment suggestions concordant with NCCN guidelines for invasive melanoma, while pathologists with a high caseload are significantly more likely to provide treatment suggestions concordant with those guidelines. Pathologists with fellowship-training or board-certification in dermatopathology were significantly more likely to provide treatment suggestions consistent with the guidelines for melanoma *in situ* after adjusting for the other parameters. More years in clinical practice correlate with treatment suggestions less than NCCN guidelines for melanoma in situ, and affiliation with an academic medical center correlates with suggestions greater than those guidelines.

Pathologists' characteristics associated with treatment recommendations for cases they interpreted as moderate and severe atypia, or as conventional and atypical Spitz are shown in Tables 3 and 4, respectively. Pathologists working in academic medical centers, those with fellowship training or board certification in dermatopathology, and those with 10 percent of caseload in melanocytic skin lesions tended to be more likely to suggest no margins for moderate atypia. Pathologists who were fellowship trained or board certified in dermatopathology, and those who had less than 10 years interpreting melanocytic skin lesions were more likely to suggest lower margins (.5) for severe dysplasia. Pathologists affiliated with an academic center were more likely to suggest a smaller margin for atypical Spitz lesions.

Discussion:

This study highlights extensive variability in treatment suggestions provided by practicing U.S. pathologists as they diagnose MSLs, even while controlling for their diagnostic interpretation of the case. The greatest variability occurs with lesions that have no standardized national treatment guidelines: MPATH-Dx Class II (e.g., moderately dysplastic nevi) and Class III diagnoses other than melanoma *in situ* (such as severely dysplastic nevi, atypical Spitz nevus/tumor)^{4,11,14}. Adverse consequences resulting from treatment variability of the Class II and III cases are likely to be rare events. We observed less variation in treatment suggestions for diagnoses of melanoma *in situ* and invasive melanoma, which have NCCN treatment guidelines, and where adherence to treatment

recommendations is more consequential.¹³ The higher variability for treatment suggestions accompanying diagnoses of severely dysplastic nevi compared to mildly and moderately dysplastic nevi may reflect disagreement within the field regarding their biological significance and appropriate treatment. The lack of standardized treatment guidelines for many of these melanocytic lesions has similar implications.

Our analysis indicates that 10 or more years of experience interpreting MSLs is positively associated with providing treatment suggestions that are discordant with national guidelines, suggesting that more recent training may lead to better familiarity with the current guidelines. ¹⁹ Notably, national guidelines for treatment of invasive melanomas have changed over time. However, since 2009¹⁸ these recommendations have remained largely unchanged, although there has been discussion regarding margin widths for lentigo maligna melanoma *in situ*, especially those on the face. ¹²

Our analysis also highlights increased concordance with national guidelines for those pathologists who interpret a higher volume of melanocytic lesion cases. This relationship may relate to the increased motivation of pathologists who spend more time interpreting these lesions to be concordant with the national guidelines.

While a previous M-Path study reported variation in pathologists' treatment suggestions based on self-reported survey data, ¹ this study provides new data on variability in the treatment suggestions that accompany actual interpretations of these lesions. Our results further expand the conclusions of the previous study, revealing evidence for substantial variability in treatment suggestions across all lesions, and in particular for those lesions not having national guidelines for their treatment.

Strengths and Limitations:

The limitations to our investigations are the test setting for interpretations; there was only one glass slide for each skin biopsy case (although pathologists were asked to assume it was representative); and pathologists were unable to perform immunohistochemical staining or other diagnostic tests. In addition, pathologists were not provided detailed clinical history for the cases, and they were not able to procure a second opinion if desired. Pathologists were also given only four different options for treatment suggestions, which may have limited the ability to fully communicate their suggestions. Furthermore, we are currently refining the MPATH-Dx schema, in light of new research evidence on Class II and III categories, and we are aware there is disagreement on some of the MPATH-Dx classifications and their respective treatment recommendations^{2–5}.

Strengths of our study include the broad spectrum and high number of cases and the large number of participating pathologists from across the U.S. While other studies have found variation in diagnostic interpretations of melanocytic lesions between pathologists^{6–9,20–31}, our study is unique in that it quantifies variation in treatment suggestions. Our study also identified pathologist characteristics associated with providing treatment suggestions that are discordant with national guidelines.

