Published in final edited form as:

Br J Dermatol. 2015 December ; 173(6): 1486–1493. doi:10.1111/bjd.14035.

Cross-Sectional Analysis of the Dermoscopic Patterns and Structures of Melanocytic Naevi on the Back and Legs of Adolescents

M. Fonseca^{#1}, M.A. Marchetti^{#1}, E. Chung¹, S.W. Dusza¹, M.E. Burnett¹, A.A. Marghoob¹, A.C. Geller², M. Bishop¹, A. Scope^{1,3}, and A.C. Halpern¹

¹Dermatology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, 16 E. 60th Street, New York, NY 10022, U.S.A.

²Harvard School of Public Health, Social and Behavioral Sciences, Boston, MA, U.S.A.

³Department of Dermatology, Sheba Medical Center, Sackler School of Medicine, Tel Aviv University, Tel Aviv 52621, Israel.

[#] These authors contributed equally to this work.

Abstract

Background—Junctional (flat) naevi predominate on the extremities whereas dermal (raised) naevi are primarily found on the head, neck, and trunk. Few studies have investigated the anatomic site prevalence of melanocytic naevi categorized using dermoscopy.

Objectives—To identify the prevalence of dermoscopic patterns and structures of naevi from the back and legs of adolescents.

Methods—Dermoscopic images of melanocytic naevi were obtained from the back and legs of students from a population-based cohort in Framingham, Massachusetts. Naevi were classified into reticular, globular, homogenous, or complex dermoscopic patterns. Multinomial logistic regression modeling assessed the associations between dermoscopic pattern and anatomic location.

Results—A total of 509 participants (mean age 14 years) contributed 2,320 back naevi and 637 leg naevi. Compared to homogeneous naevi, globular and complex naevi were more commonly observed on the back than the legs (OR=29.39, 95% CI 9.53-90.65, $p<0.001$ and OR=6.8, 95% CI 2.7-17.14, $p<0.001$, respectively), whereas reticular lesions were less likely to be observed on the back than the legs (OR=0.67, 95% CI 0.54-0.84, $p=0.001$). Naevi containing any globules were more prevalent on the back than the legs (25% v. 3.6%, $p<0.001$). Naevi containing any network were more prevalent on the legs than the back (56% v. 40.6%, $p<0.001$).

Conclusions—These findings add to a robust body of literature suggesting that dermoscopically defined globular and reticular naevi represent biologically distinct naevus subsets that differ in

Corresponding Author: Michael A. Marchetti. Dermatology Service, Memorial Sloan Kettering Cancer Center, 16 E. 60th Street, New York, NY 10022, U.S.A. Telephone: 646-888-6016. Fax: 646-227-7274. marchetm@mskcc.org.

Conflicts of Interest: The authors report no financial or personal conflicts of interest.

histopathologic growth pattern, age- and anatomic-site related prevalence, molecular phenotype, and aetiologic pathways.

Introduction

Naevi are among the strongest phenotypic markers of cutaneous melanoma risk.¹ Numerous studies have demonstrated that total body naevus counts increase during childhood and adolescence, making these critical time periods for studying naevogenesis.²⁻⁸ Understanding the normal patterns and anatomic distribution of naevi may be important to understanding the biologic mechanisms driving naevus growth.

Histopathologic classification of melanocytic naevi has previously identified that naevi on the extremities are primarily junctional naevi, and that dermal naevi are mostly found on the head and neck.⁹ Using the classification described by Ackerman and Magana-Garcia¹⁰, Schmoekel et al found that Miescher's naevi are most common on the head and neck, Unna's naevi predominate on the trunk, and flat naevi are almost exclusively found on the trunk and extremities.¹¹ Lund and Stobbe found that histologically-defined "bulky" naevi were located mainly on the head, neck, and trunk but that "narrow stratified" naevi predominated on the extremities and showed a distinct proximal to distal gradient, being most frequent on the distal extremities.¹² These observations, along with other clinical, epidemiologic, and histopathologic findings, have contributed to contradictory theories regarding naevogenesis, including Unna's "Abtropfung" (downward dropping of melanocytes from the epidermis to dermis) and Cramer's "Hochsteigerung" (upward migration of melanocytes from the dermis to epidermis).^{13, 14}

Studies incorporating the use of dermoscopy have found that among congenital melanocytic naevi, a reticular dermoscopic pattern predominates on the extremities whereas a globular pattern is most frequent on the trunk.^{15, 16} Gamo et al performed a cross-sectional analysis of the anatomic site distribution of naevi in adult patients with the atypical naevus syndrome. In this study, which was limited by sample size and inclusion criteria, a majority of leg naevi showed either reticular or homogenous dermoscopic patterns and globular naevi were more frequently observed on the back relative to the legs.¹⁷ No study to date has systematically studied the distribution of the dermoscopic patterns of melanocytic naevi in the general population.

The Study of Naevi in Children (SONIC) is the first population-based study to document the dermoscopic and clinical evolution of naevi over time.¹⁸⁻²² We previously reported that globular naevi occur more frequently on the upper back than the lower back, whereas reticular and homogenous naevi show no distribution gradient.²³ Here, we expand our anatomic site analysis to include the legs in order to further identify differences in the dermoscopic patterns and structures of naevi from adolescents stratified by anatomic site.

