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The MPATH-Dx reporting schema for melanocytic proliferations and melanoma

Michael W. Piepkorn, MD, PhD^{a,b,c}, Raymond L. Barnhill, MD^d, David E. Elder, MBChB, FRCPA^e, Stevan R. Knezevich, MD, PhD^f, Patricia A. Carney, PhD^g, Lisa M. Reisch, PhD^b, and Joann G. Elmore, MD^b

^aDivision of Dermatology, University of Washington School of Medicine, Seattle

^bDepartment of Medicine, University of Washington School of Medicine, Seattle

^cDermatopathology Northwest, Bellevue

^dDepartment of Pathology and Laboratory Medicine, University of California at Los Angeles

^eDepartment of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania

^fVeterans Affairs Medical Center, Seattle

^gDepartment of Family Medicine, Oregon Health Sciences University.

Abstract

Background—The histologic diagnosis of melanoma and nevi can be subject to discordance and errors, potentially leading to inappropriate treatment and harm. Diagnostic terminology is not standardized, creating confusion for providers and patients and challenges for investigators.

Objective—We sought to describe the development of a pathology reporting form for more precise research on melanoma and a diagnostic-treatment mapping tool for improved patient care and consistency in treatment.

Methods—Three dermatopathologists independently reviewed melanocytic lesions randomly selected from a dermatopathology database. Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis (MPATH-Dx) reporting schema evolved from iterative case review and form revision.

Results—Differences in diagnostic thresholds, interpretation, and nomenclature contributed to development of the MPATH-Dx histology reporting form, which groups lesions by similarities in histogenesis and degrees of atypia. Because preliminary results indicate greater agreement regarding suggested treatments than for specific diagnoses, the diverse terminologies of the MPATH-Dx histology reporting form were stratified by commonalities of treatments in the MPATH-Dx diagnostic-treatment mapping scheme.

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Reprint requests: Michael W. Piepkorn, MD, PhD, Division of Dermatology, Box 356524, University of Washington, Seattle, WA 98195. mpiepkor@uw.edu..

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Limitations—Without transformative advances in diagnostic paradigms, the interpretation of melanocytic lesions frequently remains subjective.

Conclusions—The MPATH-Dx diagnostic-treatment mapping scheme could diminish confusion for those receiving reports by categorizing diverse nomenclature into a hierarchy stratified by suggested management interventions.

Keywords

diagnosis; diagnostic errors; discordance; dysplasia; melanoma; nevi; observer variability

Discordance exists in the histologic diagnosis of melanoma, resulting in diagnostic uncertainty and errors and confounding both prognostication and decision making for appropriate treatment.¹⁻¹⁷ This occurs because of complexity in the histologic continuum from benign to unequivocally malignant melanocytic lesions.^{16,17} The complexity is less problematic, with high diagnostic concordance, at the opposing ends of the spectrum: eg, a stereotypic nevus at one end and a large bulky melanoma at the other, engendering but little variability in diagnosis; however, substantial difficulties emerge in the spectrum between the extremes, ie, in the gray zone between benign and malignant.^{6,16,17} Further confounding the situation is that standardized nomenclature within this continuum does not exist, and terminologies vary within the United States and elsewhere.¹⁴

The current lack of standardization is not limited to melanocytic pathology, but affects other clinical fields. To improve precision in breast imaging, Breast Imaging-Reporting and Data System (BI-RADS) emerged by US Food and Drug Administration mandate and under the auspices of the American College of Radiology, which standardized results of mammogram interpretations along a 5-point continuum.¹⁸ The principal objective is to minimize ambiguity to the clinician and patient regarding the necessity and type of therapeutic management.

The purpose of this article is to report on the development of a similar system for melanocytic proliferations. We describe here the Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis (MPATH-Dx) schema that comprise a histology reporting form and a diagnostic-treatment mapping scheme.

METHODS

The institutional review board of the University of Washington approved this project. Three experienced melanocytic lesion pathologists comprised a reference panel, whose goal was to develop and iteratively test a histology reporting form for pathologists to use during slide review in the upcoming main study, and a treatment mapping scheme for reviewing and recording diagnoses of melanocytic lesions.