Clinical and Policy Implications:

This study suggests that there may be a potential benefit from implementation of a standardized taxonomy, such as MPATH-Dx, which aims to integrate pathologists' diagnostic interpretations with corresponding treatment suggestions. It is encouraging that the majority of treatment recommendations made by these pathologists aligned with the original published MPATH-Dx suggested management for each Class. We encourage further refinement and updates on the MPATH-Dx schema, as we are currently doing in light of new research findings. Our hope is that this tool could support primary care clinicians who might be confused by pathology reports on MSL and reduce the observed variability in pathologists' evaluation of MSL and assist in aligning treatment with national guidelines.

Furthermore, our results suggest that clinicans should bear in mind the significant variability present in treatment recommendations, especially for diagnoses with no standardized national guidelines. Clinical practice guidelines are needed, and are now being suggested through collaborations in dermatology and dermatopathology.⁹

Finally, this study suggests the need for a more robust continuing education system to inform pathologists about developments in the field. The positive association between fewer years of experience interpreting melanocytic lesions and concordance with national guidelines indicates that pathologists who recently trained are more likely to be aware of current treatment guidelines. Further developments in continuing medical education could improve standardization of patient care and conformity with evidence-based standards where these exist.

Conclusion:

Our study identifies substantial variability in treatment suggestions provided by pathologists when interpreting MSLs. The variability is less for lesions for which there are national treatment guidelines and when interpreted by pathologists with fellowship training or board certification in dermatopathology, suggesting the potential for educational opportunities and national guidelines to improve the concordance of treatment.

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Citations:

1. Lee KC, Peacock S, Weinstock MA, et al. Variation among pathologists' treatment suggestions for melanocytic lesions: A survey of pathologists. J Am Acad Dermatol. 2017;76(1):121–128. [PubMed: 27692732]

 Hocker TL, Alikhan A, Comfere NI, Peters MS. Favorable long-term outcomes in patients with histologically dysplastic nevi that approach a specimen border. J Am Acad Dermatol. 2013;68(4):545–551. [PubMed: 23127472]

- Goodson AG, Florell SR, Boucher KM, Grossman D. Low rates of clinical recurrence after biopsy of benign to moderately dysplastic melanocytic nevi. J Am Acad Dermatol. 2010;62(4):591–596.
 [PubMed: 20018406]
- Fleming NH, Egbert BM, Kim J, Swetter SM. Reexamining the Threshold for Reexcision of Histologically Transected Dysplastic Nevi. JAMA Dermatol. 2016;152(12):1327–1334. [PubMed: 27542070]
- 5. Engeln K, Peters K, Ho J, et al. Dysplastic nevi with severe atypia: Long-term outcomes in patients with and without re-excision. J Am Acad Dermatol. 2017;76(2):244–249. [PubMed: 27838051]
- Duncan LM, Berwick M, Bruijn JA, Byers HR, Mihm MC, Barnhill RL. Histopathologic recognition and grading of dysplastic melanocytic nevi: an interobserver agreement study. J Invest Dermatol. 1993;100(3):318S–321S. [PubMed: 8440913]
- Duray PH, DerSimonian R, Barnhill R, et al. An analysis of interobserver recognition of the histopathologic features of dysplastic nevi from a mixed group of nevomelanocytic lesions. J Am Acad Dermatol. 1992;27(5 Pt 1):741–749. [PubMed: 1430397]
- 8. 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(4):1218–1223. [PubMed: 8648377]
- 9. Elmore JG, Barnhill RL, Elder DE, et al. Pathologists' diagnosis of invasive melanoma and melanocytic proliferations: observer accuracy and reproducibility study. BMJ. 2017;357:1–11.
- 10. Lott JP, Elmore JG, Zhao GA, et al. 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. Journal of the American Academy of Dermatology. 2016;75(2):356–363. [PubMed: 27189823]
- Kim CC, Swetter SM, Curiel-Lewandrowski C, et al. Addressing the knowledge gap in clinical recommendations for management and complete excision of clinically atypical nevi/dysplastic nevi: Pigmented Lesion Subcommittee consensus statement. JAMA Dermatol. 2015;151(2):212– 218. [PubMed: 25409291]
- 12. Bichakjian CK, Halpern AC, Johnson TM, et al. Guidelines of care for the management of primary cutaneous melanoma. American Academy of Dermatology. J Am Acad Dermatol. 2011;65(5):1032–1047. [PubMed: 21868127]
- Coit DG, Andtbacka R, Anker CJ, et al. Melanoma, version 2.2013: featured updates to the NCCN guidelines. Journal of the National Comprehensive Cancer Network. 2013;11(4):395–407.
 [PubMed: 23584343]
- 14. Piepkorn MW, Barnhill RL, Elder DE, et al. The MPATH-Dx reporting schema for melanocytic proliferations and melanoma. J Am Acad Dermatol. 2014;70(1):131–141. [PubMed: 24176521]
- 15. Onega T, Reisch L, Frederick P, et al. Use of Digital Whole Slide Imaging in Dermatopathology. J Digit Imaging. 2016;29(2):243–253. [PubMed: 26546178]
- Carney PA, Reisch LM, Piepkorn MW, et al. Achieving consensus for the histopathologic diagnosis of melanocytic lesions: use of the modified Delphi method. J Cutan Pathol. 2016;43(10):830–837. [PubMed: 27247109]
- 17. Dalkey NC BB, Cochran N. . The Delphi Method, III. Use of Self Ratings to Improve Group Estimates. Rand Corp. 1969.
- 18. Johnson TM. Guidelines of care for the management of primary cutaneous melanoma. J Am Acad Dermatol. 2013;69(6):1049–1050. [PubMed: 24238159]
- Choudhry NK, Fletcher RH, Soumerai SB. Is an Older, More Experienced Doctor a Better Doctor? Annals of Internal Medicine. 2005;142:260–273. [PubMed: 15710959]
- 20. Colloby PS, West KP, Fletcher A. Observer variation in the measurement of Breslow depth and Clark's level in thin cutaneous malignant melanoma. The Journal of pathology. 1991;163(3):245–250. [PubMed: 2013827]