Materials and Methods

Institutional Review Board approval for this study was obtained in accordance with the Helsinki Declaration. SONIC is a population-based study exploring the constitutional and behavioral factors associated with naevus phenotype in children.¹⁸⁻²⁷ Details on participant

and data collection procedures have been described previously.²⁰ Briefly, the study population included students in the graduating classes of 2012, 2014, and 2015 from a single high school in the Framingham, Massachusetts school system. A list of all eligible participants was obtained from the school system during the 8th (classes 2014, 2015) or 9th grade (class 2012). Mailings were sent to all families, requesting participation and including a description of the study, consent, and assent form. Consented participants underwent skin examination and digital photography of the back and legs in the spring months.

For this study, participants had clinical overview images of their back and legs taken as well as clinical close-up and contact, non-polarized dermoscopic images of select back and leg naevi. Up to 6 back naevi were imaged per participant. The largest naevus and up to 2 random naevi were selected from both the upper and lower back, if present. The upper back was defined as the area from the nape of the neck to the bilateral acromion processes to the level of the lower tips of the scapulae. The lower back was defined as the area bordered by the lower tips of the scapulae superiorly and the posterior iliac crests inferiorly. Leg naevi were chosen similarly, with up to 6 leg naevi imaged per participant; the largest naevus and up to 2 random naevi selected from both the upper and lower leg, if present. Due to time constraints imposed by the school, naevi from only one randomly selected leg were imaged. The upper third of the thigh marked the superior border, the ankle the inferior border, and the popliteal fossa the boundary between upper and the lower leg.

Dermoscopic images were obtained using a Fuji S2 SLR digital camera and 60 mm Macro Nikkor lens with Epi-Lume dermoscopy attachment (Canfield Scientific, Inc., Fairfield, NJ, U.S.A.). A contact liquid medium was used during dermoscopic imaging. Images were stored in Mirror™ software, a clinical imaging database that permits a resolution of 3 million pixels (Canfield Scientific, Inc.). Naevus counts were performed semi-automatically using a colour-based segmentation method and Seg3D²⁸, an open-source manual mark-up software tool. Dermoscopic assessments were performed on high-resolution monitors jointly by two trained observers (M.F. and M.M.) for consensus agreement. Observers reviewed the dermoscopic images blinded to anatomic location. Lesions were assessed for global dermoscopic pattern and grouped into 1 of 4 categories: (1) primarily reticular: a distinct pigment network was present with <3 globules; (2) primarily globular: 3 globules were present without a pigment network; (3) homogenous: tan, brown, blue, or pink structureless lesion with neither a pigment network nor 3 globules present; and (4) complex: both network and 3 globules were present, with or without structureless areas. Furthermore, any naevus with a distinct peripheral rim of globules or starburst pattern was classified into the complex category. Globules were defined as symmetric, round to oval, well-demarcated structures with a diameter >0.1 mm. The presence of any network, globules, or dots was also recorded (yes, no). Each naevus was categorized as raised or flat. Non-lesional normal appearing skin surrounding each naevus was assessed for background skin pattern in each dermoscopic image.²¹ These patterns were categorized as previously described: reticular (brown or black pigmented network in background skin); globular (brown to grey round structures dispersed at a variable density in the background skin); reticular/globular (having both pigmented network and round structures in the background skin); or no apparent pattern in the background skin.²¹

Naevus surface area was calculated from dermoscopic images using an open-source manual mark-up software tool and colour-based segmentation method.²⁸ Lesion borders were visually identified. The number of pixels in the circumscribed area was obtained and converted to square millimeters. Concordance for lesion measurements between reviewers has previously been shown to be high ($\rho=0.96$).²⁰

A study nurse assessed participant characteristics on the day of imaging. Sex and race/ethnicity data were obtained from the Framingham School District. Recent sun exposure was assessed via survey. Participants were asked: "On a typical day during the week in the past summer, how many hours did you spend outside?" The same question was asked regarding weekend exposure. A composite variable was created to quantify total outdoor exposure for a typical week by combining weekday and weekend responses for each participant by their relative contributions. This composite variable was further categorized into low, medium, and high levels of exposure by creating cut points at tertiles of the distribution.

Descriptive statistics were used to characterize the study population. Descriptive frequencies were calculated to assess the distribution of student and naevus characteristics. Mean naevus log area was calculated by taking the natural logarithm (i.e., logarithm to base 10) of the surface area of each nevus and determining the mean. Agreement between reviewers for dermoscopic pattern was assessed with Cohen's κ . Pearson's χ^2 statistics were used to compare lesion dermoscopic characteristics by anatomic location (back v. leg). Stratified, random effects logistic regression models were used to assess the association between anatomic location and dermoscopic characteristics for reticular, globular and homogeneous lesions. Multinomial logistic regression was used to assess the association between dermoscopic pattern and location, while controlling for participant phenotypic characteristics and sun exposure. The dependent variable for these analyses was lesion dermoscopic pattern coded on four levels (reticular, globular, homogeneous and complex), with homogenous lesions acting as the referent category. The main independent variable was anatomic location, coded as a dichotomous variable with leg lesions coded as 0 and back lesions coded as 1. Since participants contributed multiple lesions to the analysis, standard error estimates were adjusted for intraclass correlation. Participant characteristics and lesion dermoscopic characteristics were evaluated for inclusion. Odds ratio (OR) estimates along with 95% confidence intervals (CI) are presented. All analyses were carried out using Stata v.12.1 software (Stata Corp., College Station, TX).

Results

The study included 509 consented participants [mean age ($\pm$ SD) =14 years, 5 months ($\pm$ 8 months)]. The consent rate was 29% of the eligible students. Sixty-three percent of participants (n=319) were male and 89% (n=452) were non-Hispanic White. Demographic and phenotypic characteristics of the study population are depicted in Table 1. A spectrum of hair and skin pigment phenotypes was observed in the study population.