Selection and preparation of histologic cases

We developed by computer randomization 5 test sets collectively comprising 240 test cases of melanocytic lesions. The cases were culled from accessions of skin specimens at Dermatopathology Northwest, Bellevue, WA, between January 1, 2010, and December 31,

2011. We excluded cases that were consultations, re-excisions from earlier biopsies, unknown anatomic site, unknown gender, and patient age younger than 20 years. We included only 1 randomly selected biopsy specimen per patient identifier. Cases were randomly selected using a stratified approach with oversampling from younger patients and patients with atypical lesions, melanoma in situ, and melanoma (Appendix). New slides were prepared by conventional histologic methods for each case. Serial sections, 5- μ m thick, were prepared with only 1 or 2 sections per slide and stained with hematoxylin-eosin.

Independent review of cases

The panel performed blinded independent assessments on each deidentified patient case. From 1 microscopic slide per case, the members provided assessments of their primary diagnosis, recommended treatment, presence of solar elastosis, and special considerations, in addition to their confidence in diagnosis, level of difficulty of the case, and desire for a second opinion.

Consensus development meetings

The panel met on 4 separate occasions to review 279 cases at a multiheaded microscope. We used a modified Delphi approach¹⁹ to establish the final consensus reference diagnosis for each slide. This involved compiling the independent reviews for each case, facilitating discussion of areas where disagreement existed, and rereviewing the slides at a multiheaded microscope. The facilitated discussion continued until a final consensus diagnosis was reached. Research team members entered the diagnoses and treatments for each case into the evolving MPATH-Dx forms. The meetings were audiotaped and transcribed for quality control.

RESULTS

Development of the MPATH-Dx histology reporting form

For the goals of the upcoming main project, we developed a histology reporting form that would standardize the diagnoses for future participating pathologists. The development of the form was iterative and occurred during a 1-year period (Fig 1). It involved consensus building derived from concepts integrated into the MPATH-Dx histology reporting form. It became clear early on that each panel member uses a personalized set of nomenclatures in their interpretations; it was therefore decided to make diagnostic categories as inclusive as possible. The subsequent grouping of diagnostic categories within a treatment hierarchy (below) then imposed a semblance of order from the chaos of nomenclature.

The histology reporting form stratifies diagnostic and conceptual entities considered to be related either histogenetically, by type and degree of atypia, or by stage of tumor progression; collectively, the hierarchy covers the spectrum from unequivocally benign to conclusively malignant. Both the American Joint Committee on Cancer (AJCC) Staging Manual (7th edition)²⁰ and the World Health Organization classification of melanocytic tumors²¹ were consulted during form development. We included a wide range of diagnostic terms that might be used by pathologists from different backgrounds, approximating the

situation in the current universe of melanocytic lesion diagnoses. The final form has 7 diagnostic categories.

In addition to the final diagnostic categories, a provisional category declares incomplete examination because of limitations of the sample or to technical constraints of processing; yet other categories solicit confidence in the diagnosis for each case, treatment considerations, desire for second opinions, indications for molecular testing, degree of difficulty, and miscellany.

Because preliminary indications during the consensus meetings were that there is less variability in achieving consensus as to appropriate treatment interventions for the lesions than with their definitive diagnostic terminologies, we considered an approach based on the BI-RADS precedent, namely a diagnostic-treatment mapping scheme.

Development of the MPATH-Dx diagnostic-treatment mapping scheme

Five clinically relevant hierarchical groupings emerged that correspond to specific treatment categories (Fig 2). The diagnostic-treatment mapping scheme and the histology reporting form developed concurrently. The mapping scheme has 1 provisional category and 5 final groupings, which progressively escalate in level of suggested treatment (Fig 2). In provisional category 0, the limitations of the evaluation and advisability of short-term follow-up are addressed. Definitive categories 1 to 5 range from no further treatment to high-level intervention, with the categories correlating with incremental levels of intervention.