21. Heenan PJ, Matz LR, Blackwell JB, et al. Inter-observer variation between pathologists in the classification of cutaneous malignant melanoma in western Australia. Histopathology. 1984;8(5):717–729. [PubMed: 6519646]

- 22. Boiko PE, Piepkorn MW. Reliability of skin biopsy pathology. J Am Board Fam Pract. 1994;7(5):371–374. [PubMed: 7810353]
- 23. Barnhill RL, Argenyi ZB, From L, et al. Atypical Spitz nevi/tumors: lack of consensus for diagnosis, discrimination from melanoma, and prediction of outcome. Hum Pathol. 1999;30(5):513–520. [PubMed: 10333219]
- 24. Cook MG, Clarke TJ, Humphreys S, et al. The evaluation of diagnostic and prognostic criteria and the terminology of thin cutaneous malignant melanoma by the CRC Melanoma Pathology Panel. Histopathology. 1996;28(6):497–512. [PubMed: 8803593]
- 25. Krieger N, Hiatt RA, Sagebiel RW, Clark WH Jr., Mihm MC Jr. Inter-observer variability among pathologists' evaluation of malignant melanoma: effects upon an analytic study. Journal of clinical epidemiology. 1994;47(8):897–902. [PubMed: 7730893]
- Piepkorn MW, Barnhill RL, Cannon-Albright LA, et al. A multiobserver, population-based analysis of histologic dysplasia in melanocytic nevi. J Am Acad Dermatol. 1994;30(5 Pt 1):707– 714. [PubMed: 8176008]
- Spatz A, Cook MG, Elder DE, Piepkorn M, Ruiter DJ, Barnhill RL. Interobserver reproducibility of ulceration assessment in primary cutaneous melanomas. European Journal of Cancer. 2003;39(13):1861–1865. [PubMed: 12932663]
- Meyer LJ, Piepkorn M, Goldgar DE, et al. Interobserver concordance in discriminating clinical atypia of melanocytic nevi, and correlations with histologic atypia. J Am Acad Dermatol. 1996;34(4):618–625. [PubMed: 8601651]
- 29. Braun RP, Gutkowicz-Krusin D, Rabinovitz H, et al. Agreement of dermatopathologists in the evaluation of clinically difficult melanocytic lesions: how golden is the 'gold standard'? Dermatology (Basel, Switzerland). 2012;224(1):51–58.
- 30. Gerami P, Busam K, Cochran A, et al. Histomorphologic assessment and interobserver diagnostic reproducibility of atypical spitzoid melanocytic neoplasms with long-term follow-up. Am J Surg Pathol. 2014;38(7):934–940. [PubMed: 24618612]
- 31. Carli P, De Giorgi V, Naldi L, Dosi G. Reliability and inter-observer agreement of dermoscopic diagnosis of melanoma and melanocytic naevi. Dermoscopy Panel. European journal of cancer prevention: the official journal of the European Cancer Prevention Organisation (ECP). 1998;7(5):397–402. [PubMed: 9884886]

