STUDY

The Impact of Partial Biopsy on Histopathologic Diagnosis of Cutaneous Melanoma

Experience of an Australian Tertiary Referral Service

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Objective: To compare partial and excisional biopsy techniques in the accuracy of histopathologic diagnosis and microstaging of cutaneous melanoma.

Design: Prospective case series.

Setting: Tertiary referral, ambulatory care, institutional practice.

Patients: Consecutive cases from 1995 to 2006.

Interventions: Partial and excisional biopsy. Other factors considered were anatomic site, physician type at initial management, hypomelanosis, melanoma subtype, biopsy sample size, multiple biopsies, and tumor thickness.

Main Outcome Measures: Histopathologic diagnosis (false-negative misdiagnosis—overall or with an adverse outcome—and false-positive misdiagnosis) and microstaging accuracy. Odds ratios (ORs) and 95% confidence intervals (CIs) obtained from multinomial logistic regression.

Results: Increased odds of histopathologic misdiagnosis were associated with punch biopsy (OR, 16.6; 95% CI, 10-27) ($P<.001$) and shave biopsy (OR, 2.6; 95% CI, 1.2-5.7) ($P=.02$) compared with excisional biopsy. Punch biopsy was associated with increased odds of misdiagnosis with an adverse outcome (OR, 20; 95% CI, 10-41) ($P<.001$). Other factors associated with increased odds of misdiagnosis included acral lentiginous melanoma (OR, 5.1; 95% CI, 2-13) ($P<.001$), desmoplastic melanoma (OR, 3.8; 95% CI, 1.1-13.0) ($P=.03$), and nevoid melanoma (OR, 28.4; 95% CI, 7-115) ($P<.001$). Punch biopsy (OR, 5.1; 95% CI, 3.4-7.6) ($P<.001$) and shave biopsy (OR, 2.3; 95% CI, 1.5-3.6) ($P<.001$) had increased odds of microstaging inaccuracy over excisional biopsy. Tumor thickness was the most important determinant of microstaging inaccuracy when partial biopsy was used (odds of significant microstaging inaccuracy increased 1.8-fold for every 1 mm increase in tumor thickness; 95% CI, 1.4-2.4) ($P<.001$).

Conclusions: Among melanoma seen at a tertiary referral center, histopathologic misdiagnosis is more common for melanomas that have been assessed with punch and shave biopsy than with excisional biopsy. Regardless of biopsy method, adverse outcomes due to misdiagnosis may occur. However, such adverse events are more commonly associated with punch biopsy than with shave and excisional biopsy. The use of punch and shave biopsy also leads to increased microstaging inaccuracy.

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THE RECOMMENDED BIOPSY technique for suspected melanoma is excision with narrow margins.[1,2] Partial biopsy techniques (such as punch or shave) may lead to histopathologic misdiagnosis through unrepresentative sampling,[3-5] inability to assess overall architecture,[6] and induction of pseudomelanoma.[7] Yet the use of partial biopsy to sample suspected melanoma is common, being routinely used among 31% of US dermatologists.[8] It was also used in 30% and 22% of cases referred by general practitioners and dermatologists, respectively, to a United Kingdom surgical unit,[9] and in 27% of melanoma cases in Victoria, Australia, in the year 2000 (increased from 18% in 1996).[10]

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The risk of melanoma misdiagnosis by partial biopsy has not been clearly established in the literature. Punch biopsy failed to identify melanoma (subsequently confirmed after excision) in 7% of clinically dysplastic nevus cases in a recent series.[11] Partial biopsy was responsible for over 50% of false-negative melanoma misdiagnoses among surgical pathology claims to a US medical indemnity provider.[12] In compari-

son, excisional biopsy has been associated with false-negative misdiagnosis in 1.2%,[13] 7.2%,[14] and 42.4%[15] of melanoma cases among pathology review studies with different inclusion criteria.

