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Changes in the Presentation of Nodular and Superficial Spreading Melanomas Over 35 Years

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Abstract

BACKGROUND—Nodular melanoma (NM) may be biologically aggressive compared with the more common superficial spreading melanoma (SSM), with recent data suggesting underlying genetic differences between these 2 subtypes. To better define the clinical behavior of NMs, the authors compared their clinical and histopathologic features to those of SSMs at their institution, a tertiary referral center, over 3 decades.

METHODS—A total of 1684 patients diagnosed with 1734 melanomas were prospectively enrolled. Of these, 1143 patients (69% SSM, 11% NM, 20% other) were diagnosed between 1972 and 1982; 541 patients (54% SSM, 23% NM, 23% other) were diagnosed between 2002 and the present. Differences between the features of NM and SSM within each time period as well as changes over time were analyzed.

RESULTS—The authors found that SSMs are now diagnosed as thinner lesions ($P < .0001$) with a low incidence of histologic ulceration ($P < .0001$), whereas there was no significant change in the median tumor thickness or ulceration status of NMs over time ($P = .10$, $P = .30$, respectively). The median age at diagnosis of NM, however, did significantly increase over time (51 years to 63 years, $P < .01$). The median duration of NMs was reported to be only 5 months compared with 9 months in SSM patients.

CONCLUSIONS—The authors' data suggest that improvements have been made in the early detection of SSM but not NM. Modifications of current screening practices, including increased surveillance of high-risk patients with an emphasis on the "E" for "evolution" criterion of the ABCDE acronym used for early detection of melanoma, are thus warranted.

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Patients enrolled in the NYU Melanoma Cooperative Group Database between 1972 and 1982 gave verbal informed consent. Subsequent approval to use data from these patients was obtained from the NYU Institutional Review Board (IRB). Prospective accrual of patients from August 2002 to the present has been approved by the NYU IRB, with written informed consent obtained from all patients at the time of enrollment.

Keywords

melanoma; nodular melanoma; superficial spreading melanoma; histopathologic subtype; clinicopathologic characteristics

Although the traditional classification of melanoma by histopathologic subtype (eg, superficial spreading, nodular, lentigo maligna, acral lentiginous) has been criticized for its lack of independent prognostic value, previous studies have demonstrated that nodular melanoma (NM) may be a distinct biologic entity.[1,2] In support of this theory, a recent microarray study of primary and meta-static melanoma specimens identified a characteristic gene expression profile unique to NMs.[3] NMs have also been shown to have lower rates of *BRAF* mutations compared with the more common superficial spreading subtype (SSM). The largest study to date found a *BRAF* mutation rate of 39.1% for NMs, compared with 55.3% for SSMs.[4] Furthermore, our group has recently demonstrated that NMs are associated with increased shedding of collagen epitope HU177 into the bloodstream compared with other subtypes, independent of tumor thickness.[5] Taken together, these findings suggest the possibility that NMs develop along distinct genetic pathways.

Although NM accounts for 15% to 30% of all cutaneous melanomas, it comprises nearly half of all melanomas >2 mm in thickness.[6,7] This finding is thought to reflect their increased rate of growth and biologic aggressiveness compared with other subtypes, with a typical history of onset over several months compared with a few years for SSMs.[8,9] NMs often fail to fulfill the original ABCD diagnostic criteria, possibly contributing to their advanced stage at presentation.[10,11] Evidence in support of the distinct clinical behavior of NMs has also been demonstrated in data on sentinel lymph node (SLN) status, where NMs have been associated with a higher incidence of recurrence in the SLN basin compared with other subtypes.[12,13]

Given the higher proportion of NMs among thick tumors, previous studies have sought to better define their clinical presentation and biologic behavior in attempts to facilitate early detection. Several of these studies suffer limitations, including a small sample size,[11,14] the reporting of a few select parameters,[12,15] or the failure to provide follow-up information.[16] Our study represents the largest analysis of NMs from a single United States institution that we are aware of to date, and reports on both clinical and histopathologic features of these tumors. This comprehensive approach allows us to make specific recommendations impacting the early detection of NM.