Some of the nomenclature in infrequent use has the specific intent of explicitly disclosing in pathology reports the uncertainty in predicting the biological potential of unusual melanocytic lesions. We incorporated examples of this intentionally ambiguous and provisional language, as follows:

- Atypical intraepidermal melanocytic proliferation: disordered lentiginous and/or junctional nested to focally pagetoid pattern of proliferation, in association with nuclear atypia, but without sufficiently advanced criteria for conclusive diagnosis of melanoma in situ.
- Pagetoid intraepidermal melanocytic proliferation: as above, but with accentuated prominence of pagetoid melanocytosis.
- Superficial atypical melanocytic proliferation of uncertain significance: as per atypical intraepidermal melanocytic proliferation, with the additional finding of melanocytic cells in the papillary dermis having cytologic abnormalities, but to a degree insufficient for conclusive diagnosis of invasive melanoma; implies some potential for disease progression in the event of incomplete re-excision.
- Melanocytic tumor of uncertain malignant potential: a melanocytic tumor with more substantial dermal involvement, with or without an intraepidermal component, in which the cytologic characteristics are unusual but not conclusively those of the common form(s) of melanoma; implies some, but presently unquantifiable, risk for metastatic competence after complete excision.

Consensus was not always achieved in assigning individual lesions classified under the above terms to unique treatment categories in the mapping scheme; however, their use may be in providing the pathologist with the flexibility to determine which MPATH-Dx mapping category is deemed appropriate for prognosis and management purposes based on the perceived level of risk.

DISCUSSION

Our approach of iterative interpretation, review, and rereview of cases while revising the MPATH-Dx forms to ensure accurate capture of histologic criteria for the diagnosis and treatment of melanocytic lesions yielded a histology reporting form and a diagnostic-treatment mapping scheme. The MPATHDx histology reporting form may prove useful in population-based research on melanocytic lesions because it categorizes for researchers outside the field of dermatopathology a diversity of arcane nomenclature into categories based on shared histogenesis, type and degree of atypia, or putative stage of tumor progression. The MPATH-Dx diagnostic-treatment mapping scheme could prove helpful in clinical practice by reducing (but clearly not eliminating) diagnostic variation and confusion for clinicians and patients, in that pathology reports incorporating the assignment of any given diagnosis to a specific MPATH-Dx category will convey the level of perceived risk and attendant level of suggested treatment intervention.

The screening of the general public for cancers has, over time, created similar issues not only in melanocytic pathology but also across other organ systems, collectively constraining the use of existing screening strategies. There are high rates of noncancerous findings and concerns regarding cancer overdiagnosis (false positives), evoking important public health debates related to misdirected expenditures and other unintended consequences.²²⁻²⁴

Screening for melanoma as promulgated by organizations within dermatology has also highlighted limitations in the reliability of the histologic diagnosis of melanocytic lesions.¹⁻¹⁷ Although the proximate bases for the current limitations in diagnostic reliability have not been fully elucidated, the nature of the diagnostic process is criteria based and requires observers to recognize the presence or absence of histologic findings, alone or in combination. The logic of the process is inductive, and the end result is a diagnosis that represents a hypothesis about the nature of disease as inferred from observation.¹⁶ Primary factors contributing to diagnostic uncertainty are the soft nature of some criteria, ie, limited sensitivity, specificity, and predictive values, and the frequent subjectivity in recognizing the presence or absence of subtle findings.¹⁶ Secondary factors include sampling limitations in partial biopsy specimens and observer concerns regarding uncontrollable effects, among which are the sometimes fickle nature of melanocytic neoplasms, patient safety, and legal liability.

Although there are subjective elements to melanocytic tumor diagnosis, general agreement exists for the diagnosis of most nevi and melanoma from criteria that are by and large reproducible and are managed without controversy. Nevertheless, previous literature¹⁻¹⁷ and our current study suggest a significant prevalence of histologically ambiguous lesions that are difficult to accurately classify as high or low risk. Whereas the referenced literature well

documents interobserver discordances in diagnosis and variability in the use of nomenclatures, our experience in the development of the reporting and mapping schema is that diagnostic discordance is greater than is generally acknowledged, even among pathologists experienced in melanocytic pathology. The MPATH-Dx schema described in this report are intended to help quantify and further characterize these subjective cases.