In addition to misdiagnoses, partial biopsies may lead to inaccurate histopathologic assessments of tumor thickness and other factors affecting the prognosis of melanoma (microstaging). Significant microstaging inaccuracy has been reported in 16% to 43% of partial biopsies,[16-21] but generalization from these studies may be limited by their inclusion criteria (lentigo maligna melanoma only),[20,21] small sample size,[16] variable definitions of partial biopsy,[16-21] and difficulty with the definition of microstaging accuracy.[17,18]

We set out to assess prospectively the accuracy of histopathologic diagnosis and microstaging of partial biopsy compared with excisional biopsy for melanoma in a large series from a single tertiary referral center.

METHODS

PATIENTS

The Victorian Melanoma Service (VMS) is a tertiary referral multidisciplinary center that manages approximately 25% of cutaneous melanoma in Victoria, Australia. Data from VMS cases are comparable to population data from the Victorian Cancer Registry, with in situ disease making up 35% and 36% of all VMS and registry cases, respectively, and invasive disease of less than 1.00 mm, 1.00 to 1.99 mm, 2.00 to 2.99 mm, and 3 mm or more in tumor thickness making up 59%, 19%, 8%, and 13% of invasive VMS cases, respectively, and 64%, 18%, 7%, and 13% of invasive registry cases, respectively [written communication, August 2008, Graham Giles, PhD].

The VMS accepts referrals for histopathologically confirmed melanoma either at the time of initial intervention (partial or excisional biopsy) or after an adverse outcome (where the initial intervention failed to diagnose melanoma) such as persistent primary disease or metastatic melanoma. The histopathologic diagnosis of melanoma is made either independently prior to referral (with subsequent unblinded VMS review) or in consultation with the VMS pathologist prompted by histopathologic or clinical uncertainty relating to lesions excised recently or in the more distant past. The study included consecutive referrals to the VMS from 1995 to 2006 and was approved by the Alfred Human Research Ethics Committee, The Alfred Hospital, Melbourne, Australia.

MELANOMA MISDIAGNOSIS

For each referral, clinical and histopathologic data were recorded, including the initial managing physician type, type of biopsy, anatomic location of the lesion, lesion hypomelanosis, multiple biopsy specimens of the lesion, lesion size, biopsy sample size, histopathologic diagnosis, subtype of melanoma, tumor thickness, Clark level, presence or absence of ulceration, and margins. For shave biopsy, no distinction is made between the superficial and the deeper "saucerization" shave biopsy. Punch or shave biopsies were considered partial except in instances where no residual melanoma was identifiable microscopically on definitive excision (when excisions were considered complete).

Using the VMS assessment of the definitive excision as reference, the initial pathology reports were categorized into correct diagnosis, false-negative misdiagnosis (including misdiagnosis with an adverse outcome), or false-positive misdiagnosis. An adverse outcome was defined as the persistence or progression of primary disease or development of nodal or distant metastasis occurring prior to the correct diagnosis being made. A sampling error was considered present if the initial partial biopsy of an excision-proven melanoma was not retrospectively identifiable as melanoma by VMS review.

Cases were excluded from analysis subject to the following criteria: absence of prior histopathologic assessment or VMS review of an excisional biopsy specimen (no comparison possible), absence of VMS review of the excision for patients assessed with initial partial biopsy (no reference available), subungual melanoma (requiring biopsy of specialized nature), and clinical trial participation where it interfered with microstaging.

MELANOMA MICROSTAGING ACCURACY

Correct diagnoses were assessed for microstaging accuracy by comparing initial histopathologic assessment of the biopsy (both partial and excisional) against that of the VMS assessment of the final excision. Microstaging inaccuracy was defined as a prognostically significant underestimation of microstaging by the initial biopsy, where prognostic significance was defined as a change in prognostic stage grouping according to the 2001 American Joint Committee on Cancer (AJCC) staging system.[22] Among excisional biopsies, inaccurate microstaging was attributed to interobserver error, with the VMS microstaging being the reference.