MATERIALS AND METHODS

Patients

The study cohort was comprised of 2 groups of primary cutaneous melanoma patients who had been prospectively enrolled in the New York University Melanoma Cooperative Group (NYU-MCG). The earlier cohort was enrolled between November 1972 and November 1982, with follow-up until 1991. The second group of patients was enrolled between August 2002 and April 2007. From the years 1992 to 2002, there was no active enrollment or follow-up of patients in the melanoma program.

From the years 1972 to 1982, a total of 1143 patients (583 women and 560 men, median age of 53 years) diagnosed with 1170 primary melanomas were enrolled in the NYU-MCG. All patients within this registry were treated at NYU Medical Center. During this time, clinical and pathologic data were collected on a total of 415 fields, of which 21 were reviewed for purposes of this study. Data on melanoma features were also collected by the examining

physician, including an assessment of border regularity, first dominant color, second dominant color, color pattern, largest diameter (measured in millimeters), and elevation (measured in millimeters). At this time, patients also provided yes/no responses as to whether they had noted a change in the melanoma lesion, including whether there had been a change in size, elevation, or color. Patients also provided an estimate of the duration of melanoma (in months). All available pathologic slides were reviewed by 1 of 3 dermatopathologists at the time of patient enrollment, with central review of all cases performed by 1 dermatopathologist. The melanoma subtypes from this earlier time period included 812 SSMs, 126 NMs, 25 acral lentiginous melanomas, 60 lentigo maligna melanomas, 54 other, and 93 unknown. For purposes of this study, patients were restaged pathologically according to the sixth edition American Joint Committee on Cancer (AJCC) staging system.[17] Patients enrolled into the NYU-MCG during this time period gave verbal informed consent. Subsequent approval to use data from these patients was obtained from the NYU Institutional Review Board (IRB).

From the years 2002 to 2007, a total of 541 patients (232 women and 309 men, median age of 59 years) diagnosed with 564 primary melanomas were enrolled in the NYU Interdisciplinary Melanoma Cooperative Group. All patients within this registry were prospectively accrued and had received definitive treatment at NYU Medical Center. In this time period, clinical and pathologic data were collected on a total of 371 fields, of which 10 were reviewed for purposes of this study. Data on melanoma features were not collected in this time period. All available pathologic slides were centrally reviewed by 2 pathologists, 1 of whom reviewed all surgical pathology, and 1 of whom reviewed all dermatopathology. The melanoma subtypes in this cohort included 307 SSMs, 127 NMs, 14 acral lentiginous melanomas, 19 lentigo maligna melanomas, 38 other, and 59 unknown. All patients were staged pathologically according to the sixth edition AJCC staging system.[17] Prospective accrual of patients from August 2002 to present is approved by the NYU IRB, with written informed consent obtained at the time of enrollment.

In this study, only patients with a histopathologic diagnosis of either NM or SSM within both time periods were included, as these are the most common subtypes of invasive melanoma among the US population. Nodular melanomas were histologically defined as melanomas exclusively in the vertical growth phase, without evidence of an intraepidermal melanocytic proliferation beyond 3 epidermal ridges on either side of the tumor mass.[18] Differences between the features of NM and SSM within each time period as well as over time were compared with respect to age, sex, primary tumor thickness, anatomic site, Clark level, histologic ulceration, histologic regression, and pathologic stage. Mitotic rate was also assessed within each database; however, because the format in which these data were recorded differed between the 2 time periods (mitoses per mm^2 in the earlier time period vs categorical [0, ≤2, 3-5, or >5 mitoses/high-power field (HPF)] in the current time period), we could not make a direct comparison of mitotic rate across time. Lastly, we also compared data regarding the clinical features of NM and SSM that had been collected in the earlier time period only.