In the case of breast cancer screening with mammography, the BI-RADS lexicon¹⁸ had the objective of standardizing reporting terms and formats that previously were inconsistent across the field. Consistency in assessment categories, it was hoped, would help the clinicians and patients alike in understanding the appropriate dispositions of results from imaging. In fact, these efforts have clearly facilitated research, improved patient care, and reduced adverse medicolegal events²⁵ (see also: breastscreening.cancer.gov/). BI-RADS specifies a category 0, where assessment and information are incomplete, and 6 final categories stratified by the hierarchical degree of abnormality and the corresponding level of intervention. These are: category 1, negative, no abnormalities; category 2, benign findings, no evidence for malignancy; category 3, “probably” benign findings, short-term follow-up recommended, less than 2% chance of cancer; category 4, suspicious abnormality, not classic for cancer, but wide range of probability for cancer exceeding 2%; category 5, highly suggestive of cancer, probability more than 95%, appropriate action should be taken; and category 6, proven malignancy, appropriate action should be taken.

The development of an analogous adjunctive scheme in the field of pathology of melanocytic lesions, as a supplement to conventional reporting, will be helpful in modulating the current ambiguity in diagnosis and variability in nomenclature among pathologists and more specifically in providing the patients with a sense of what the report means in pragmatic terms relating to prognosis and to management. Toward this end, we offer the MPATH-Dx schema as a starting point for discussion in the field of melanocytic lesion pathology (Figs 1 and 2). In analogy with BI-RADS, the diagnostic-treatment mapping tool has a provisional category 0 (repeated diagnostic intervention recommended because of limitations in sampling or to significant technical constraints) and 5 clinical outcome categories that correlate with no recommended intervention as a result of no apparent risk for continued local proliferation (MPATH-Dx category 1) and with MPATH-Dx categories 2 through 5 specifying an increasing degree of suggested treatment interventions. The implication of category 2 is that the probability of progressive disease is deemed unlikely but that if lesional cells are left in place there is risk (albeit low level risk) for continued local proliferation, with potentially adverse consequences in some cases. With category 3, the likelihood of local tumor progression is considered higher and need for intervention greater, although reliable quantitative data for actual risk associated with various diagnoses do not presently exist. Although evidence-based treatment recommendations also do not exist for the categories 2 and 3, and opinions in the professional community differ, we offer the suggestions in the diagnostic-treatment mapping scheme as a basis for dialogue. Categories 4 and 5 accommodate lesions classified by AJCC²⁰ as microstages T1a and greater than or equal to T1b, respectively, wherein there is substantial risk for locoregional tumor progression/metastasis and even greater risk for regional and distant metastasis, respectively, and wherein there exists consensus regarding standard therapy.

To illustrate the potential use of the mapping scheme, consider the hypothetical diagnosis of “atypical nevus of special anatomical site with moderate melanocytic dysplasia.” That verbiage would clearly be opaque to the patient and likely the clinician as well; however, the insertion of a notation in the report mapping the lesion to MPATHDx category 2 would alert the parties that perceived risk from residual disease after biopsy would confer some, but most probably low, likelihood of persistent local proliferation, which in some cases could ultimately result in adverse consequences; accordingly, consideration of narrow but complete re-excision could be justified to eliminate low probability risk, although follow-up monitoring could be a reasonable alternative.

Substantial health care resources are directed to the screening of populations considered to be at increased risk of melanoma. Ambiguities in diagnostic reports are common, and there is a prevalent tendency to electively treat ambiguous lesions. How much of this effort is actually necessary is presently unclear.²²⁻²⁴ Harm to patients can result not only from undertreatment but also from overtreatment of ambiguous disease in the forms of false fear of cancer, of morbidity from unnecessary treatment, and of misdirection of health care resources. These issues, which result not only from intrinsic limitations of the diagnostic processes but also as a response to medicolegal pressures and patient safety concerns, present no immediate pathway for resolution. The MPATH-Dx diagnostic-treatment mapping scheme may serve as an aid in assuaging (albeit not eliminating) uncertainty and ambiguity in melanocytic lesion reporting until such time as transformative shifts occur in the diagnostic paradigms.