STATISTICAL ANALYSIS

The odds for false-negative misdiagnosis (overall and misdiagnosis with an adverse outcome) were compared between biopsy types and other variables by calculating odds ratios (ORs), 95% confidence intervals (CIs), and *P* values with multinomial (polytomous) logistic regression. Microstaging inaccuracy was analyzed with OR from logistic regression followed by multivariate logistic regression to adjust for potential confounding factors. All statistical analyses were performed using Stata 9.0 (Stata Statistical Software, College Station, Texas).

RESULTS

Of 3348 referrals, 878 (26.2%) were excluded from analysis owing to absence of VMS pathology review (588 in total, 565 by excisional biopsy, and 23 by partial biopsy); absence of prior histopathologic assessment (261 by excisional biopsy); insufficient information (20 by partial biopsy); subungual melanoma (7 by partial biopsy); or involvement in a clinical trial (2 by partial biopsy). Biopsy by curettage (8 cases) and fusiform incisional techniques (10 cases) were excluded owing to small numbers.

Of 2470 referrals included in the study (2127 excisional biopsies, 163 punch biopsies, and 180 shave biopsies), there were 83 false-negative misdiagnoses (3.4%) including 37 associated with an adverse outcome (1.5%); 135 false-positive misdiagnoses (5.5%); and 2252 correct diagnoses (91.2%) (**Table 1**).

FALSE-NEGATIVE MELANOMA MISDIAGNOSES

The odds of misdiagnosis (both overall and associated with an adverse outcome) were very much higher with punch biopsy than with excisional biopsy, whereas shave biopsy was only weakly associated with misdiagnosis (**Table 2**). After adjusting for other clinical and histopathologic factors on multivariate analysis, the increased odds for mis-

Table 1. Misdiagnosis of Melanoma by Type of Biopsy

Characteristic	Biopsy Type[a]			
	Excisional	Punch	Shave	Total
False-negative misdiagnosis overall	37 (1.7)	38 (23.3)	8 (4.5)	**83** (3.4)
False-negative misdiagnosis with an adverse outcome	15 (0.7)	19 (11.6)	3 (1.7)	**37** (1.5)
False-positive misdiagnosis	123 (5.8)	3 (1.8)	9 (5.0)	**135** (5.5)
Correct diagnosis	1967 (92.5)	122 (74.8)	163 (90.5)	**2252** (91.2)
Total	2127	163	180	**2470** (100)

[a] All data are reported as number (percentage) of cases.

Table 2. The Relationship Between Clinical Factors and the Odds of a False-Negative Diagnosis Rather Than a Correct Diagnosis

Comparison	False-Negative Misdiagnosis Overall		False-Negative Misdiagnosis With an Adverse Outcome	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Punch biopsy (n=160) vs excisional biopsy (n=2004)	16.6 (10.2-27.0)	<.001	20.4 (10.1-41.2)	<.001
Shave biopsy (n=171) vs excisional biopsy (n=2004)	2.6 (1.2-5.7)	.02	2.4 (0.7-8.4)	.17
General practitioner (n=637) vs dermatologist (n=638)[a]	4.2 (2.3-7.6)	<.001	7.6 (2.7-21.8)	<.001
H&N (n=480) vs non-H&N locations (n=1829)	1.0 (0.6-1.7)	.94	1.6 (0.8-3.3)	.19
Hypomelanotic (n=147) vs melanotic lesions (n=2188)	1.2 (0.5-2.7)	.72	1.8 (0.6-5.2)	.26
SSM (n=1428) vs all other melanoma subtypes (n=907)	0.5 (0.3-0.8)	.002	0.5 (0.2-0.9)	.02
LMM (n=328) vs all other melanoma subtypes (n=2007)	1.3 (0.7-2.3)	.45	2.0 (0.9-4.2)	.08
NM (n=299) vs all other melanoma subtypes (n=2036)	0.5 (0.2-1.2)	.13	1.0 (0.4-2.7)	.93
ALM (n=40) vs all other melanoma subtypes (n=2295)	5.1 (2.1-12.5)	<.001	1.8 (0.2-13.6)	.56
Desmoplastic melanoma (n=25) vs all other melanoma subtypes (n=2310)	3.8 (1.1-13.0)	.03	2.8 (0.4-21.2)	.32
Nevoid melanoma (n=8) vs all other melanoma subtypes (n=2327)	28.4 (7.0-115)	<.001	15.6 (1.7-143.2)	.01

Abbreviations: ALM, acral lentiginous melanoma; CI, confidence interval; H&N, head and neck; LMM, lentigo maligna melanoma; NM, nodular melanoma; OR, odds ratio; SSM, superficial spreading melanoma.

