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ORIGINAL RESEARCH

The anatomic distribution of cutaneous melanoma: A detailed study of 5141 lesions

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ABSTRACT

Background/Objectives: There is evidence that cutaneous melanomas at different anatomic sites present with distinctive clinicopathologic features. We examined the anatomic distribution of cutaneous melanoma and its variation by patient characteristics, subtype and Breslow thickness, using high-resolution anatomic site data.

Methods: A cross-sectional study was performed of all primary cutaneous melanoma cases managed at a tertiary referral centre, analysing prospectively collected clinical data across 50 anatomic subsites.

Results: The study included 5141 in situ or invasive melanomas; most were invasive (76.2%), and the median Breslow thickness of invasive lesions was 1.0 mm. Superficial spreading (57.2%), lentigo maligna (20.8%) and nodular (12.2%) were the most common histopathological subtypes. Sun-exposed sites such as the female nose and cheek, the male ear, as well as the upper back in both sexes had the highest incidence of melanoma per unit area. When compared to the posterior forearm, the scalp, ear, preauricular, perioral, subungual and plantar sites had thicker invasive melanomas (each $P < 0.05$). The peri-auricular, ear and cheek had the highest incidence of nodular melanoma per unit area. There were subtype-, age- and sex-specific differences in melanoma anatomic distribution.

Conclusion: Melanoma most commonly arises in sun-exposed facial areas, as well as the upper back. Increased thickness is found for melanoma in acral and many head and neck sites. Nodular melanoma is more likely to occur in head and neck sites including the peri-auricular area, ear and cheek. Clinicians should carefully assess these sites during skin examinations.

Key words: anatomic location, Breslow thickness, cutaneous melanoma, nodular melanoma, sun exposure.

INTRODUCTION

The anatomic location of cutaneous melanoma is of clinical importance. There is evidence that melanomas at different sites present with unique clinicopathologic characteristics,[1–7] and location itself has been identified as an independent prognostic factor.[7]

The anatomic distribution of melanoma varies according to gender,[8–13] age[8–13] and histopathological subtype.[13,14] This is thought to reflect differences in site-specific sun exposure, and at least two distinct biological pathways associated with different somatic mutations are involved in melanoma pathogenesis.[15–18] These include a naevus-prone pathway promoted by intermittent sun exposure in areas such as the trunk and limbs, as well as a pathway involving chronic cumulative sun exposure in areas such as the head and neck.[15]

An improved understanding of the anatomic distribution of melanoma may guide both clinicians and patients, potentially leading to earlier detection and improved outcomes. Significantly, population studies have demonstrated that the incidence rate of thick melanomas in many countries is increasing or stable[19–21] and that early detection of certain subtypes, such as nodular melanoma, continues to be a challenge.[21,22] Nevertheless, previous studies of

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melanoma distribution have involved small numbers of patients or typically divided the body into relatively few subsites,[9–12] precluding more comprehensive analysis of the relationship between melanoma distribution, thickness and subtype.

The aims of our study were to examine the anatomic distribution of cutaneous melanoma in detail, and to investigate variations in this distribution by patient characteristics, tumour subtype and Breslow thickness.

METHODS

The Victorian Melanoma Service (VMS) is a statewide, multidisciplinary tertiary referral service based at the Alfred Hospital in Melbourne; it reviews approximately one-quarter of new melanoma cases in Victoria, Australia. The VMS research database is prospectively maintained and includes all patients treated at the service. Data for all patients with primary cutaneous melanoma managed at the VMS between 1994 and 2016 were included in the study. After exclusion of noncutaneous melanomas ($n = 20$), and cases with unknown subtype ($n = 17$) or thickness ($n = 30$), 5141 melanomas were included for analysis.

Clinical features assessed and recorded in the database by the treating physician for each patient included age, gender, date of diagnosis, tumour location and Fitzpatrick skin type. Tumour location was recorded using detailed coding across 232 anatomic sites, based on a system developed by the Pigmented Lesion Study Group (see Figure S1).[23] Histopathologic features assessed included tumour subtype and Breslow thickness. Tumour subtype was classified according to World Health Organization guidelines as superficial spreading, lentigo maligna, acral lentiginous, nodular or desmoplastic melanoma. Unclassified and rare subtypes such as Spitzoid and naevoid melanoma were grouped as 'other'.