Capsule Summary—

- National treatment guidelines exist for managing in situ and invasive melanoma, but not for other melanocytic lesions.
- Pathologists' treatment suggestions were found to vary significantly for melanocytic lesions, with lower variability for lesion types with national guidelines and when interpreted by pathologists with fellowship training or board certification in dermatopathology.

■ No tx ■ Excise <0.5cm ■ Excise 0.5 to <1cm

■ Excise >=1cm

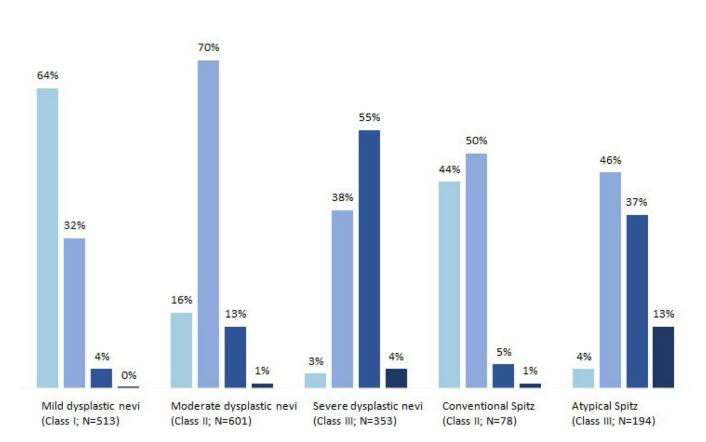


Figure 1: Pathologist treatment suggestions for cases diagnosed as dysplastic nevi and Spitz tumors. N's represent total interpretations.

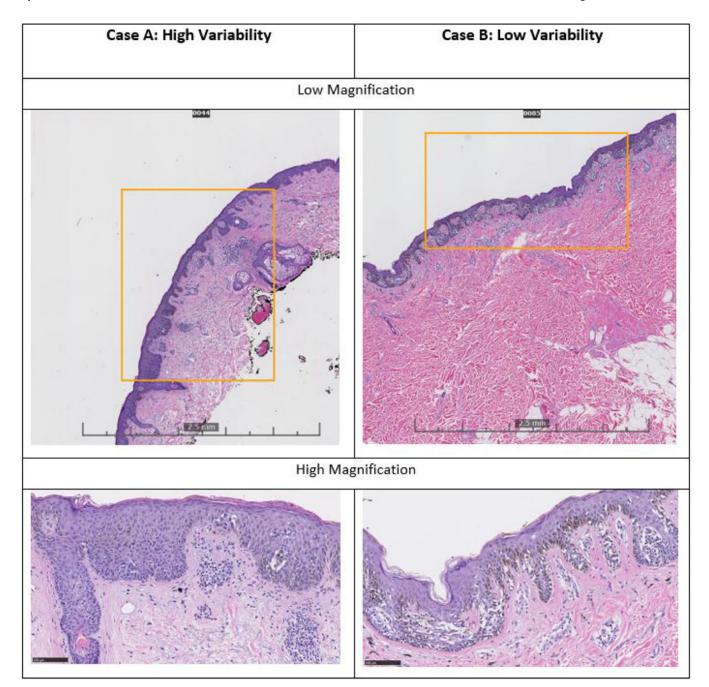


Figure 2: Two Examples of Melanoma *In Situ* Glass Slide Biopsies evoking High and Low Variability in Treatment Suggestions by the Study Participants.

Both cases were diagnosed as melanoma *in situ* by consensus panel and 17 out of 18 pathologists. For Case A, 29% of participating pathologists suggested a lower treatment (<0.5cm) and 18% suggested a higher treatment (1cm margin) than NCCN guidelines, showing relatively large variability in treatment suggestions. Case A is relatively small (~4mm) and does not have an obviously atypical melanocytic proliferation at low magnification. Higher magnification allows the identification of a poorly circumscribed intraepidermal melanocytic proliferation. In contrast, Case B had a smaller proportion of

pathologists (12%) rendering a treatment suggestion lower than NCCN guidelines, and no pathologists suggested a higher treatment than NCCN guidelines. Case B is a larger lesion (\sim 8mm) that more readily is identifiable as an atypical lentiginous and nested proliferation with pagetoid scatter.

