Guideline Resource Unit
guru@ahs.ca

Biopsy of a Suspicious Pigmented Lesion

Effective Date: August 2021

Background

Biopsy is used to diagnose and stage a suspicious lesion, which in turn permits prognostication and determining the best management plan. The purpose of this guideline is to describe the preferred biopsy techniques for patients presenting with a mole or lesion that is suspicious for melanoma, as well as to outline the appropriate reporting elements.

Guideline Questions

1. What types of biopsies are appropriate for diagnosis of a suspicious lesion in melanoma?
2. What elements should be collected from the biopsy?

Search Strategy

For the 2021 guideline update, a search of systematic reviews, meta-analyses, randomized controlled trials, clinical trials, and practice guidelines was conducted in PubMed using the MeSH search terms “biopsy” and “melanoma”. The search was expanded back to 10 years. The websites of national and international oncology guideline developers were also searched for relevant recommendations published in the last five years. The details of the literature search and results are available upon request.

Target Population

The following recommendations apply to adults over the age of 18 years with melanoma. Different principles may apply to pediatric patients.

Recommendations

1. Excisional/complete biopsy (elliptical, punch, saucerization/deep shave) with 1-3 mm margins is preferred. Avoid wider margins to permit accurate subsequent lymphatic mapping.[1]
2. Plan the orientation of an elliptica/fusiform excisional biopsy with definitive wide local excision in mind (e.g., longitudinally [axially] and parallel to the underlying lymphatics on the extremities).[1]
3. Full-thickness incisional or punch biopsy of the clinically thickest or most atypical portion of lesion is acceptable in certain anatomic areas (e.g., palm/sole, digit, face, ear) or for very large lesions. Multiple “scouting” biopsies may help guide management for very large lesions.[1]
4. Superficial shave biopsy may compromise pathologic diagnosis and complete assessment of Breslow thickness, but is acceptable for melanoma in situ, lentigo maligna type (i.e., melanoma on skin with high cumulative sun damage.[1]
5. Biopsy should be read by a pathologist experienced with pigmented lesions and should include the following elements:[2]
    - Biopsy procedure (shave, punch, incisional, other, not specified)
    - Specimen laterality (right, left, midline, not specified)
    - Tumour site
    - Histologic Type

    - Invasive melanoma subtype: superficial spreading (low-cumulative sun damage), lentigo maligna, desmoplastic (pure or mixed), acral, arising in a blue nevus, arising in a giant congenital nevus, spitz, nodular, nevoid, not otherwise classified, other
    - Melanoma in situ subtype: superficial spreading (low-cumulative sun damage), lentigo maligna, acral, arising in a giant congenital nevus, not otherwise classified, other
- Peripheral and deep margins (negative for invasive melanoma, invasive melanoma present at margin, negative for melanoma in situ, melanoma in situ present at margin, cannot be assessed)
- Tumour Regression (not identified, present, indeterminate)
- Pathologic stage classification (pTNM, AJCC 8th Edition)
- Applicable to invasive tumour only:
    - Maximum tumour (Breslow) thickness (specify mm or at least mm, indeterminate)
    - Ulceration (not identified, present, indeterminate)
    - Microsatellite(s) (not identified, present, indeterminate)
    - Mitotic rate (none identified, specify [mitoses/mm^2], indeterminate)
    - Lymphovascular invasion (not identified, present, indeterminate)
    - Neurotropism (not identified, present, indeterminate)
    - Tumour-infiltrating lymphocytes (not identified, present non-brisk, present brisk, indeterminate)
    - Optional, anatomic (Clark) Level (at least level __, II, III, IV, V, indeterminate)

Discussion

When performing an excisional biopsy, a definitive treatment plan should be developed so that any possible future procedures (i.e., lymphatic mapping or sentinel node biopsy) are considered; in this regard wider margins should be avoided. An excisional biopsy may not be feasible for certain sites, such as the face, palmar surface of the hand, sole of the foot, ear, etc. or for very large lesions. Alternatively, a full-thickness incisional biopsy (including deep saucerization) or punch biopsy may be appropriate, rather than a shave biopsy, as they are accurate[3] and do not interfere with local therapy.[4] It should be noted, however, that in a case series, the odds ratio (OR) for a histopathologic misdiagnosis with punch biopsy and shave biopsy were 16.6 (95% CI 10-27; P<0.001) and 2.6 (95% CI 1.2-5.7; P=0.02), respectively, versus excisional biopsy. The OR for a misdiagnosis with adverse outcome with punch biopsy was 20.0 (95% CI 10-41; P<0.01) versus excisional biopsy. Primary care physicians should perform excisional biopsy, if feasible, or promptly refer to a dermatologist for assessment and biopsy. For large flat lesions, a deep shave biopsy may be preferred over a scouting punch biopsy. Regarding microstaging, the odds of inaccuracy (versus excisional biopsy) was higher for punch biopsy (OR 5.1, 95% CI 3.4-7.6; P<0.001) than for shave biopsy (OR 2.3, 95% CI 1.5-3.6; P<0.001).[5] If the biopsy is unable to provide enough information to make a diagnosis or to accurately microstage the tumour, a repeat biopsy is recommended.[1] Ideally, the specimen should be