[a] Physician type at initial management (general practitioners, dermatologists, and surgeons) with data available for 1536 cases.

diagnosis and adverse outcome remained significant for punch biopsy (OR for misdiagnosis, 14.7 [$P<.001$]; OR for adverse outcome, 13.2 [$P<.001$]) and were accentuated with shave biopsy (OR for misdiagnosis, 4.5 [$P=.002$]; OR for adverse outcome, 4.4 [$P=.01$]).

The delay in diagnosis was shorter following misdiagnosis with punch and shave biopsies (median delay, 30.6 months) than with excisional biopsies (median delay, 49.1 months). Peripheral margins and deep margins were involved, respectively, in 11 of 15 (73%) and 1 of 15 (6%) misdiagnosed cases with an adverse outcome by excisional biopsy. Adverse outcomes manifested as persistence and progression of primary disease in all partial biopsies (n=22) and in 11 of 15 excisional biopsies (in particular, in 10 of 12 excisional biopsies associated with positive margins) and as metastatic disease in 4 of 15 excisional biopsies. Forty-five percent of adverse outcomes did not lead to progression by any AJCC prognostic stage grouping. Sampling error by partial biopsy was implicated in 22% of false-negative misdiagnoses and in 18% of cases with an adverse outcome; the remaining misdiagnoses were attributed to errors in histopathologic interpretation.

Increased odds of misdiagnosis were associated with initial management by general practitioners (compared with dermatologists), acral-lentiginous melanoma, desmoplastic melanoma, and nevoid melanoma. Increased odds of adverse outcomes were associated with initial management by general practitioners and nevoid melanoma (Table 2). Of 1536 cases where information for physician type was available, dermatologists (42%) were overrepresented among shave biopsy (82%), lentigo maligna melanoma (61%), acral lentiginous melanoma (47%), desmoplastic melanoma (68%), hypomelanotic melanoma (47%), and head and neck locations (57%). In contrast, general practitioners (41%) were overrepresented among false-negative misdiagnoses overall (72%) and with adverse outcomes (81%) (**Table 3**). After adjusting for other clinical and histopathologic factors on multivariate analysis, general practitioners remained at increased odds of misdiagnosis (OR, 6.1) ($P<.001$) and adverse outcomes (OR, 25) ($P<.001$) compared with dermatologists.

In situ disease at presentation was more common among misdiagnosed cases (36%) than among those correctly diagnosed (16%). Adverse outcomes were avoided in 24 misdiagnosed cases by partial biopsy because the pathologist recommended complete excision (58%); persisting clinical suspicion led to excision (25%); or misdiagnosis as nonmelanoma skin cancer led to excision (16%). Most false-negative misdiagnoses with an adverse outcome were initially assessed as melanocytic (86% by excisional biopsy and 68% by partial biopsy) (**Table 4**).

MICROSTAGING ACCURACY

Inaccurate microstaging was present in 34% of cases correctly diagnosed with punch biopsy (41 of 122), 19% with shave biopsy (31 of 163), and 9.1% with excisional biopsy (179 of 1967). The increased odds of microstaging

Table 3. Distribution of Characteristics by Initial Managing Physician Type[a]