Table 1:Distribution of Treatment Suggestions for Melanoma In Situ and Invasive Melanoma Case Diagnoses by Pathologist Characteristics

		Melanoma i	<i>n situ</i> treatme	nt suggestion	IM treatmen	nt suggestion ^a
		excision	excision	Excision	excision	Excision
		< 0.5cm	0.5-<1cm ^b	1cm	< 1cm	1cm ^b
	No. case readings	111	665	137	438	2711
Affiliation with	academic medical ce	nter				
No	2833	80 (13%)	449 (72%)	96 (15%)	339 (15%)	1869 (85%)
Yes	1229	31 (11 %)	216 (75%)	41 (14%)	99 (11 %)	842 (89%)
Fellowship or b	oard certified in derr	natopatholog	y			
No	2308	89 (17%)	330 (62%)	114 (21%)	328 (18%)	1447 (82%)
Yes	1754	22 (6%)	335 (88%)	23 (6%)	110 (8%)	1264 (92%)
Years interpret	ing melanocytic skin	lesions				
< 10 years	1583	19 (6%)	273 (80%)	50 (15%)	56 (5%)	1185 (95%)
10 years +	2479	92 (16%)	392 (69%)	87 (15%)	382 (20%)	1526 (80%)
Percent of casel	oad represented by n	nelanocytic sl	cin lesions			
< 10 percent	1581	62 (17%)	219 (61%)	76 (21 %)	250 (20%)	974 (80%)
10 percent	2481	49 (9%)	446 (80%)	61 (11 %)	188 (10%)	1737 (90%)

a. IM=invasive melanoma

b-NCCN guidelines for surgical margins for primary melanoma (exceptions to these guidelines exist for both melanoma in situ and invasive melanoma).

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Table 2:

Multivariable Analysis Examining Pathologist Characteristics Associated with Treatment Suggestions as Referenced to National Comprehensive Cancer Network (NCCN)

	Likelihood of Suggesting with NCCN Guidelines	Likelihood of Suggesting Treatment Concordant with NCCN Guidelines for Invasive Melanoma $^{\it d}$	g Treatment Concordant for Invasive Melanoma	Likelihood o NCCN G	Likelihood of Suggesting Lesser Treatment than NCCN Guidelines for Melanoma $In \ Situ^a$	Treatment than toma In Situ ^a	Likelihood o	Likelihood of Suggesting Greater Treatment than NCCN Guidelines for Melanoma $\ln Situ^a$	r Treatment than oma <i>In Situ^a</i>
Characteristic	Odds Ratio Lower Confid	Lower Confidence	Upper Confidence	Odds Ratio Lower Confid	Lower Confidence	Upper Confidence	Odds Ratio	Lower Confidence	Upper Confidence
Affiliated with academic medical center	1.27	96.0	1.7	1.21	9.76	1.93	1.61 *	1.06	2.44
Fellowship or board certified in dermatopathology	1.24	26:0	1.58	0.33 *	0.18	0.63	0.17 *	0.09	0.32
Years interpreting melanocytic skin lesions (10+ years)	0.21 *	0.16	0.29	2.35 *	1.30	4.24	0.75	0.48	1.16
Percent of caseload represented by melanocytic skin leions (10%+ of caseload)	1.70 *	1.39	2.08	0.76	0.48	1.20	0.84	0.56	1.27

 $^{^{}a}$ Odds ratios are adjusted odds ratios (adjusted for the other variables in the multivariable model).

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^{*} Statistically significant at p 0.05

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Table 3:

Suggested Treatment Recommendations for Cases Interpreted as Moderate or Severe Dysplasia by Pathologists' Characteristics.