A total of 3,253 lesions were imaged, of which 9.1% (n=296) were excluded because they were either not naevi [n=284 (8.7%), including lentigines and acneiform lesions] or because of poor image quality [n=12 (0.4%)]. In sum, 2,957 naevi from the back (n=2,320) and legs

(n=637) were included in the study. The primary reason for the sample size differences was that nevi were more prevalent on the back than on the legs. Of all naevi included in the study, 41.4% (n=1,224) were reticular, 12.2% (n=360) globular, 42.3% (n=1,250) homogenous, and 4.2% (n=123) complex (Table 2). On the back, 42% (n=977) were homogenous, 37% (n=868) reticular, 15% (n=357) globular, and 5% (n=118) complex. On the legs, 43% (n=273) were homogenous, 56% (n=356) reticular, <1% (n=3) globular, and <1% (n=5) complex. Agreement between reviewers for dermoscopic pattern was assessed on a random subset of lesions (n=302) and was high ($\kappa=0.77$).

On the back, race, hair colour, and skin colour were significantly associated with the relative frequency of reticular, globular, homogenous, and complex naevi (all $p<0.001$); Hispanic ethnicity, darker hair color (dark brown to black) and darker skin color were associated with relatively higher percentage of reticular back naevi and lower percentage of homogenous back naevi than non-Hispanic Whites, lighter hair and skin colors, respectively (Table 3). On the legs, skin color was also significantly associated with naevus dermoscopic patterns ($p=0.015$), with darker skin color having higher percentage of reticular naevi and lower percentage of homogenous naevi than lighter skin color. Tendency to sunburn and outdoor sun exposure were not associated with naevus dermoscopic patterns.

Lesion-level dermoscopic features by anatomic location are shown in Table 4. The presence of any network in a lesion was higher on the legs v. back (56% v. 40.6%, $p<0.001$) whereas the presence of any globules was higher on the back v. legs (25% v. 3.6% $p<0.001$). Dots were more commonly present in back lesions than leg lesions (44.7% v. 20.6%, $p<0.001$). The presence of a background skin pattern was more common on the back v. legs (42.3% v. 11.8%, $p<0.001$); among 981 naevi showing a pattern in the surrounding skin, reticular pattern was most prevalent (61%), followed by globular (25%), and reticular/globular (14%). Naevi on the back were more likely to be raised than naevi on the legs. The mean surface area of back naevi was larger than leg naevi (6.4mm² v. 4.9mm², $p<0.001$). No differences in naevus mean surface area by gender and anatomic site were observed, with male and female back naevi measuring 6.6mm² v. 6.2mm² ($p=0.49$) and male and female leg naevi measuring 4.9mm² v. 4.8mm² ($p=0.18$), respectively.

Using homogenous naevi as a referent group in multinomial logistic regression modeling, reticular naevi were less likely to occur on the back (OR 0.67, 95% CI 0.54-0.84, $p=0.001$) and globular naevi were more likely to occur on the back (OR 29.39, 95% CI 9.53-90.65, $p<0.001$) (Table 5). Reticular naevi were also less likely to be raised (OR 0.08, 95% CI 0.04-0.17, $p<0.001$) and to occur in lighter individuals (OR 0.46, 95% CI 0.34-0.62, $p<0.001$). Globular and complex naevi were more likely to be larger in size than homogenous naevi (OR 1.86, 95% CI 1.52-2.27, $p<0.001$ and OR 2.25, 95% CI 1.72-2.94, $p<0.001$, respectively).

There were no significant differences in the mean log lesion area of reticular, globular, and complex naevi by anatomic site, although small sample sizes of globular and complex naevi on the legs preclude a meaningful comparison for these subtypes (Figure 1). The mean log lesion area of homogenous naevi from the back was significantly greater than the legs (1.64mm² v. 1.48mm², $p=0.001$).

Discussion

We report the prevalence of the dermoscopic patterns of back and leg naevi in 8th and 9th grade adolescents and show a distinct anatomic distribution of globular and reticular naevi. Globular naevi are significantly more likely to be found on the back than the legs whereas reticular naevi predominate on the legs compared to other dermoscopic patterns. This data adds to a growing, robust body of literature suggesting that reticular and globular naevi represent biologically distinct naevus subsets that differ in histopathologic growth pattern, age- and anatomic-site related prevalence, growth characteristics, molecular phenotype, and aetiologic pathways,^{20, 23, 29-32} and not simply different stages in the life cycle of a nevus, as suggested by the “Abtropfung” and “Hochsteigerung” theories of Unna and Cramer, respectively.

Naevus development follows an arc-like trajectory; naevus counts begin to increase in childhood, plateau in the 4th decade, and then decrease steadily thereafter.^{31, 33-38} Dermoscopy studies have demonstrated that globular naevi are more common in children whereas reticular naevi are more common in adults.^{17, 31} We have previously shown that globular naevi occur more frequently on the upper back than the lower back but that reticular and homogenous naevi show no site predilection on the back. Prospective longitudinal follow-up of individual reticular and globular naevi has demonstrated that the dermoscopic classification of these naevi is stable from childhood through adolescence.²⁰

The age and anatomic differences observed in naevus dermoscopic patterns has led to suggestions that naevogenesis occurs by at least two distinct pathways.^{23, 39, 40} In the ‘constitutional’ pathway of naevogenesis, globular naevi have been suggested to derive from melanoblasts, which migrate from the neural crest to the skin in a sequence of cephalo-caudal, dorsal-ventral, and proximal-to-distal directions.⁴¹⁻⁴³ Melanoblasts first localize to the dermis at about 6-8 weeks post-fertilization, and migrate into the epidermis at 12-17 weeks.^{41, 42, 44, 45} A delay or arrest in this sequence may cause melanoblasts to remain in the dermis and in more proximal anatomic sites accounting for the clinically-observed cephalad to caudal distribution of globular naevi. This theory of arrest is supported by the fact that globular naevi histologically correspond to a predominantly dermal growth pattern^{30, 46} and by the identification of melanocytes expressing melanoblast markers in the dermis.⁴²