Characteristic	Dermatologist	General Practitioner	Surgeon	Total
Total	638 (42)	637 (41)	261 (17)	**1536**
Excisional biopsy	426 (35)	537 (44)	245 (20)	**1208**
Punch biopsy	73 (46)	75 (47)	10 (6)	**158**
Shave biopsy	139 (82)	25 (15)	6 (4)	**170**
False-negative misdiagnosis with adverse outcome	4 (11)	29 (81)	3 (8)	**36**
False-negative misdiagnosis overall	15 (20)	55 (72)	6 (8)	**76**
Correct diagnosis	623 (43)	582 (40)	255 (17)	**1460**
SSM	337 (37)	435 (47)	146 (16)	**918**
LMM	166 (61)	71 (26)	33 (12)	**270**
NM	64 (36)	68 (38)	47 (26)	**179**
ALM	14 (47)	11 (37)	5 (17)	**30**
Desmoplastic melanoma	13 (68)	4 (21)	2 (11)	**19**
Nevoid melanoma	3 (43)	3 (43)	1 (14)	**7**
Unclassified melanoma	21 (38)	25 (45)	9 (16)	**55**
Other melanoma	20 (34)	20 (34)	18 (31)	**58**
Hypomelanotic melanoma	60 (47)	43 (34)	24 (19)	**127**
Melanotic melanoma	578 (41)	594 (42)	237 (17)	**1409**
Head and neck location	206 (57)	101 (28)	56 (15)	**363**
Trunk location	155 (33)	220 (48)	88 (19)	**463**
Upper limb location	120 (38)	150 (47)	49 (15)	**319**
Lower limb location	154 (41)	160 (42)	63 (17)	**377**
Unknown location	3 (21)	6 (43)	5 (36)	**14**

Abbreviations: ALM, acral lentiginous melanoma; LMM, lentigo maligna melanoma; NM, nodular melanoma; SSM, superficial spreading melanoma.
[a]Unless otherwise indicated, data are reported as number (percentage) of physicians.

Table 4. Initial Diagnostic Label of Cases of False-Negative Misdiagnosis

	With Adverse Outcome		Without Adverse Outcome	
Characteristic	Excisional Biopsy	Partial Biopsy	Excisional Biopsy	Partial Biopsy
Benign melanocytic nevus	7 (47)	11 (50)	4 (18)	3 (13)
Dysplastic melanocytic nevus	5 (33)	3 (14)	14 (64)	11 (46)
Spitz nevus	1 (7)	NA	NA	1 (4)
Sclerotic blue nevus	NA	NA	NA	1 (4)
Deep penetrating nevus	NA	NA	1 (5)	NA
NMSC	1 (7)	NA	NA	4 (17)
Solar lentigo and/or solar damage	NA	5 (23)	NA	NA
Scar	NA	2 (9)	NA	NA
Other	1 (7)	1 (5)	3 (14)	3 (13)
Deferred	NA	NA	NA	1 (4)
Total	**15**	**22**	**22**	**24**

Abbreviations: NA, not applicable; NMSC, nonmelanotic skin cancer.

inaccuracy by punch and shave biopsy compared with excisional biopsy were statistically significant (**Table 5**). On univariate analysis, other significant associations of microstaging inaccuracy by partial biopsy included hypomelanotic melanoma, multiple biopsies of the lesion, nodular melanoma, and acral-lentiginous melanoma. There were no clear correlations with biopsy sample size (as a proportion of the lesion surface area), initial managing physician type (nondermatologist vs dermatologist), or anatomic location (head and neck vs non–head and neck locations) (Table 5). On multivariate analysis adjusted for the other clinical and histopathologic factors, the only variable with significant impact on microstaging accuracy was tumor thickness: for every 1-mm increase in tumor thickness, the risk of inaccurate microstaging increased 1.8-fold (95% CI, 1.4-2.4) ($P < .001$).

FALSE-POSITIVE MISDIAGNOSES

There were a total of 135 false-positive misdiagnoses, making up 5.8% of excisional biopsies (123 of 2127 cases) and 3.5% of partial biopsies (12 of 343 cases). Diagnoses were most commonly revised to Spitz nevus (36.3%), dysplastic nevus (28.9%), and benign melanocytic nevus (17%).