For statistical analysis, tumour location was categorised into 50 subsites (Tables 2 and 3). Percentage surface area in each subsite was determined using a three-dimensional anatomic model (based on an average person with 1.7 m^2 surface area) in the Apple iOS program Skin3D (Table S1). Age was dichotomised (≤60, >60 years), and Breslow thickness was classified as in situ, >0 to <1, 1 to <4 and ≥4 mm. Incidence of melanoma by site was analysed with Poisson regression, with rates per site surface area further examined in subgroups defined by age, gender and melanoma subtype. To assess differences in melanoma distribution between subgroups, chi-square tests were used to select a reference site for Poisson regression that had similar proportions of melanoma with respect to the subgroups being compared. The thickness of invasive tumours was compared across sites in univariable and multivariable ordered logistic regression analyses. The odds of an in situ tumour were compared in univariable and multivariable logistic regression analyses. Results were considered statistically significant if $P < 0.05$. All statistical analyses were performed in Stata 14 (StataCorp).

Institutional ethics approval for the study was obtained from the Alfred Hospital.

RESULTS

Clinicopathologic characteristics

The clinical and pathological characteristics of melanomas included in the study are summarised in Table 1. The study included 5141 primary cutaneous melanomas of which 1228 (23.4%) were in situ and 3913 (76.6%) were invasive; the median Breslow thickness among invasive lesions was 1 mm. Superficial spreading (57.2%), lentigo maligna (20.8%) and nodular (12.2%) were the most common histopathologic subtypes. Men (median age, 61 years) were diagnosed at an older age than women (median age, 54 years) and tended to have thicker invasive tumours (unadjusted OR, 1.8; CI 1.6–2.0, $P < 0.001$). Patients >60 years had thicker tumours than those ≤60 years (OR adjusted for sex, 2.5; CI 2.2–2.8, $P < 0.001$).

Anatomic distribution of melanoma by sex and age

The anatomic distribution of melanoma per unit area in men and women diagnosed at ≤60 or >60 years of age, including both in situ and invasive tumours, is summarised in Figure 1. Overall melanoma distribution patterns remained similar when in situ lesions were excluded.

Facial sites had the highest incidence rate of melanoma per unit area in both sexes and all ages (Tables 2 and 3). In men, the ear (incidence rate ratio (IRR), 5.3; 95% CI 3.4–7.0, $P < 0.001$), preauricular (IRR, 4.8; 95% CI 3.3–7.0, $P < 0.001$), nose (IRR, 4.9; 95% CI 3.5–6.8, <0.001) and cheek (IRR, 4.3; 95% CI 3.3–5.5, $P < 0.001$) had the highest incidence of melanoma per unit area relative to the posterior forearm. In women, the nose (IRR, 4.8; 95% CI 3.5–6.6, $P < 0.001$) and cheek (IRR, 4.8; 95% CI 3.8–6.0, $P < 0.001$) had the highest incidence rate of melanoma per unit area relative to the posterior forearm. Excluding the head and neck, relative to the posterior forearm, the areas with the highest incidence of melanoma per unit area were the upper back (IRR, 3.7; 95% CI 2.9–4.6, $P < 0.001$) in men as well as the upper back (IRR, 1.6; 95% CI 1.3–2.1, $P < 0.001$) and posterior lower leg (IRR, 1.4; 95% CI 1.1–1.7, $P = 0.006$) in women.

For comparisons of lesion distribution between men ($n = 2660$) and women ($n = 2481$), the posterior forearm was chosen as the reference site; it contained similar proportions of melanoma amongst men (3.2%) and women (4.1%) (χ^2 test; $P = 0.12$). Relative to the posterior forearm, a number of sites had differing incidence rate ratios between the sexes, as indicated by an interaction ($P < 0.05$) between subsite and gender (Table 2). Compared to women, men had higher incidence in areas such as the hair-bearing scalp, pre- and postauricular, ear, forehead, posterior neck, supramammary chest, abdomen and back areas. Compared to men, women had higher incidence in lower limb areas such as the anterior thigh,