Statistical Analysis

Descriptive statistics were calculated for baseline demographic and clinicopathologic characteristics. To determine changes in NM and SSM over time, demographic and clinicopathologic features during both time periods were compared (separately for NM and SSM) using the Student *t* test, Wilcoxon rank sum test, or chi-square test, as appropriate. Differences between the features of NM and SSM within each time period were also analyzed using the tests referenced above. All *P* values are 2-sided, with statistical significance evaluated at the .05 alpha level. All analyses were performed in SAS Version 9.1 (SAS Institute Inc., Cary, NC) and SPSS Version 15.0 (SPSS Inc., Chicago, Ill).

RESULTS

Characteristics of the Early Cohort (1972-1982)

The earlier cohort consisted of 920 patients diagnosed with 126 NMs and 812 SSMs. Table 1 summarizes the noted differences in the demographic and histopathologic features of NMs and SSMs within this time period. A statistically significant difference between NMs and SSMs was observed with respect to primary tumor thickness, Clark level, ulceration, mitotic rate, regression, and stage distribution. Specifically, NMs presented as substantially thicker lesions compared with SSMs (median tumor thickness 3.2 mm for NM vs 1.1 mm for SSM; $P < .0001$, Wilcoxon test), and were more likely to be ulcerated ($P < .0001$, chi-square test) or invasive to Clark level IV or V ($P < .0001$, chi-square test). NMs also had a high mitotic rate, with the median number of mitoses per mm^2 for NMs more than double that of SSMs (2.5 vs 1.0; $P < .0001$, Wilcoxon test). Conversely, regression was more often a feature of SSMs compared with NMs ($P = .0002$, chi-square test). There were no observed differences between NMs and SSMs regarding age at diagnosis, sex, or anatomic site ($P = .69$, $P = .33$, $P = .09$, respectively, Wilcoxon test and chi-square test).

Characteristics of the Current Cohort (2002-2007)

The current cohort consisted of 425 patients diagnosed with 127 NMs and 307 SSMs. Table 1 summarizes differences in the demographic and histopathologic features of NMs and SSMs within the current time period. As in the earlier cohort, a statistically significant difference between NMs and SSMs was noted with respect to primary tumor thickness, Clark level, ulceration, mitotic rate, and stage distribution. Unlike the earlier time period, we observed a statistically significant increase in the age at diagnosis of NMs compared with SSMs ($P = .001$, Wilcoxon test). We found that NMs continued to present as thick lesions and were more often diagnosed with regionally advanced disease compared with SSMs ($P < .0001$, Wilcoxon test, $P < .0001$, chi-square test, respectively). NMs were also more mitotically active, with nearly 70% of NMs having either “moderate” (3-5 mitoses/HPF) or “many” (>5 mitoses/HPF) mitoses, whereas approximately 80% of SSMs had either “none” or “few” (≤2 mitoses/HPF; $P < .0001$, chi-square test) mitoses. In contrast to the earlier cohort, where regression was more often a feature of SSMs, we observed no differences between SSMs and NMs with respect to regression in the current time period ($P = .24$, chi-square test). There were also no differences in the sex distribution or anatomic site between NMs and SSMs ($P = .57$, $P = .75$, respectively, chi-square test).

Changes in the Presentation of SSMs and NMs Over 35 Years

The clinicopathologic features of SSMs within the 2 time periods are presented in Table 1. We found nearly a 50% reduction in the median thickness of SSMs over time (1.10 mm vs 0.60 mm; $P < .0001$, Wilcoxon test). This was consistent with an overall migration toward earlier stages of disease, with a 25% increase in the proportion of stage I disease across both time periods (68.8% vs 86.0%; $P < .0001$, chi-square test). Similarly, the proportion of SSMs that presented as Clark level IV or V decreased over time ($P = .02$, chi-square test). There was also a significant decrease in the percentage of ulcerated SSMs, but an increase in the proportion of tumors with histologic evidence of regression ($P < .0001$ and $P = .02$, respectively, chi-square test). A small but statistically significant increase in the median age at diagnosis as well as in the proportion of men with SSMs was also noted ($P < .0001$, Wilcoxon test; $P = .01$, chi-square test, respectively).