COMMENT

The present study demonstrates quantitatively the increased risks of melanoma histopathologic misdiagnosis and microstaging inaccuracy by punch and shave biopsy compared with excisional biopsy in the experience

Table 5. Univariate Analysis of Inaccurate Microstaging by Partial Biopsy[a]

Comparison	OR (95% CI)	*P* Value
Punch biopsy (n=122) vs excisional biopsy (n=1967)	5.1 (3.4-7.6)	<.001
Shave biopsy (163) vs excisional biopsy (n=1967)	2.3 (1.5-3.6)	<.001
Multiple biopsies (n=35) vs single biopsy (n=250)	2.5 (1.2-5.3)	.01
H&N location (n=155) vs non-H&N locations (n=130)[b]	0.9 (0.5-1.5)	.56
Nondermatologist (n=82) vs dermatologist (n=203)	1.1 (0.6-2.0)	.70
Hypomelanotic (n=25) vs melanotic lesions (n=260)	4.4 (1.9-10.3)	.001
Proportion of lesion sampled: 10%-25% (n=37) vs 10% (n=77)[c]	0.2 (0.1-0.7)	.01
Proportion of lesion sampled: 25%-80% (n=26) vs 10% (n=77)[c]	0.7 (0.3-1.9)	.52
SSM (n=99) vs all other melanoma subtypes (n=186)[b]	0.6 (0.3-1.1)	.09
LMM (n=135) vs all other melanoma subtypes (n=150)[b]	0.6 (0.4-1.1)	.10
NM (n=19) vs all other melanoma subtypes (n=266)[b]	2.9 (1.1-7.5)	.03
ALM (n=7) vs all other melanoma subtypes (n=278)[b]	19.3 (2.3-163.0)	.01

Abbreviations: ALM, acral lentiginous melanoma; CI, confidence interval; H&N, head and neck; LMM, lentigo maligna melanoma; NM, nodular melanoma; OR, odds ratio; SSM, superficial spreading melanoma.

[a] Univariate analysis only, not taking into account effects of tumor thickness.

[b] Desmoplastic and nevoid melanoma not included owing to insufficient numbers.

[c] Proportion of lesion sampled, data available for 140 cases.

of a tertiary melanoma treatment center. The findings are of particular relevance in view of recent reports of common[8-10] and increasing[10] usage of partial biopsies to sample suspected melanoma in spite of the recommendations of national guidelines to the contrary.[1,2] Our findings help to explain the disproportionate representation of partial biopsy among cases of melanoma misdiagnosis leading to litigation against pathologists.[12] In some circumstances (eg, where the lesion is large or located in an area where excision would lead to cosmetic and/or functional impairment such as the face or acral skin), a partial biopsy is necessary, but histopathologic conclusions need to be interpreted in correlation with clinical findings and with full understanding of the limitations of the biopsy type used.

The finding that general practitioners had more adverse outcomes due to melanoma misdiagnosis than did dermatologists may be explained by a less selected or more difficult spectrum of presenting lesions in general practice, differences in clinical diagnostic skills, lesion selection for partial biopsy, selection of areas for sampling within a lesion by partial biopsy, the use of less experienced histopathologists, critical appraisal of the histopathology report in decision making, or duration of follow-up. Regardless of reasons, there appears to be a case for more caution in the use of partial biopsy for possible melanomas, particularly in the general practice context. The use of ancillary techniques such as dermoscopy is likely to help avoid melanoma histopathologic misdiagnosis through improved bedside diagnosis, guidance of biopsy, and dermoscopic-histopathologic correlation.[23]

The observation of increased histopathologic misdiagnosis of desmoplastic melanoma, acral-lentiginous melanoma, and nevoid melanoma is consistent with recognized difficulties associated with these lesions.[24] Misdiagnoses in this study are mainly attributable to errors in histopathologic interpretation rather than sampling error, and common pitfalls have been reported to include failure to recognize pagetoid spread of intraepidermal melanocytes, failure to recognize severe solar elastosis underlying junctional nests, and incorrect assignment of cell lineage.[25] However, the unblinded nature of VMS pathology review may underestimate the role of sampling error. Bisection or targeted representative laboratory sampling of shave and punch specimens should be considered to optimize morphologic interpretation of the specimens.