In contrast, reticular naevi are suggested to originate from epidermal melanocytes through an ‘acquired’ pathway, possibly as a response to intermittent ultraviolet radiation (UVR).⁴⁷ The discovery that melanocyte precursors migrate to their final destination in the skin through not only a dorsolateral route as melanoblasts but also a ventral route as Schwann cell precursors suggests the possibility of biologically-unique melanocyte populations.⁴⁸ We have previously shown a molecular differences in these naevus subsets with globular naevi more than three times likely to express BRAF V600E than reticular naevi (86.7% v. 20%, $P = 0.002$).³⁰

Regional variations in background skin anatomy may play an important role in the observed differences in dermoscopic patterns of naevi.⁴⁹⁻⁵¹ For example, the rete ridge pattern of the epidermis is reflected in the pigment network, whose lines are delineated by the melanin

distribution within the keratinocytes and melanocytes.⁴⁹ The morphology of rete ridges has been shown to vary among different anatomic sites; rete ridges from the lower extremities are shorter whereas back skin has well-developed, deep epidermal ridges.^{52, 53}

Phenotype-related differences are evident in the distribution of dermoscopic patterns among this cohort. We previously reported that naevi with a distinct dermoscopic pattern (reticular, globular or complex naevi) were 2.4 times more likely to be found among dark-skinned children.²⁰ In this study, we found that darker phenotypes were more likely to have reticular naevi when compared to lighter phenotypes, which supports our previous findings. These data support the notion that there may be an underlying genetic basis for the association of pigmentation and naevus pattern. It has been postulated that such pattern of naevus development may reflect the increased constitutive activity of melanocytes and possible greater transfer of melanin to keratinocytes.²³

Multiple limitations exist in our study. First, the majority of participants were White and our study may not be generalizable to other racial groups. In addition, morphological characteristics of the naevi presented here are not established with histopathologic examination. Imaging of naevi occurred in spring during a prolonged period of low UVR intensity at this latitude. It is well established that UVR exposure leads to dermoscopic changes in naevi, including darkening, increase in dots/globules, regression, blurred pigment network, and increased vascularity.⁵⁴ Therefore, our results may not be applicable to populations that live in areas with different UVR exposure levels. Low UVR exposure may also be a potential contributing factor to the higher prevalence of homogenous naevi observed in our study cohort compared to other study cohorts.⁵⁵⁻⁵⁷ While measures of solar exposure were ascertained in participants, temporal differences in UVR exposure across anatomic sites were not estimated.

In addition, dermoscopic imaging was not performed using polarized dermoscopy, which limits comparison of our results to studies using this technique. Only a select subset of back and leg naevi were imaged and our findings may not be representative of all naevi present at these anatomic sites. Randomization in the selection of naevi was used to minimize such selection bias. Naevi on the upper third of the thigh were not imaged due to privacy concerns, which may have led to lower prevalence estimates of globular and complex naevi on the legs. Finally, there is no universally accepted dermoscopic definition of the distinguishing characteristics between dots and globules. As the morphologic differences in naevi located at different anatomic sites are partially determined by differences in underlying microanatomy, we cannot exclude the possibility that globules present in naevi on the lower extremity are smaller in size, which may have led to misclassification. In vivo non-invasive molecular techniques may someday permit better characterization of naevus subsets, including more refined definitions of their clinical, dermoscopic, and confocal appearance.^{58, 59}

In conclusion, we found that globular and reticular naevi have a distinct anatomical distribution in adolescents. Globular naevi show a cephalad to caudal distribution, which recapitulates the pattern of melanoblast migration during embryogenesis. The predominant pattern of leg naevi is reticular. This data supports previous findings suggesting that globular

and reticular naevi are biologically distinct, which may have strong implications for the progression of naevi to melanoma. Future studies on the genotypic differences among these naevi and the regional variations of skin may provide further insight into the biologic basis of these subsets.

Acknowledgments

Funding Sources: Research reported in this publication was supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health under Award Number R01-AR049342 as well as the National Institute of General Medical Sciences of the National Institutes of Health under grant number P41GM103545. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