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APPENDIX

Description of the data pull of potential cases for the MPATH-Dx study

To fill the cells in the final Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis (MPATH-Dx) study slide set, we queried the Dermatopathology Northwest database (Bellevue, WA) with the inclusion and exclusion criteria specified under the “Methods” section and with specific modifications in search terms, which were: the use of “dysplas” to retrieve “dysplasia” and “dysplastic”; “ephil” to retrieve “ephelid” and “ephelis”; “nev” to retrieve “nevus” and “nevi”; “atypi” to capture “atypical” and “atypia”; and “in situ” to include “in situ” and “in-situ.” The following were the categorical groupings of the search terms:

Category 1: nevus and mild, melanocytic proliferation, congenital, nev, solar lentigo, lentigo simplex, ephil.

Category 2: deep and penetrating, nev and moderate, atyp and melanocytic proliferation and mild, dyplas and melanocytic proliferation and mild, blue and cellular, pigmented and spindle cell, Spitz.

Category 3: melanoma and in situ, lentigo and maligna, atyp and melanocytic proliferation and severe, dyspl and melanocytic proliferation and severe, atyp and melanocytic proliferation and moderate, dyspl and melanocytic proliferation and moderate, pigmented spindle cell and atypi, Spitz and atypi, Spitz and dysplas, atypi and melanocytic tumor, dysplas and melanocytic tumor.

Category 4: melanoma and not in situ.

Category 5: melanoma and not in situ and 1 mitotic figures or 1 mm.

Abbreviations used

AJCC	American Joint Committee on Cancer
BI-RADS	Breast Imaging-Reporting and Data System
MPATH-Dx	Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis

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CAPSULE SUMMARY

- The histologic diagnosis of melanocytic lesions is not standardized and can be prone to discordance and errors, potentially leading to inappropriate treatment and harm.
- The Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis (MPATH-Dx) diagnostic-treatment mapping scheme categorizes diverse nomenclature into a hierarchy of management interventions.
- The mapping tool could diminish ambiguity in pathology reports by standardizing management options.

Ia. Histologic Assessment: Diagnoses (check the single best diagnosis)☐ No diagnostic alteration☐ Incomplete examination due to sampling or technical limitations☐ Lentigo related☐ Lentigo simplex☐ Solar lentigo☐ Ephelis☐ Nevus and related☐ Common nevus☐ Junctional ☐ Compound ☐ Intradermal ☐ Combined ☐ Congenital pattern☐ Lentiginous nevus (junctional or compound)☐ Spitz nevus conventional (junctional, compound, or intradermal)☐ Blue nevus and related lesions:☐ Common ☐ Cellular ☐ Epithelioid ☐ Ito/Ota/Mongolian spot☐ Congenital melanocytic nevus (junctional, compound, or intradermal)☐ Deep penetrating nevus/ plexiform spindle cell nevus☐ Pigmented spindle cell nevus (junctional or compound)☐ Halo nevus☐ Nevus of special anatomic site: acral, genital, flexural, milkline and breast, scalp☐ Atypia☐ Dysplastic nevus (nevus with architectural disorder and cytological atypia; Clark's nevus, junctional or compound) ☐ Mild ☐ Moderate ☐ Severe☐ Lentiginous melanocytic proliferation of sun-damaged or non-sun-damaged skin with atypia
☐ Mild ☐ Moderate ☐ Severe☐ Proliferative nodules in congenital melanocytic nevi☐ Minimal or no atypia or mitotic activity ☐ Moderate/severe atypia and/or mitotic activity☐ Persistent (recurrent) nevus☐ Atypical nevus NOS, including atypical nevus of special anatomic site (e.g. acral, genital,

flexural, milkline and breast, scalp, etc.)