Table 1 Clinicopathologic characteristics of melanomas in the study cohort

Characteristic	All n = 5141	Male n = 2660 (51.7%)	Female n = 2481 (48.6%)
Age at diagnosis			
Median (IQR), years	58 (44–70)	61 (48–71)	54 (41–68)
≤60 years	2820 (54.9%)	1292 (48.6%)	1528 (61.6%)
>60 years	2321 (45.2%)	1368 (51.4%)	953 (38.4%)
Fitzpatrick skin type[†,‡]			
I	1438 (28.7%)	642 (24.7%)	796 (32.9%)
II	2127 (42.4%)	1126 (43.4%)	1001 (41.1%)
III	1168 (23.3%)	661 (25.5%)	507 (21.0%)
IV–VI	280 (5.6%)	167 (6.4%)	113 (4.7%)
Histopathological subtype			
Superficial spreading	2938 (57.2%)	1463 (55.0%)	1475 (59.5%)
Lentigo maligna	1069 (20.8%)	553 (20.8%)	516 (20.8%)
Nodular	626 (12.2%)	382 (14.4%)	244 (9.8%)
Desmoplastic	130 (2.5%)	86 (3.2%)	44 (1.8%)
Acral lentiginous	131 (2.6%)	54 (2.0%)	77 (3.1%)
Unclassified or other[§]	247 (4.8%)	122 (4.6%)	125 (5.0%)
Breslow thickness in mm			
0 (in situ)	1228 (23.4%)	602 (22.6%)	626 (25.2%)
>0 to <1	1854 (36.1%)	848 (31.9%)	1006 (40.6%)
1 to <4	1628 (31.7%)	915 (34.4%)	713 (28.7%)
≥4	431 (8.4%)	295 (11.1%)	136 (5.5%)
Median thickness of invasive lesions (IQR) in mm	1 (0.6–2.2)	1.2 (0.6–2.6)	0.85 (0.5–1.75)
Anatomic location			
Head and neck	1445 (28.1%)	864 (32.5%)	581 (23.4%)
Trunk	1465 (28.5%)	965 (36.3%)	500 (20.2%)
Upper limb	966 (18.8%)	414 (15.6%)	552 (22.3%)
Lower limb	1265 (24.6%)	417 (15.7%)	848 (34.2%)

[†]Tabulations for this variable exclude cases with unknown or missing values.

[‡]I = always burns, never tans; II = burns easily, tans poorly; III = burns moderately, then develops a light tan; IV = burns minimally to rarely, then develops a moderate tan; V = rarely burns, tans darkly easily; VI = never burns, always tans darkly.

[§]Other includes naevoid and Spitzoid melanomas. IQR, interquartile range.

lower leg and dorsal foot. The differences in melanoma distribution between men and women were similar in both age groups ≤60 and >60 years (Figure 1).

For comparisons of lesion distribution between patients diagnosed at age ≤60 (n = 2820) and >60 years (n = 2321), the posterior forearm was chosen as the reference site; it contained similar proportions of melanoma in age groups ≤60 (3.6%) and >60 years (3.8%) (χ^2 test; P = 0.70). Relative to the posterior forearm, a number of sites had differing incidence rate ratios between age groups, as indicated by an interaction (P < 0.05) between subsite and age group (Table 3). Compared to patients ≤60 years, those >60 years had higher incidence in the hair-bearing scalp, postauricular, forehead, nose, cheek, periocular and foot ungual areas. In addition, those >60 years had lower incidence in the abdomen, buttock and thigh areas. There was also a trend for those >60 years to have a lower incidence on the back and lower leg (Figure 1 and Table 3). The differences in melanoma distribution between age groups ≤60 and >60 years were similar in both men and women (Figure 1).

Histopathologic subtype

The anatomic distribution of melanoma per unit area for superficial spreading (n = 2938), nodular (n = 636) and lentigo maligna (n = 1069) subtypes, including both in situ and invasive tumours, is summarised in Figure 2. The anatomic location of lentigo maligna subtype predominantly involved chronically sun-exposed sites of the head and neck. Relative to the posterior forearm, central facial areas such as the nose (IRR, 17.2; 95% CI 12.1–24.4, P < 0.001) and cheek (IRR, 15.0; 95% CI 11.0–20.6, P < 0.001) had the highest incidence rate of lentigo maligna subtype per unit area.

For comparisons between superficial spreading (n = 2938) and nodular (n = 636) subtypes, the posterior arm was selected as the reference area; it contained similar proportions of melanoma amongst superficial spreading (7.7%) and nodular (6.9%) subtypes (χ^2 test; P = 0.52). For superficial spreading subtype, the upper back (IRR, 2.8; 95% CI 2.4–3.3, P < 0.001) and ear (IRR, 1.7; 95% CI 1.3–2.3, P < 0.001) had the highest incidence rate of melanoma per unit area relative to the posterior arm. For nodular subtype, the preauricular (IRR 5.2; 95% CI 2.7–9.8, P < 0.001), postauricular (IRR 3.9; 95% CI 1.9–8.0, P < 0.001), ear (IRR, 3.5; 95% CI 2.0–5.9, P < 0.001) and cheek (IRR 2.7; 95% CI 1.7–4.2, P < 0.001) areas had the highest incidence rate of melanoma per unit area relative to the posterior arm. Relative to the posterior arm, a number of sites had differing incidence rate ratios between superficial spreading and nodular subtypes, as indicated by