interpreted by a dermatopathologist or a pathologist experienced with pigmented skin lesions.[6] For staging definitions, please refer to the Appendix.

References

1. National Comprehensive Cancer Network. Melanoma: Cutaneous. Version 2.2021. 2021.
2. College of American Pathologists. *Protocol for the Examination of Biopsy Specimens From Patients with Melanoma of the Skin. Version 4.1.0.0*. 2019.
3. Fraga GR, Warren N. The effect of sampling method on the quality of histologic preparations in the diagnosis of melanoma: A retrospective study of 103 melanomas procured via shave, punch, and scalpel excision. *Journal of Histotechnology*. 2010;33(2):65-70.
4. Moore P, Hundley J, Levine EA, Williford P, Sangueza O, McCoy T, et al. Does shave biopsy accurately predict the final breslow depth of primary cutaneous melanoma? *Am Surg*. May 2009;75(5):369-73; discussion 374.
5. Ng JC, Swain S, Dowling JP, Wolfe R, Simpson P, Kelly JW. The impact of partial biopsy on histopathologic diagnosis of cutaneous melanoma: experience of an Australian tertiary referral service. *Arch Dermatol*. Mar 2010;146(3):234-9.
6. Michielin O, van Akkooi ACJ, Ascierto PA, Dummer R, Keilholz U. Cutaneous melanoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. *Ann Oncol*. Dec 1 2019;30(12):1884-1901.

Appendix

AJCC 2017 (8th Edition) Anatomic Stage Groupings for Cutaneous Melanoma

	Clinical Staging [a]				Pathologic Staging [b]			5-year Survival (%)
	T	N	M		T	N	M	
0	Tis	N0	M0	0	Tis	N0	M0	100%
IA	T1a	N0	M0	IA	T1a T1b	N0	M0	99%
IB	T1b T2a	N0	M0	IB	T2a	N0	M0	97%
IIA	T2b T3a	N0	M0	IIA	T2b T3a	N0	M0	94%
IIB	T3b T4a	N0	M0	IIB	T3b T4a	N0	M0	87%
IIC	T4b	N0	M0	IIC	T4b	N0	M0	82%
III	Any T, Tis	≥N1	M0	IIIA IIIB IIIC IIID	T1a/b-T2a T0 T1a/b-T2a T2b/T3a T1a-T3a T3b/T4a T4b T4b	N1a or N2a N1b, N1c N1b/c or N2b N1a-N2b N2c or N3a/b/c Any N ≥N1 N1a-N2c N3a/b/c	M0	93% 77% 60% 24%
IV	Any T	Any N	M1	IV	Any T, Tis	Any N	M1	<10%

[a] Clinical staging includes microstaging of the primary melanoma and clinical/radiologic/biopsy evaluation for metastases. By convention, clinical staging should be used after biopsy of the primary melanoma, with clinical assessment for regional and distant metastases.

[b] Pathologic staging includes microstaging of the primary melanoma, including any additional staging information from the wide-excision (surgical) specimen that constitutes primary tumour surgical treatment and pathological information about the regional lymph nodes after SLN biopsy or therapeutic lymph node dissection for clinically evident regional lymph node disease.

AJCC 2017 (8th Edition) TNM Staging Categories for Cutaneous Melanoma

T	Thickness (mm)	Ulceration Status
Tx: Primary tumour thickness cannot be assessed (e.g., diagnosis by curettage)	NA	NA
T0: No evidence of primary tumour (e.g., unknown primary or completely regressed melanoma)	NA	NA
Tis (melanoma *in situ*)	NA	NA
T1	≤ 1.0	Unknown or unspecified
T1a	< 0.8	Without ulceration
T1b	< 0.8	With ulceration
	0.8 to 1.0	With or without ulceration
T2	>1.0 to 2.0	Unknown or unspecified
T2a	>1.0 to 2.0	Without ulceration