1. Gandini S, Sera F, Cattaruzza MS, et al. Meta-analysis of risk factors for cutaneous melanoma: I. Common and atypical naevi. *Eur J Cancer*. 2005; 41:28–44. [PubMed: 15617989]
2. Harrison SL, MacLennan R, Speare R, et al. Sun exposure and melanocytic naevi in young Australian children. *Lancet*. 1994; 344:1529–32. [PubMed: 7983952]
3. Green A, Siskind V, Green L. The incidence of melanocytic naevi in adolescent children in Queensland, Australia. *Melanoma Res*. 1995; 5:155–60. [PubMed: 7640516]
4. Siskind V, Darlington S, Green L, et al. Evolution of melanocytic nevi on the faces and necks of adolescents: a 4 y longitudinal study. *J Invest Dermatol*. 2002; 118:500–4. [PubMed: 11874490]
5. Milne E, Simpson JA, English DR. Appearance of melanocytic nevi on the backs of young Australian children: a 7-year longitudinal study. *Melanoma Res*. 2008; 18:22–8. [PubMed: 18227704]
6. Luther H, Altmeyer P, Garbe C, et al. Increase of melanocytic nevus counts in children during 5 years of follow-up and analysis of associated factors. *Arch Dermatol*. 1996; 132:1473–8. [PubMed: 8961877]
7. Bauer J, Buttner P, Wiecker TS, et al. Risk factors of incident melanocytic nevi: a longitudinal study in a cohort of 1,232 young German children. *Int J Cancer*. 2005; 115:121–6. [PubMed: 15645451]
8. English DR, Milne E, Simpson JA. Ultraviolet radiation at places of residence and the development of melanocytic nevi in children (Australia). *Cancer Causes Control*. 2006; 17:103–7. [PubMed: 16411059]
9. Winkelmann RK, Rocha G. The dermal nevus and statistics. An evaluation of 1,200 pigmented lesions. *Arch Dermatol*. 1962; 86:310–5. [PubMed: 14007520]
10. Ackerman AB, Magana-Garcia M. Naming acquired melanocytic nevi. Unna's, Miescher's, Spitz's Clark's. *Am J Dermatopathol*. 1990; 12:193–209. [PubMed: 2184692]
11. Schmoeckel C. Classification of melanocytic nevi: do nodular and flat nevi develop differently? *Am J Dermatopathol*. 1997; 19:31–4. [PubMed: 9056651]
12. Lund HZ, Stobbe GD. The natural history of the pigmented nevus; factors of age and anatomic location. *Am J Pathol*. 1949; 25:1117–55. incl 4 pl. [PubMed: 15392467]
13. Worret WI, Burgdorf WH. Which direction do nevus cells move? Abtropfung reexamined. *Am J Dermatopathol*. 1998; 20:135–9. [PubMed: 9557780]
14. Krengel S. Nevogenesis--new thoughts regarding a classical problem. *Am J Dermatopathol*. 2005; 27:456–65. [PubMed: 16148419]
15. Changchien L, Dusza SW, Agero AL, et al. Age- and site-specific variation in the dermoscopic patterns of congenital melanocytic nevi: an aid to accurate classification and assessment of melanocytic nevi. *Arch Dermatol*. 2007; 143:1007–14. [PubMed: 17709659]
16. Seidenari S, Pellacani G, Martella A, et al. Instrument-, age- and site-dependent variations of dermoscopic patterns of congenital melanocytic naevi: a multicentre study. *Br J Dermatol*. 2006; 155:56–61. [PubMed: 16792752]

17. Gamo R, Malvey J, Puig S, et al. Dermoscopic features of melanocytic nevi in seven different anatomical locations in patients with atypical nevi syndrome. *Dermatol Surg*. 2013; 39:864–71. [PubMed: 23464729]
18. Oliveria SA, Geller AC, Dusza SW, et al. The Framingham school nevus study: a pilot study. *Arch Dermatol*. 2004; 140:545–51. [PubMed: 15148098]
19. Oliveria SA, Satagopan JM, Geller AC, et al. Study of Nevi in Children (SONIC): baseline findings and predictors of nevus count. *Am J Epidemiol*. 2009; 169:41–53. [PubMed: 19001133]
20. Scope A, Dusza SW, Marghoob AA, et al. Clinical and dermoscopic stability and volatility of melanocytic nevi in a population-based cohort of children in Framingham school system. *J Invest Dermatol*. 2011; 131:1615–21. [PubMed: 21562569]
21. Scope A, Marghoob AA, Chen CS, et al. Dermoscopic patterns and subclinical melanocytic nests in normal-appearing skin. *Br J Dermatol*. 2009; 160:1318–21. [PubMed: 19416274]
22. LaVigne EA, Oliveria SA, Dusza SW, et al. Clinical and dermoscopic changes in common melanocytic nevi in school children: the Framingham school nevus study. *Dermatology*. 2005; 211:234–9. [PubMed: 16205068]
23. Scope A, Marghoob AA, Dusza SW, et al. Dermoscopic patterns of naevi in fifth grade children of the Framingham school system. *Br J Dermatol*. 2008; 158:1041–9. [PubMed: 18363751]
24. Dusza SW, Halpern AC, Satagopan JM, et al. Prospective study of sunburn and sun behavior patterns during adolescence. *Pediatrics*. 2012; 129:309–17. [PubMed: 22271688]
25. Oliveria SA, Scope A, Satagopan JM, et al. Factors Associated with Nevus Volatility in Early Adolescence. *J Invest Dermatol*. 2014
26. Dusza SW, Oliveria SA, Geller AC, et al. Student-parent agreement in self-reported sun behaviors. *J Am Acad Dermatol*. 2005; 52:896–900. [PubMed: 15858486]
27. Geller AC, Oliveria SA, Bishop M, et al. Study of health outcomes in school children: key challenges and lessons learned from the Framingham Schools' Natural History of Nevi Study. *J Sch Health*. 2007; 77:312–8. [PubMed: 17600588]
28. Institute SCAI. “Seg3D” Volumetric Image Segmentation and Visualization.. Scientific Computing and Imaging Institute (SCI). Available from: <http://www.seg3d.org>
29. Zalaudek I, Grinschgl S, Argenziano G, et al. Age-related prevalence of dermoscopy patterns in acquired melanocytic naevi. *Br J Dermatol*. 2006; 154:299–304. [PubMed: 16433800]
30. Marchetti MA, Kiuru MH, Busam KJ, et al. Melanocytic Naevi with Globular and Reticular Dermoscopic Patterns Display Distinct BRAF V600E Expression Profiles and Histopathologic Patterns. *Br J Dermatol*. 2014
31. Zalaudek I, Schmid K, Marghoob AA, et al. Frequency of dermoscopic nevus subtypes by age and body site: a cross-sectional study. *Arch Dermatol*. 2011; 147:663–70. [PubMed: 21690528]
32. Fonseca M, Burnett M, S. D, et al. Dermoscopic patterns of nevi have a distinct anatomical distribution in adolescents. Abstract #315 presented at the 2014 Society for Investigative Dermatology Meeting in Albuquerque, New Mexico. *J Invest Dermatol*. 2014; 134(Suppl 1):S49–60.
33. Stegmaier OC. Natural regression of the melanocytic nevus. *J Invest Dermatol*. 1959; 32:413–21. [PubMed: 13641818]
34. Nicholls EM. Development and elimination of pigmented moles, and the anatomical distribution of primary malignant melanoma. *Cancer*. 1973; 32:191–5. [PubMed: 4716772]
35. Cooke KR, Spears GF, Skegg DC. Frequency of moles in a defined population. *J Epidemiol Community Health*. 1985; 39:48–52. [PubMed: 3989434]
36. MacKie RM, English J, Aitchison TC, et al. The number and distribution of benign pigmented moles (melanocytic naevi) in a healthy British population. *Br J Dermatol*. 1985; 113:167–74. [PubMed: 4027184]
37. Halpern AC, Guerry Dt, Elder DE, et al. Natural history of dysplastic nevi. *J Am Acad Dermatol*. 1993; 29:51–7. [PubMed: 8315078]
38. Bataille V, Grulich A, Sasieni P, et al. The association between naevi and melanoma in populations with different levels of sun exposure: a joint case-control study of melanoma in the UK and Australia. *Br J Cancer*. 1998; 77:505–10. [PubMed: 9472652]