The clinicopathologic features of NMs within the 2 time periods are presented in Table 1. Although we observed a 25% reduction in the median thickness of NMs over time, this decrease was not statistically significant ($P = .10$, Wilcoxon test). Whereas the proportion of NMs with ulceration remained unchanged ($P = .30$, chi-square test), the percentage of NMs

invasive to Clark level IV or V increased over time ($P = .008$, chi-square test). The resulting stage distribution of NMs remained relatively constant over the 2 time periods, although a trend toward an increase in stage I disease was suggested ($P = .05$, chi-square test). We did detect a statistically significant increase in the median age at diagnosis of NMs over time (51 years vs 63 years; $P < .0001$, Wilcoxon test). The overall sex distribution of NMs was not significantly different between time periods, although an increase in the relative proportion of men diagnosed with NM over time was observed ($P = .28$, chi-square test).

Differences in Clinical Features Between NMs and SSMs

Table 2 presents the clinical features of NMs and SSMs within the earlier time period. NMs were more likely to exhibit border regularity compared with SSMs ($P = .004$, chi-square test), although the majority of lesions among both histologic subtypes had moderately irregular borders. The dominant color of NMs was black, compared with brown in SSMs ($P < .0001$, chi-square test), with the second dominant color being brown in NMs and light brown in SSMs ($P = .003$, chi-square test). Red was the dominant color in 13.5% of NMs, compared with 6.8% in SSMs. SSMs were more likely to present with color variegation compared with NMs ($P = .006$, chi-square test). Approximately 90% of both NM and SSM patients reported a change in the lesion before presentation, with approximately 54% of both NM and SSM patients reporting an increase in size of the lesion. A slightly higher percentage of NM patients reported a change in elevation or color compared with SSM patients ($P < .0001$, $P = .01$, respectively, chi-square test). The median duration of NMs as assessed by patient recall was 5 months, compared with 9 months in SSM patients ($P = .01$, t test). SSMs had a larger diameter, although NMs were more often elevated ($P = .01$, $P < .0001$, respectively, Wilcoxon test).

DISCUSSION

Our study provides evidence that advances in the early detection of melanoma have led to statistically significant and clinically relevant migration to earlier stages of disease at diagnosis for SSMs. Although these findings reflect data that have been generated through a hospital-based prospective database, our results are consistent with previous epidemiological studies using population-based registries, including the Surveillance, Epidemiology, and End Results (SEER) cancer registry.[6] In contrast, evidence of progress in the early diagnosis of NMs is lacking. In fact, the presenting clinical and histopathologic features of NM have not changed substantially over the last 30 years. Although we observed a 25% reduction in the median thickness of NMs over time, this did not amount to significant improvements in stage distribution.

To our knowledge, ours is the first study to report these findings based on data from a United States academic center. Although no change in the median tumor thickness of NM has been documented in the SEER registry from 1988 to 1999, data on other histopathologic features are not available for comparison.[6] Ulceration is a known poor prognostic feature of melanoma and, thus, can provide insight into the overall aggressiveness of melanoma. Considering that ulceration is more often a feature of thick tumors, the stable rate of ulcerated NMs detected across both time periods is another indication that limited progress has been made at diagnosing NMs at earlier stages in their progression. NMs were also found to be more proliferative than SSMs as assessed by the number of mitoses detected in these tumors. High mitotic rate has previously been associated with rapid tumor growth independent of thickness, as well as correlated with the NM subtype.[8,19] Some have also found mitotic rate to be a significant predictor of SLN positivity.[20,21] Thus, our data on mitotic rate lend further support to the distinct biologic behavior of NMs.