			Mode	Moderate dysplasia	ia			Se	Severe dysplasia	а	
		None	ιċ	.5-1	1	-	None	3:	.5-1	1	-
Z	No. case readings	66	420	79	8	F-value	10	134	193	16	P-value
Affiliation with a	Affiliation with academic medical center	center									
No	6432	59 (14%)	59 (14%) 316 (72%) 60 (14%) 1 (0%)	60 (14%)	1 (0%)	<0.01	6 (2%)		99 (40%) 130 (53%) 12 (5%)	12 (5%)	0.51
Yes	2544	40 (24%)	40 (24%) 104 (63%) 19 (12%)	19 (12%)	2 (1 %)		4 (4%)	35 (33%)	63 (59%)	4 (4%)	
Fellowship or bo	Fellowship or board certified in dermatopathology	ermatopatho	logy								
No	5424	35 (10%)	35 (10%) 235 (69%)	70 (20%)	3 (1 %)	<0.001	6 (3%)	67 (35%)	107 (55%)	14 (7%)	0.03
Yes	3552	64 (25%)	64 (25%) 185 (72%)	9 (3%)	(%0)0		4 (3%)	67 (42%)	86 (54%)	2 (1 %)	
Years interpretir	Years interpreting melanocytic skin lesions	in lesions									
< 10 years	3552	39 (16%)	39 (16%) 182 (73%)	27 (11%)	2 (1 %)	0.34	2 (1 %)	44 (28%)	100 (65%)	(%9)6	<0.01
10 years +	5424	60 (17%)	60 (17%) 238 (68%)	52 (15%)	1 (0%)		8 (4%)	90 (45%)	93 (47%)	7 (4%)	
Percent of caselo	Percent of caseload is melanocytic skin lesions	skin lesions									
< 10 percent	3792	27 (11%)	27 (11%) 173 (72%)	40 (17%)	0 (0%)	<0.01	4 (3%)	52 (36%)	83 (57%)	6 (4%)	0.87
10 percent	5184	72 (20%)	72 (20%) 247 (68%) 39 (11%) 3 (1 %)	39 (11%)	3 (1 %)		6 (3%)		82 (39%) 110 (53%)	10 (5%)	

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Table 4.

Suggested Treatment Recommendations for Cases Interpreted as Conventional Spitz or Atypical Spitz by Pathologists' Characteristics.

			Conve	Conventional Spitz	oitz			Ą	Atypical Spitz	z	
	No. case readings	None 34	39	5-1	1 1	P-value	None 8	s. 90	.5-1	1 25	P-value
Affiliation wit	Affiliation with academic medical center	center									
No	6432	23 (43%)	23 (43%) 28 (53%) 2 (4%) 0 (0%)	2 (4%)	(%0)0	0.35	3 (2%)	65 (45%)	65 (45%) 59 (40%) 19 (13%)	19 (13%)	0.04
Yes	2544	11 (44%)	11 (44%) 11 (44%) 2 (8%)	2 (8%)	1 (4%)		5 (10%)		25 (52%) 12 (25%)	6 (13%)	
Fellowship or	Fellowship or board certified in dermatopathology	ermatopatho	logy								
No	5424	19 (42%)	19 (42%) 22 (49%) 3 (7%) 1 (2%)	3 (7%)	1 (2%)	0.89	4 (4%)		47 (46%) 38 (37%) 14 (14%)	14 (14%)	0.98
Yes	3552	15 (45%)	15 (45%) 17 (52%) 1 (3%)	1 (3%)	(%0)0		4 (4%)	43 (47%)	33 (36%)	11 (12%)	
Years interpre	Years interpreting melanocytic skin lesions	in lesions									
< 10 Years	3552	8 (31%)	17 (65%) 1 (4%) 0 (0%)	1 (4%)	(%0)0	0.24	2 (2%)		41 (48%) 32 (37%) 11 (13%)	11 (13%)	0.78
10 years +	5424	26 (50%)	26 (50%) 22 (42%) 3 (6%)	3 (6%)	1 (2%)		(%9)9	49 (45%)	39 (36%)	14 (13%)	
Percent of cas	Percent of caseload is melanocytic skin lesions	skin lesions	7-								
< 10 percent	3792	18 (50%)	18 (50%) 15 (42%) 2 (6%) 1 (3%)	2 (6%)	1 (3%)	0.34	2 (3%)		32 (45%) 27 (38%) 10 (14%)	10 (14%)	6.0
10 percent	5184	16 (38%)	24 (57%) 2 (5%)	2 (5%)	(%0)0		(%5) 9	58 (47%)	44 (36%)	44 (36%) 15 (12%)	