39. Zalaudek I, Hofmann-Wellenhof R, Kittler H, et al. A dual concept of nevogenesis: theoretical considerations based on dermoscopic features of melanocytic nevi. *J Dtsch Dermatol Ges.* 2007; 5:985–92. [PubMed: 17976139]
40. Zalaudek I, Hofmann-Wellenhof R, Soyer HP, et al. Naevogenesis: new thoughts based on dermoscopy. *Br J Dermatol.* 2006; 154:793–4. [PubMed: 16536840]
41. Alexeev V, Yoon K. Distinctive role of the cKit receptor tyrosine kinase signaling in mammalian melanocytes. *J Invest Dermatol.* 2006; 126:1102–10. [PubMed: 16410786]
42. Gleason BC, Crum CP, Murphy GF. Expression patterns of MITF during human cutaneous embryogenesis: evidence for bulge epithelial expression and persistence of dermal melanoblasts. *J Cutan Pathol.* 2008; 35:615–22. [PubMed: 18312434]
43. Cramer SF. Speckled lentiginous nevus (nevus spilus): the “roots” of the “melanocytic garden”. *Arch Dermatol.* 2001; 137:1654–5. [PubMed: 11735723]
44. Horikawa T, Norris DA, Yohn JJ, et al. Melanocyte mitogens induce both melanocyte chemokinesis and chemotaxis. *J Invest Dermatol.* 1995; 104:256–9. [PubMed: 7530272]
45. Thomas AJ, Erickson CA. The making of a melanocyte: the specification of melanoblasts from the neural crest. *Pigment Cell Melanoma Res.* 2008; 21:598–610. [PubMed: 19067969]
46. Pellacani G, Scope A, Ferrari B, et al. New insights into nevogenesis: in vivo characterization and follow-up of melanocytic nevi by reflectance confocal microscopy. *J Am Acad Dermatol.* 2009; 61:1001–13. [PubMed: 19833408]
47. Zalaudek I, Manzo M, Savarese I, et al. The morphologic universe of melanocytic nevi. *Semin Cutan Med Surg.* 2009; 28:149–56. [PubMed: 19782938]
48. Adameyko I, Lallemand F, Aquino JB, et al. Schwann cell precursors from nerve innervation are a cellular origin of melanocytes in skin. *Cell.* 2009; 139:366–79. [PubMed: 19837037]
49. Braun RP, Rabinovitz HS, Oliviero M, et al. Dermoscopy of pigmented skin lesions. *J Am Acad Dermatol.* 2005; 52:109–21. [PubMed: 15627088]
50. Massi D, De Giorgi V, Soyer HP. Histopathologic correlates of dermoscopic criteria. *Dermatol Clin.* 2001; 19:259–68. vii. [PubMed: 11556235]
51. Soyer HP, Kenet RO, Wolf IH, et al. Clinicopathological correlation of pigmented skin lesions using dermoscopy. *Eur J Dermatol.* 2000; 10:22–8. [PubMed: 10694293]
52. Szabo G. Regional Anatomy of Human Integument with Special Reference to Distribution of Hair Follicles Sweat Glands and Melanocytes. *Philosophical Transactions of the Royal Society of London Series B-Biological Sciences.* 1967; 252:447.
53. Szabo, G. Melanocyte system of human epidermis. Gordon, M., editor. Vol. xiv. Academic Press; New York: 1959. p. 647
54. Carrera C, Puig-Butlle JA, Aguilera P, et al. Impact of sunscreens on preventing UVR-induced effects in nevi: in vivo study comparing protection using a physical barrier vs sunscreen. *JAMA Dermatol.* 2013; 149:803–13. [PubMed: 23699984]
55. Sosa-Seda IM, Valentin-Nogueras S, Figueroa LD, et al. Clinical and dermoscopic patterns of melanocytic nevi in Hispanic adolescents: a descriptive study. *Int J Dermatol.* 2014; 53:280–7. [PubMed: 23968120]
56. Aguilera P, Puig S, Guilabert A, et al. Prevalence study of nevi in children from Barcelona. Dermoscopy, constitutional and environmental factors. *Dermatology.* 2009; 218:203–14. [PubMed: 19060476]
57. Patruno C, Scalvenzi M, Megna M, et al. Melanocytic nevi in children of southern Italy: dermoscopic, constitutional, and environmental factors. *Pediatr Dermatol.* 2014; 31:38–42. [PubMed: 23721171]
58. Grichnik JM. Stratum corneum RNA levels are diagnostic for melanoma. *Br J Dermatol.* 2011; 164:693–4. [PubMed: 21457197]
59. Wachsman W, Morhenn V, Palmer T, et al. Noninvasive genomic detection of melanoma. *Br J Dermatol.* 2011; 164:797–806. [PubMed: 21294715]

What's already known about this topic?