There is no clear explanation for the observed increase in NMs with regression across the 2 time periods. Several reports have commented on the lack of consistent criteria for defining regression, making the reproducibility of this finding potentially difficult.[22,23] The prognostic importance of regression has also been disputed, with a recent study reporting that patients with regression of the primary tumor had a better survival profile than those without regression.[24] Thus, it is difficult to comment on the implications of the increased rate of regression we observed in NMs over time.

We found that patients who develop NM tend to be significantly older compared with those who develop SSM. These findings are in support of a US population-based analysis where age-specific melanoma incidence rates were shown to have a bimodal distribution, with distinct early onset and late-onset peak frequencies at 54 and 74 years of age, respectively.[25] Although the specific age distribution of NMs was not presented in this referenced study, their data suggest that older patients are at significant risk for melanoma development. In a separate study of the SEER Registry, patients >60 years of age, in particular men, had the most precipitous increase in the incidence of thick melanomas ≥4 mm, nearly 50% of which were of the nodular subtype.[6,26] The association of older age and male sex with NM has also been documented in Australian-based registries.[16,27] Taken together, these results suggest that older male patients need to be carefully considered for secondary prevention efforts. The HARMM (History of previous melanoma, Age over 50, Regular dermatologist absent, Mole changing, Male sex) melanoma risk assessment model, an acronym derived from the American Academy of Dermatology Skin Cancer Screening Program Data from 2001 to 2005, identified both age >50 years (“A”) and male sex (“M”) as risk factors for melanoma development and suggests that targeted screening of this subgroup, especially those who tan poorly, may help to improve rates of melanoma detection.[28] The recognition of those at high risk for NM is critical, as the diagnosis of this melanoma subtype often presents a clinical challenge to dermatologists and general practitioners alike.

In this study, we found that NMs typically lacked the ABCD criteria, exhibiting a high degree of border regularity, a more uniform color pattern, with dominant colors of black and brown, and a smaller diameter compared with SSMs. Chamberlain et al, in their assessment of the presenting features of NMs within an Australian registry, also noted that these tumors were more likely to be symmetric and elevated in comparison to SSMs. However, in their study, the predominant color of NMs was pink, with 60.6% of NM patients reporting no evidence of pigmentation within the lesion.[11] Given these discordant data, it seems reasonable to conclude that although NMs in the United States are more likely to be amelanotic compared with SSMs, it is not uncommon for these tumors to present as black or brown pigmented lesions. Although the specific changes that NMs undergo before presentation can also be disputed, it is important to emphasize that any change in a persistent pigmented or nonpigmented lesion warrants further attention.[11,29] In our study alone, >90% of NM patients reported a history of change in the lesion, lending clinical relevance to evolving, or the “E” criterion, in the ABCDE acronym for the early diagnosis of melanoma.[30] It must also be emphasized that the time over which this change occurs is typically shorter for NMs than for SSMs.[11] Consistent with this, we found that the median duration of NMs was only 5 months compared with 9 months for SSMs, suggesting that the clinically aggressive biology of these tumors, rather than delays in seeking medical attention, may account for their advanced thickness. Given this rapid rate of growth, the implementation of self-detection strategies, including education on how to perform skin self-examinations, becomes critically important as a means of secondary prevention for NM.[31]

Although the traditional classification of melanoma by histopathologic subtype has been criticized for its lack of independent prognostic value, our data demonstrate the distinct clinical behavior among melanoma subtypes. These findings should not be ignored when

considering the adoption of newer classification strategies for melanoma. Furthermore, our group has recently demonstrated that NMs are associated with increased shedding of collagen epitope HU177 into the blood compared with other subtypes, independent of tumor thickness.[5] In support of these findings, a recent gene expression study of melanoma identified a characteristic gene expression profile unique to NM.[3] Still others have shown that the proto-oncogene *hPTTG1* (human pituitary tumor-transforming gene 1) is differentially overexpressed in NMs, a finding that remained significant when controlling for tumor thickness.[32] Recognized limitations in adequately addressing the biologic behavior of melanomas with distinct histopathologic subtypes are largely inconsistent reporting and the lack of a universal classification system. In the SEER database alone, over 30% of melanomas lack a designated histopathologic subtype.[6] Although some authors debate the existence of fundamental histopathologic differences among melanoma subtypes, to facilitate future correlative studies, we support the continued classification of melanoma by histopathologic subtype and encourage its reporting by all dermatopathologists.[33] Further research efforts directed toward improving our understanding of the etiology and underlying biologic properties of melanoma subtypes are also warranted.