☐ Mild ☐ Moderate ☐ Severe☐ **Atypical spitzoid lesion**

- ☐ Atypical/dysplastic Spitz lesion (junctional, compound, or dermal)
- ☐ Atypical pigmented spindle cell lesion (junctional or compound)

☐ **Melanocytic lesion of uncertain malignant potential (cannot decide whether the lesion is clearly benign or malignant)**

- ☐ Atypical melanocytic neoplasm, junctional
- ☐ Atypical intraepithelial melanocytic proliferation (AIMP)
- ☐ Pagetoid intraepidermal melanocytic proliferation (PIMP)
- ☐ Superficial atypical melanocytic proliferation of uncertain significance (SAMPUS)
- ☐ Melanocytic tumor of uncertain malignant potential (MELTUMP)
- ☐ Atypical melanocytic neoplasm, compound

☐ **Melanoma in situ (MIS)**

- ☐ common/pagetoid/superficial spreading melanoma
- ☐ lentiginous, sun damaged skin (lentigo maligna)
- ☐ lentiginous, non-solar (i.e., acral or other)
- ☐ Not otherwise specified (NOS)

☐ **Invasive melanoma**

Breslow thickness: ____mm

☐ The tumor is transected at base and subsequent excision likely will show a deeper component.Ulceration No ____ Yes ____ ☐ IndeterminateMitotic rate per mm² ____ per mm²

Subtype (check all that apply)

- ☐ Acral-lentiginous melanoma
- ☐ Blue nevus-like (a melanoma resembling or originating from a blue nevus)
- ☐ Desmoplastic melanoma
- ☐ Heavily pigmented melanoma (a melanoma resembling epithelioid blue nevi or melanomas developing in animals)
- ☐ Lentigo maligna melanoma
- ☐ Melanoma arising in a congenital nevus
- ☐ Metastatic melanoma
- ☐ Neurotropic melanoma
- ☐ Nevoid (a melanoma resembling a common nevus)
- ☐ Nodular melanoma

- ☐ Persistent melanoma
- ☐ Pigmented spindle cell-like (a melanoma resembling pigmented spindle cell nevus or plexiform spindle cell nevus)
- ☐ Spitz-like (a melanoma that resembles a Spitz nevus/tumor)
- ☐ Superficial spreading melanoma
- ☐ Unclassifiable

1b. Histologic Assessment: Further information on diagnosis

Please assess the degree of solar elastosis:

- ☐ Absent ☐ Mild ☐ Moderate ☐ Severe ☐ Indeterminate

Special Considerations:

Would you need additional information to make a definitive diagnosis in real clinical practice?

- ☐ No
- ☐ Yes, I would need to know if it is a partial sampling of a larger lesion, and may not be representative of the larger lesion
- ☐ Yes, to make a definitive diagnosis, I would need to know additional clinical history:

- ☐ Lesional diameter ☐ History of change

☐ I would order special stains or ancillary tests in this case (check all that apply)

i. Immunohistochemical tests:

- ☐ BAP1
- ☐ BRAF
- ☐ cKit
- ☐ HMB45
- ☐ Ki-67
- ☐ Mart-1
- ☐ MITF
- ☐ P16
- ☐ S100
- ☐ Sox10
- ☐ Tyrosinase
- ☐ Vimentin

ii. Molecular tests:

- ☐ aCGH
- ☐ FISH
- ☐ Genomic sequencing (e.g., BRAF, cKit, etc.)

Additional comments (optional)

II. Do you consider your most advanced diagnosis for this case to be borderline between two diagnoses?

If yes, section I needs to be completed for borderline assessment.

☐ No ☐ Yes
III. Recommendations

- a. Although final treatment decisions may rest with the clinician and the patient, what clinical course would you suggest for consideration? (Assume this biopsy is representative of the entire lesion and that the margin is positive.)

- ☐ No further treatment required
☐ Re-excision <5 mm margins (narrow but complete)
☐ Re-excision ≥ 5 mm margins (but < 1cm)
☐ Re-excision ≥ 1cm (wide excision)
☐ Sentinel lymph node sampling
☐ Adjuvant therapy (e.g., interferon)

- b. What is your perception of the patient's prognosis?

Poor prognosis 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ Excellent prognosis

IV. Additional questions regarding this case

- a. Please rate on the following scale your opinion of the **level of diagnostic difficulty** of this case
Very easy 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ Very challenging
- b. Please rate on the following scale your **confidence in your assessment** of this case
Very confident 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ Not at all confident
- c. Would you ask for a **second pathologist's opinion** of this case before finalizing the report? (Assume a second pathologist is available; check all that apply)
- ☐ No
☐ Yes, because it is our policy to get a second opinion on cases with this diagnosis.
☐ Yes, because I would want a second pathologist's opinion for diagnostic reasons (e.g. the diagnosis is challenging/borderline/uncertain).