- Differences in the prevalence of melanocytic naevi by age and anatomic site have led to conflicting theories regarding naevogenesis.

What does this study add?

- Dermoscopically-defined globular and reticular naevi show a distinct anatomic site distribution in adolescents. Globular naevi are significantly more likely to be found on the back than the legs. Reticular naevi predominate on the legs compared to other dermoscopic patterns.

†Reticular back v. legs (1.58mm^2 v. 1.65mm^2 , $p=0.19$); globular back v. legs (2.04mm^2 v. 1.39mm^2 , $p=0.07$); homogenous back v. legs (1.64mm^2 v. 1.48mm^2 , $p=0.001$); complex back v. legs (2.15mm^2 v. 2.13mm^2 , $p=0.78$). All values refer to mean log lesion area.

Figure 1.

Boxplots of naevus log lesion area by dermoscopic pattern and anatomic location.

Table 1

Participant characteristics (n=509).

Characteristic		n (%)
Sex	Female	190 (37.3)
	Male	319 (62.7)
Race	Asian	9 (1.8)
	Black	5 (1)
	Hispanic	41 (8.1)
	Multi-racial	2 (0.4)
	White	452 (88.8)
Hair Color	Blonde	39 (7.7)
	Blonde/ Light brown	49 (9.6)
	Light brown	86 (16.9)
	Medium brown	152 (29.9)
	Red	10 (2)
	Dark brown	118 (23.2)
	Black	55 (10.8)
Skin color	Very fair	84 (16.5)
	Fair	273 (53.6)
	Light olive	104 (20.4)
	Dark olive	11 (2.2)
	Light brown	24 (4.7)
	Medium brown	11 (2.2)
	Dark brown/ Black	2 (0.4)
Outdoor sun exposure	Low	164 (32.2)
	Medium	171 (33.6)
	High	169 (33.2)
	Missing	5 (1)
Burns easily	Yes	147 (28.9)
	No	287 (56.4)
	Don't know	65 (12.8)
	Missing	10 (2.0)

		Median (IQR)	Mean (SD)
Naevus counts	Back	11 (14)	14.3 (11.7)
	Legs	3 (7)	6.1 (8.9)
	Total	15 (19)	20.4 (17.2)

Table 2

Dermoscopic patterns by anatomic location.

	Back		Legs		Total
	Upper	Lower	Upper	Lower	
Reticular	418	450	190	166	1,224
<i>Row %</i>	<i>34.1</i>	<i>36.8</i>	<i>15.5</i>	<i>13.6</i>	<i>100</i>
<i>Col %</i>	<i>31.4</i>	<i>45.4</i>	<i>56.0</i>	<i>55.7</i>	<i>41.4</i>
Globular	271	86	2	1	360
<i>Row %</i>	<i>75.3</i>	<i>23.9</i>	<i>0.6</i>	<i>0.3</i>	<i>100</i>
<i>Col %</i>	<i>20.4</i>	<i>8.7</i>	<i>0.6</i>	<i>0.3</i>	<i>12.2</i>
Homogenous	556	421	144	129	1,250
<i>Row %</i>	<i>44.5</i>	<i>33.7</i>	<i>11.5</i>	<i>10.3</i>	<i>100</i>
<i>Col %</i>	<i>41.8</i>	<i>42.5</i>	<i>42.5</i>	<i>43.3</i>	<i>42.3</i>
Complex	84	34	3	2	123
<i>Row %</i>	<i>68.3</i>	<i>27.6</i>	<i>2.4</i>	<i>1.6</i>	<i>100</i>
<i>Col %</i>	<i>6.3</i>	<i>3.4</i>	<i>0.9</i>	<i>0.7</i>	<i>4.2</i>
Total	1,329	991	339	298	2,957
<i>Row %</i>	<i>44.9</i>	<i>33.5</i>	<i>11.5</i>	<i>10.1</i>	<i>100</i>
<i>Col %</i>	<i>100</i>	<i>100</i>	<i>100</i>	<i>100</i>	<i>100</i>

Table 3

Dermoscopic patterns by participant characteristics, stratified by anatomic location.