Over the last few years, newer classification strategies focused on the underlying biology of melanoma, with an emphasis on the categorization of distinct genetic alterations, have been proposed. Specifically, differences in chromosomal aberrations and mutation frequencies have been documented in melanomas based on the extent of sun exposure and anatomic site. For example, melanomas on skin without chronic sun-induced damage have been shown to have frequent mutations in *BRAF* and losses of chromosome 10, whereas melanomas on skin with chronic sun-induced damage, mucosal membranes, or acral skin have a low rate of *BRAF* mutation but frequent oncogenic mutations and/or copy number increases in *KIT*.[34,35] Although it has yet to be determined whether this classification of melanomas based on ultraviolet light exposure and anatomic site can accurately stratify patients into prognostic groups, this strategy may prove to be clinically useful in selecting patients for targeted therapeutic interventions. Moving forward, classification systems will likely evolve to integrate tumor genetics with histopathologic findings, thus providing both practical and clinically relevant information.[36]

We recognize that our study does not include information on patients diagnosed with melanoma in the 1990s, a time when we were not actively recruiting patients into our melanoma registries. Nevertheless, we believe that our conclusions are valid, as they are based on a large-scale, comprehensive prospective database. We also realize that the incidence of NM at our institution is higher than that typically reported in the literature; however, our results are largely consistent with those of the SEER registry, including a similar median thickness for NM, which suggests that misdiagnosis or discrepancies in dermatopathologic expertise were less of a concern in our study.[6] We also acknowledge the possibility that our observation of an increasing age at diagnosis of NM patients might be confounded by possible changing referral patterns over time. However, the fact that these findings have also been reported in analyses of Australian-based registries lends support to our observations.[16,27]

In conclusion, NM presents with aggressive histological features and at advanced stages of disease. Targeted screening of older patient populations, with an emphasis on men, is critical if melanoma mortality rates are to be impacted. Healthcare practitioners need to be vigilant for these aggressive melanomas and should perform total cutaneous examinations in this high-risk group. Considering that NMs often fail to exhibit the ABCD criteria, alerting patients to the significance of evolution within a lesion, the “E” criterion, may serve as a more effective means of early melanoma recognition in this patient population.

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TABLE 1

Characteristics of Superficial Spreading Melanoma and Nodular Melanoma Within Each Time Period and Over Time