T	Thickness (mm)	Ulceration Status
T2b	>1.0 to 2.0	With ulceration
T3	>2.0 to 4.0	Unknown or unspecified
T3a	>2.0 to 4.0	Without ulceration
T3b	>2.0 to 4.0	With ulceration
T4	> 4.0	Unknown or unspecified
T4a	> 4.0	Without ulceration
T4b	> 4.0	With ulceration
N	**Number of Tumour-Involved Regional Lymph Nodes**	**Presence of In-Transit, Satellite, and/ore Microsatellite Metastases**
NX	Regional nodes not assessed (e.g., SLNB not performed, regional nodes previously removed for another reason) Exception: Pathological N category is not required for T1 melanomas, use cN	No
N0	No regional metastases detected	NA
N1	1 tumour-involved node or in-transit, satellite, and/or microsatellite metastases with no tumour-involved nodes	
N1a	1 clinically occult (i.e., detected by SLN biopsy)	No
N1b	1 clinically detected	No
N1c	No regional lymph node disease	Yes
N2	2 or 3	
N2A	2 or 3 tumour-involved nodes or in-transit, satellite, and/or microsatellite metastases with one tumour-involved node	No
N2B	2 or 3 clinically occult (i.e., detected by SLN biopsy)	No
N2C	1 clinically occult or clinically detected	Yes
N3	≥4 tumour-involved nodes or in-transit, satellite, and/or microsatellite metastases with ≥2 tumour-involved nodes, or any number of matted nodes without or with in-transit, satellite, and/or microsatellite metastases	
N3A	≥4 clinically occult (i.e., detected by SLNB biopsy)	No

N3B	≥4, at least 1 of which was clinically detected, or presence of any number of matted nodes	No
N	**Number of Tumour-Involved Regional Lymph Nodes**	**Presence of In-Transit, Satellite, and/ore Microsatellite Metastases**
N3C	≥2 clinically occult or clinically detected and/or presence of any number of matted nodes	Yes
M	**Site**	**LDH (lactate dehydrogenase) Level**
M0	No evidence of distant metastases	Not applicable
M1	Evidence of distant metastasis	See below
M1a	Distant metastasis to skin, soft tissue including muscle, and/or nonregional lymph node	Not recorded or unspecified
M1a(0)		Not elevated
M1b(1)		Elevated
M1b	Distant metastasis to lung with or without M1a sites of disease	Not recorded or unspecified
M1b(0)		Not elevated
M1b(1)		Elevated
M1c	Distant metastasis to non-CNS visceral sites with or without M1a or M1b sites of disease	Not recorded or unspecified
M1c(0)		Not elevated
M1c(1)		Elevated
M1d	Distant metastasis to CNS with or without M1a, M1b, or M1c sites of disease	Not recorded or unspecified
M1d(0)		Not elevated
M1d(1)		Elevated

Development and Revision History

This guideline was reviewed and endorsed by the Alberta Provincial Cutaneous Tumour Team. Members include surgical oncologists, radiation oncologists, medical oncologists, dermatologists, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Cutaneous Tumour Team, external participants identified by the Working Group Lead, and a methodologist from the Guideline Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Resource Unit Handbook.

This guideline was originally developed in May 2008 and updated in June 2009, May 2010, February 2011, March 2012, February 2013, August 2021.

Levels of Evidence

I	Evidence from at least one large randomized, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity
II	Small, randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case-control studies
V	Studies without control group, case reports, expert opinion

Strength of Recommendations

A	Strong evidence for efficacy with a substantial clinical benefit; strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit; generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.); optional
D	Moderate evidence against efficacy or for adverse outcome; generally, not recommended
E	Strong evidence against efficacy or for adverse outcome; never recommended

Maintenance

A formal review of the guideline will be conducted in 2024. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

Abbreviations

AHS, Alberta Health Services; CCA, Cancer Care Alberta; OR, odds ratio

Disclaimer

The recommendations contained in this guideline are a consensus of the Alberta Provincial Cutaneous Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

Funding Source

Financial support for the development of Cancer Care Alberta's evidence-based clinical practice guidelines and supporting materials comes from the Cancer Care Alberta operating budget; no outside commercial funding was received to support the development of this document.

All cancer drugs described in the guidelines are funded in accordance with the Outpatient Cancer Drug Benefit Program, at no charge, to eligible residents of Alberta, unless otherwise explicitly stated. For a complete list of funded drugs, specific indications, and approved prescribers, please refer to the *Outpatient Cancer Drug Benefit Program Master List*.

Conflict of Interest Statements

Dr. Thomas Salopek (guideline lead) has nothing to disclose.
Brae Surgeoner has nothing to disclose.