Variable	Coding	Back				P-value	Legs				P-value
		Reticular	Globular	Homogenous	Complex		Reticular	Globular	Homogenous	Complex	
Sex	Female	287 (38.8)	117 (15.8)	285 (38.6)	50 (6.8)	0.02	149 (49.5)	3 (1)	146 (48.5)	3 (1)	0.007
	Male	581 (36.8)	240 (15.2)	692 (43.8)	68 (4.3)		207 (61.6)	0 (0)	127 (37.8)	2 (0.6)	
Race	Asian	9 (40.9)	3 (13.6)	9 (40.9)	1 (4.6)	<0.001	5 (71.4)	0 (0)	2 (28.6)	0 (0)	0.887
	Black	3 (37.5)	3 (37.5)	2 (25)	0 (0)		1 (100)	0 (0)	0 (0)	0 (0)	
	Hispanic	88 (57.9)	16 (10.5)	43 (28.3)	5 (3.3)		21 (70)	0 (0)	9 (30)	0 (0)	
	Multi-racial	0 (0)	1 (33.3)	2 (66.7)	0 (0)		(0)	(0)	(0)	(0)	
	White	768 (36)	334 (15.6)	921 (43.1)	112 (5.3)		329 (54.9)	3 (0.5)	262 (43.7)	5 (0.8)	
Hair color	Blonde	33 (17.2)	45 (23.4)	101 (52.6)	13 (6.8)	<0.001	27 (42.9)	1 (1.6)	35 (55.6)	0 (0)	0.187
	Blonde/ Light brown	75 (30.0)	39 (15.6)	123 (49.2)	13 (5.2)		43 (54.4)	0 (0)	36 (45.6)	0 (0)	
	Light brown	144 (30.5)	76 (16.1)	227 (48.1)	25 (5.3)		69 (51.1)	1 (0.7)	65 (48.2)	0 (0)	
	Medium brown	263 (37.6)	104 (14.9)	290 (41.4)	43 (6.1)		109 (58)	1 (0.5)	75 (39.9)	3 (1.6)	
	Red	17 (34.0)	9 (18.0)	23 (46.0)	1 (2.0)		10 (50)	0 (0)	10 (50)	0 (0)	
	Dark brown	226 (47.6)	67 (14.1)	164 (34.5)	18 (3.8)		72 (60.5)	0 (0)	45 (37.8)	2 (1.7)	
	Black	110 (60.8)	17 (9.4)	49 (27.1)	5 (2.8)		26 (78.8)	0 (0)	7 (21.2)	0 (0)	
	Lighter	612 (34.1)	277 (15.4)	809 (45.1)	96 (5.4)		292 (53.4)	3 (0.6)	247 (45.2)	5 (0.9)	
Skin color	Darker	256 (48.7)	80 (15.2)	168 (31.9)	22 (4.2)	<0.001	64 (71.1)	0 (0)	26 (28.9)	0 (0)	0.015
Skin burns easily	No	231 (33.2)	113 (16.3)	317 (45.6)	34 (4.9)	0.11	127 (49.8)	2 (0.8)	125 (49.0)	1 (0.4)	0.28
	Yes	612 (39.0)	236 (15.1)	636 (40.6)	83 (5.3)		227 (60.4)	1 (0.3)	144 (38.3)	4 (1.1)	
Sun exposure	Low	257 (40.2)	98 (15.3)	252 (39.4)	32 (5.0)	0.505	102 (53.7)	2 (1.0)	85 (44.7)	1 (0.5)	0.77
	Medium brown	297 (35.6)	130 (15.6)	366 (43.9)	41 (4.9)		116 (54.5)	0 (0)	94 (44.1)	3 (1.4)	
	High	309 (37.6)	126 (15.3)	344 (41.8)	44 (5.3)		133 (59.4)	1 (0.5)	89 (39.7)	1 (0.5)	

Table 4

Lesion level characteristics by anatomic location.

Variable	Back	Legs	P-value
Any Network			
No	1,379 (59.4)	280 (44)	<0.001
Yes	941 (40.6)	357 (56)	
Any Globules			
No	1,739 (75)	614 (96.4)	<0.001
Yes	581 (25)	23 (3.6)	
Any Dots			
No	1,281 (55.2)	506 (79.4)	<0.001
Yes	1,037 (44.7)	131 (20.6)	
Raised lesion			
No	2,174 (93.7)	634 (99.5)	<0.001
Yes	146 (6.3)	3 (0.5)	
Background Skin Pattern			
None	1,339 (57.7)	562 (88.2)	<0.001
Reticular	603 (26)	46 (7.2)	
Globular	239 (10.3)	19 (3.0)	
Reticular/Globular	139 (6)	10 (1.6)	
Lesion area, mm ² (median, IQR)	4.1 (5.6)	3.5 (4.0)	<0.001
Lesion area, mm ² (mean, SD)	6.4 (7.8)	4.9 (4.7)	<0.001

Table 5

Multinomial logistic regression model of the association between naevus dermoscopic pattern and location (dichotomous), controlling for sex, lesion area, raised lesions, and skin color.

Naevus Dermoscopic Pattern	Variables	OR	95% CI	P-value
Reticular	Location – Back vs. Legs	0.67	(0.54-0.84)	0.001
	Sex (Males)	0.97	(0.76-1.23)	0.794
	Lesion area (log transformed)	1.1	(0.95-1.27)	0.195
	Raised Lesion	0.08	(0.04-0.17)	<0.001
	Skin color- lighter versus darker	0.46	(0.34-0.62)	<0.001
Globular	Location – Back vs. Legs	29.39	(9.53-90.65)	<0.001
	Sex (Males)	0.89	(0.65-1.21)	0.463
	Lesion area (log transformed)	1.86	(1.52-2.27)	<0.001
	Raised Lesion	1.09	(0.68-1.74)	0.729
	Skin color- lighter versus darker	0.89	(0.64-1.25)	0.515
Homogeneous	Referent Group	--	--	--
Complex	Location – Back vs. Legs	6.8	(2.7-17.14)	<0.001
	Sex (Males)	0.6	(0.39-0.94)	0.024
	Lesion area (log transformed)	2.25	(1.72-2.94)	<0.001
	Raised Lesion	0.18	(0.07-0.44)	<0.001
	Skin color- lighter versus darker	1.24	(0.72-2.13)	0.43