	Years 1972-1982			Years 2002-2007			Changes Between 1972-1982 and 2002-2007	
Characteristic	**SSM, No. (%)**	**NM, No. (%)**	***P***	**SSM, No. (%)**	**NM, No. (%)**	***P***	**SSM, *P***	**NM, *P***
Age (y, median)	51	51	.69	56	63	.001	<.0001	<.0001
Sex (men, women)	380 (48), 415 (52)	66 (52), 60 (48)	.33	168 (56), 131 (44)	74 (59), 51 (41)	.57	.01	.28
Thickness (mm, median)	1.1	3.2	<.0001	0.6	2.4	<.0001	<.0001	.10
Clark's level								
I	32 (4.0)	0 (0.0)	<.0001	0 (0.0)	0 (0.0)	<.0001	.02*	.008*
II	235 (29.1)	0 (0.0)		119 (40.2)	1 (0.9)			
III	227 (28.1)	21 (17.1)		74 (25.0)	6 (5.2)			
IV	293 (36.2)	89 (72.4)		102 (34.5)	93 (80.2)			
V	22 (2.7)	13 (10.6)		1 (0.3)	16 (13.8)			
Ulceration present	145 (18.2)	58 (47.2)	<.0001	17 (5.7)	50 (40.7)	<.0001	<.0001	.30
Regression present	166 (26.2)	4 (5.8)	.0002	96 (33.5)	30 (27.3)	.24	.02	.0004
Mitoses (per mm^2, median)	1.0	2.5	<.0001					
None				86 (31.6)	5 (4.8)	<.0001		
Few (≤2 mitoses/HPF)				132 (48.5)	27 (25.7)			
Moderate (3-5 mitoses/HPF)				27 (9.9)	23 (21.9)			
Many (>5 mitoses/HPF)				27 (9.9)	50 (47.6)			
Stage								
I	524 (68.8)	27 (22.0)	<.0001	264 (86.0)	43 (33.9)	<.0001	<.0001	.05
II	163 (21.4)	61 (49.6)		28 (9.1)	56 (44.1)		<.0001	.46
III	71 (9.3)	33 (26.8)		15 (4.9)	28 (22.1)		.02	.46
IV	4 (0.5)	2 (1.6)		0 (0.0)	0 (0.0)		.48	.46

SSM indicates superficial spreading melanoma; NM, nodular melanoma; HPF, high-power field.

*Denotes the change over time in the proportion of melanomas presenting as Clark level IV or V.

TABLE 2

Clinical Features of Superficial Spreading and Nodular Melanoma

Clinical Features	Superficial Spreading, n=812, No. (%)	Nodular, n=126, No. (%)	*P*
Border regularity			
Regular	243 (29.9)	48 (38.1)	.004
Moderately irregular	435 (53.6)	70 (55.6)	
Very irregular	94 (11.6)	3 (2.4)	
Unknown	40 (4.9)	5 (4.0)	
First dominant color			
Black	254 (31.3)	54 (42.9)	<.0001
Brown	384 (47.3)	33 (26.2)	
Red	55 (6.8)	17 (13.5)	
Other	107 (13.2)	20 (15.9)	
Unknown	12 (1.5)	2 (1.6)	
Second dominant color			
Black	113 (13.9)	6 (4.8)	.003
Brown	131 (16.1)	25 (19.8)	
Light brown	143 (17.6)	11 (8.7)	
Red	49 (6.0)	9 (7.1)	
Other	84 (10.3)	19 (15.1)	
None	292 (36.0)	56 (44.4)	
Unknown	0 (0)	0 (0)	
Color pattern			
Uniform	248 (30.5)	54 (42.9)	.006
Variegated	544 (67.0)	69 (54.8)	
Unknown	20 (2.5)	3 (2.4)	
Change in lesion			
Yes	680 (83.7)	116 (92.1)	.06
No	102 (12.6)	9 (7.1)	
Unknown	30 (3.7)	1 (0.80)	
Change in size			
Decrease	9 (1.1)	4 (3.2)	.21
Increase	439 (54.1)	69 (54.8)	
No change	305 (37.6)	49 (38.9)	
Unknown	59 (7.3)	4 (3.2)	
Change in elevation			
Increase	400 (49.3)	95 (75.4)	<.0001
Decrease	16 (2.0)	1 (0.80)	
No change	357 (44.0)	28 (22.2)	
Unknown	39 (4.8)	2 (1.6)	
Change in color			
Yes	419 (51.6)	81 (64.3)	.01

Clinical Features	Superficial Spreading, n=812, No. (%)	Nodular, n=126, No. (%)	*P*
No	333 (41.0)	38 (30.2)	
Unknown	60 (7.4)	7 (5.6)	
Duration of melanoma, mean, median (mo)	27.9, 9.0	25.3, 5.0	.004
Largest diameter, mean, median (mm)	18.3, 15.0	14.8, 12.0	.01
Elevation, mean, median (mm)	2.2, 1.0	4.2, 3.5	<.0001