The overall false-negative misdiagnosis rate of 3.4% of 2470 cases in the present study is comparable to reported rates in the literature (1.1% of 5136 cases[13] and 7.2% of 139 cases[14]). The much higher rate reported by Veenhuizen et al[15] (42.4%) arose from a study of only difficult melanocytic lesions.[15] While absolute misdiagnosis rates in the current study may be influenced by referral bias to a large tertiary referral center, the relative misdiagnosis rates as quantified by ORs allow valid comparison between the outcomes of partial and excisional biopsy techniques.

The finding that adverse outcomes were limited to persistence or progression of primary disease among cases of partial biopsies (22 of 22) and most excisional biopsy cases with incomplete margins (10 of 12) is consistent with the current view that incising a melanoma does not itself lead to metastasis or worsened prognosis.[26-28]

While in the present study adverse outcomes caused relatively little disease progression (40% not progressing by any AJCC prognostic stage grouping from the time of initial biopsy to diagnosis), the morbidity and mortality would likely have been higher if longer follow-up had been carried out. The observation that most adverse outcomes occurred in the setting of involved margins (80% of excisional biopsies and 100% of partial biopsies) and an initial incorrect diagnosis of benign melanocytic lesion (86% of excisional biopsies and 68% of partial biopsies) suggests that most adverse outcomes would have been avoided if complete excision was performed of any neoplastic lesion for which melanoma could not be excluded on clinical grounds and that was reported as melanocytic histologically.

The rates of microstaging inaccuracy by punch biopsy (34%) and shave biopsy (19%) were comparable to previously reported rates ranging from 16% to 43%.[16,19-21]

Overdiagnosis of Spitz nevi as melanomas was the most common source of false-positive misdiagnosis (36% of false-positive misdiagnosis in the current study), similar to another report in which histologic confusion with Spitz nevi was the reason for false-positive melanoma diagnosis in 51% of cases.[29]

Since the tumor thickness distributions were similar between VMS cases and those of the Victorian State Cancer Registry, the present study patients can be consid-

ered reasonably representative of the general melanoma population despite the tertiary referral setting of the study. The use of the histopathologic assessment of a single VMS expert pathologist rather than consensus assessment by a panel as the diagnostic reference raises the possibility of bias. The study may also be biased in favor of excisional biopsy, in that most melanoma misdiagnosed by excisional biopsy in the community would remain undetected (the melanomas are cured by the initial complete excision and do not persist and progress as they do after partial biopsy).

In conclusion, among tertiary referrals, punch biopsy is associated with significantly increased melanoma histopathologic misdiagnosis. Clinicians who use punch biopsy for the diagnosis of possible melanomas must be keenly aware of this finding to avoid adverse outcomes, particularly in cases of possible acral lentiginous melanoma, desmoplastic melanoma, or nevoid melanoma. Any neoplastic lesion for which melanoma cannot be clinically excluded and that is diagnosed histologically as melanocytic on partial biopsy should be considered for complete excision. The use of punch and shave biopsies reduces the accuracy of microstaging, and the results of such biopsies are less reliable for prognostication or therapeutic decision making, particularly for thicker tumors. Whenever possible, excisional biopsy should be used to sample suspected melanomas.

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Author Contributions: Dr Ng had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Ng and Kelly. *Acquisition of data:* Ng, Swain, Dowling, and Kelly. *Analysis and interpretation of data:* Ng, Swain, Wolfe, Simpson, and Kelly. *Drafting of the manuscript:* Ng and Kelly. *Critical revision of the manuscript for important intellectual content:* Ng, Swain, Dowling, Wolfe, Simpson, and Kelly. *Statistical analysis:* Wolfe and Simpson. *Obtained funding:* Kelly. *Administrative, technical, and material support:* Swain, Dowling, and Kelly. *Study supervision:* Swain and Kelly.
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