Fig 1.

Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis (*MPATH-Dx*) histology reporting form. *aCGH*, Array comparative genomic hybridization; *BAP1*, BRCA1-associated protein-1; *FISH*, fluorescence in-situ hybridization; *MART-1*, melanoma antigen recognized by T cells-1; *MITF*, microphthalmia-associated transcription factor; *NOS*, not otherwise specified; *SOX10*, SRY-related HMG-box10.

MPATH-Dx Diagnostic-Treatment Mapping Scheme – Assume the margins are positive

Class	Clinical Outcome	Terms on histology form
0	Repeat testing or short term follow up	Incomplete study due to sampling and/or technical limitations Significant pathology not necessarily ruled out by this examination
1	No apparent risk for continued local proliferation and adverse outcome	Nevus and related- Common nevus – junctional, compound, intradermal, combined, congenital pattern Nevus and related- Lentiginous nevus, junctional or compound Nevus and related- Blue nevus and related lesions: common Lentigo related- Ephelis Atypia- Dysplastic nevus (nevus with architectural disorder and cytological atypia; Clark's nevus, junctional or compound), mild Nevus and related- Congenital melanocytic nevus: junctional, compound, or intradermal Lentigo related- Solar lentigo Lentigo related- Lentigo simplex Nevus and related- Blue nevus and related lesions: Ito/Ota/Mongolian spot Nevus and related- Halo nevus Atypia- Persistent (recurrent) nevus Atypia- Lentiginous melanocytic proliferation (of sun-damaged OR non-sun-damaged skin) with atypia: mild Nevus and related- Nevus of special anatomic site: acral, genital, flexural, milkline and breast, scalp Atypia- Atypical nevus NOS including atypical nevus of special anatomic site (acral, genital, flexural, milkline/breast, etc.), mild
2	Low level risk for local proliferation of remaining cells; probability of progressive disease unlikely; potentially	Atypia- Dysplastic nevus (nevus with architectural disorder and cytological atypia; Clark's nevus, junctional or compound), moderate Atypia- Atypical nevus NOS, including atypical nevus of special anatomic site: acral, genital, flexural, milkline and breast, scalp moderate Nevus and related-Pigmented spindle cell nevus: junctional or compound Nevus and related-Spitz nevus conventional: junctional, compound, or intradermal Atypia-Lentiginous melanocytic proliferation with moderate atypia (of sun-damaged OR non-sun-damaged skin) Nevus and related- Blue nevus: cellular or epithelioid Nevus and related- Deep penetrating nevus/ plexiform spindle cell nevus

adverse outcome in some cases	Atypia- Proliferative nodules in congenital melanocytic nevi (moderate or no atypia or no mitotic activity)
3 Higher likelihood of local tumor progression and greater need for intervention; No reliable data for actual risk	<p>Atypia- Dysplastic nevus (nevus with architectural disorder and cytological atypia; Clark's nevus, junctional or compound), severe</p> <p>Melanoma, in situ (common/pagetoid/superficial spreading melanoma)</p> <p>Melanoma, in situ, lentiginous, sun-damaged skin (lentigo maligna)</p> <p>Melanoma, in situ, lentiginous non-solar (i.e., acral or other)</p> <p>Melanoma, in situ, not otherwise specified (NOS)</p> <p>Atypia- Lentiginous melanocytic proliferation with severe atypia (of sun-damaged OR non-sun-damaged skin)</p> <p>Atypical spitzoid lesion-Atypical/dysplastic/Spitz tumor (junctional, compound, or dermal)</p> <p>Atypical spitzoid lesion-Atypical pigmented spindle cell tumor, (junctional or compound)</p> <p>Atypia- Atypical nevus NOS including atypical nevus of special anatomic site (acral, genital, flexural, milkline/breast, scalp, etc.), severe</p> <p>Atypia- Proliferative nodules in congenital melanocytic nevi (moderate/severe atypia and/or mitotic activity)</p> <p>Melanocytic lesion of uncertain malignant potential- Pagetoid intraepidermal melanocytic proliferation (PIMP)</p>
4 Substantial risk for locoregional progression	<p>Repeat excision with at least 5mm (but < 1cm) margins</p> <p>Wide excision (≥1cm) T1a</p> <p>Invasive melanoma-Acral-lentiginous melanoma</p> <p>Invasive melanoma-Blue nevus-like, a melanoma resembling or originating from a blue nevus</p> <p>Invasive melanoma-Desmoplastic melanoma</p> <p>Invasive melanoma- Heavily pigmented melanoma, a melanoma resembling epithelioid blue nevi or melanomas developing in animals</p> <p>Invasive melanoma- Invasive melanoma, unclassifiable</p> <p>Invasive melanoma- Lentigo maligna melanoma</p> <p>Invasive melanoma- Melanoma arising in a congenital nevus</p> <p>Invasive melanoma- Metastatic melanoma</p> <p>Invasive melanoma- Neurotropic melanoma</p>

		Invasive melanoma- Nevoid melanoma (a melanoma resembling a common nevus)
		Invasive melanoma- Nodular melanoma
		Invasive melanoma- Persistent melanoma (if invasive melanoma – T1a)
		Invasive melanoma- Pigmented spindle cell-like, a melanoma resembling pigmented spindle cell nevus or plexiform spindle cell nevus
		Invasive melanoma- Spitz-like, a melanoma that resembles a Spitz nevus/tumor
		Invasive melanoma- Superficial spreading melanoma
		Invasive melanoma- Acral-lentiginous melanoma
		Invasive melanoma- Blue nevus-like, a melanoma resembling or originating from a blue nevus
		Invasive melanoma- Desmoplastic melanoma
		Invasive melanoma- Heavily pigmented melanoma, a melanoma resembling epithelioid blue nevi or melanomas developing in animals
		Invasive melanoma- Invasive melanoma, unclassifiable
		Invasive melanoma- Lentigo maligna melanoma
		Invasive melanoma- Melanoma arising in a giant congenital nevus
		Invasive melanoma- Metastatic melanoma
		Invasive melanoma- Nevoid (a melanoma resembling a common nevus) melanoma
		Invasive melanoma- Neurotropic melanoma
		Invasive melanoma- Nodular melanoma
		Invasive melanoma- Persistent melanoma (if invasive melanoma – $\geq$ T1b)
		Invasive melanoma- Pigmented spindle cell-like, a melanoma resembling pigmented spindle cell nevus or plexiform spindle cell nevus
		Invasive melanoma- Spitz-like, a melanoma that resembles a Spitz nevus/tumor
		Invasive melanoma- Superficial spreading melanoma
5 Greater risk for regional and/or distant metastasis	Wide excision ($\geq$ 1 cm) T1b or more	Melanocytic lesion of uncertain malignant potential- Atypical melanocytic neoplasm, junctional – Usually maps to Class 2 or 3
		Melanocytic lesion of uncertain malignant potential- Atypical intraepithelial melanocytic proliferation (AIMP) – Usually maps to Class 2 or 3
		Melanocytic lesion of uncertain malignant potential- Superficial atypical melanocytic proliferation of uncertain significance (SAMPUS) – Usually maps to Class 2, 3, or 4
		Melanocytic lesion of uncertain malignant potential- Melanocytic tumor of uncertain malignant potential (MELTUMP) – Usually maps to Class 3 or 4
		Melanocytic lesion of uncertain malignant potential- Atypical melanocytic neoplasm, compound – Usually maps to Class 3, 4, or 5

Classification of 4 vs. 5 is defined as follows:

T1a (class 4): Breslow thickness of ≤ 1.00 mm, no ulceration and no mitotic rate or mitotic rate $< 1 \text{ mm}^2$

T1b (class 5): Breslow thickness of 1.01 mm or more

or

Breslow thickness of ≤ 1.00 mm, with yes ulceration and/or mitotic rate $\geq 1 \text{ mm}^2$

Fig 2.

Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis (*MPATH-Dx*) diagnostic-treatment mapping scheme.
NOS, Not otherwise specified.