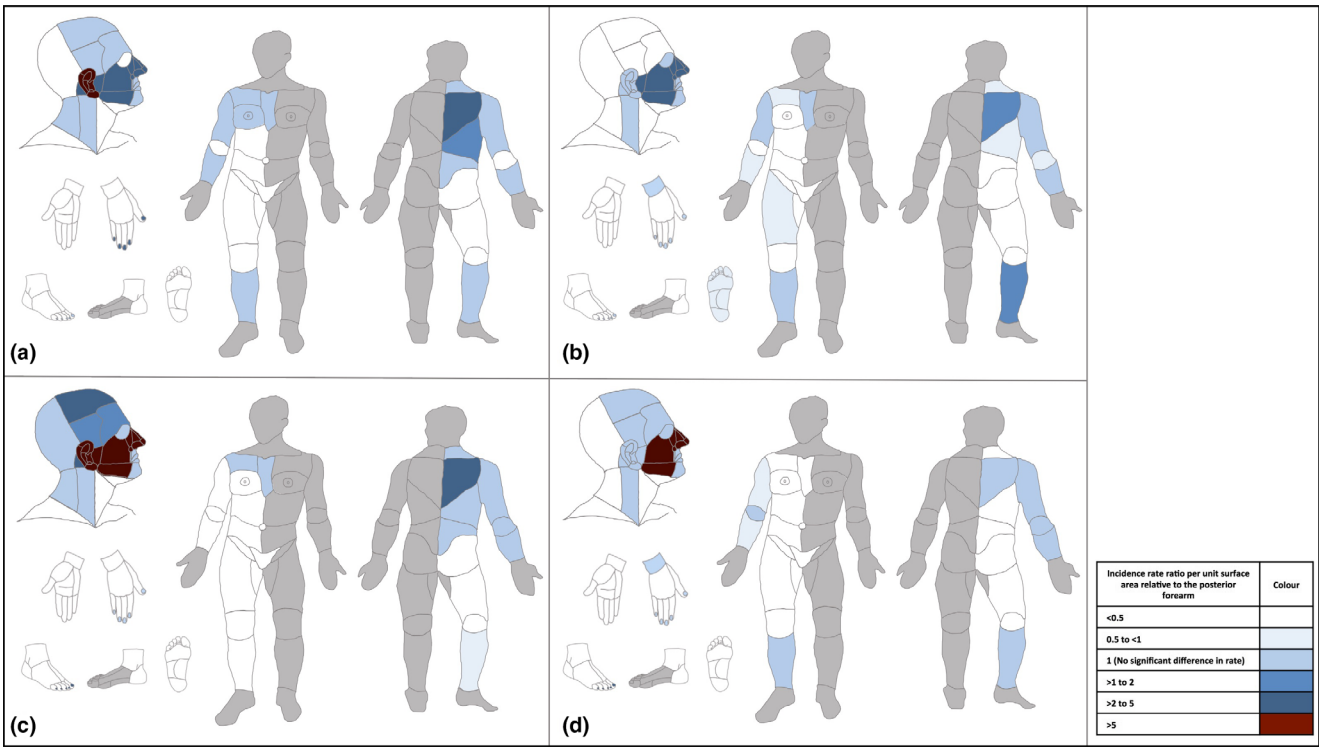

Figure 1 The anatomic distribution of melanoma for men ≤60 years of age (a), women ≤60 years of age (b), men >60 years of age (c) and women >60 years of age (d). Colours indicate the unadjusted ratio of incidence rate per unit area, relative to the posterior forearm (see legend). Laterality was not assessed and mucosal, ocular as well as genital melanomas were excluded (shaded in grey).

an interaction ($P < 0.05$) between subsite and subtype (Table S2). Compared to superficial spreading melanoma, nodular melanoma had higher incidence in the hair-bearing scalp, pre- and postauricular, ear, cheek and perioral sites. The distribution of superficial spreading and nodular subtypes was similar on the trunk and limbs. Differences in the distribution patterns between superficial spreading and nodular melanomas remained similar when in situ lesions were excluded.

Breslow thickness

To assess the anatomic distribution of Breslow thickness amongst invasive melanomas ($n = 3913$), the posterior forearm was selected as the reference area given that it had >100 lesions, with a median thickness (1.1 mm) close to that of the overall cohort (1 mm). In univariable analysis, a number of subsites had increased odds of thicker melanomas relative to the posterior forearm (Table S3). These were the posterior scalp (unadjusted OR, 8.2; 95% CI 4.3–15.3, $P < 0.001$), anterior scalp (unadjusted OR, 6.4; 95% CI 3.9–10.3, $P < 0.001$), lateral scalp (unadjusted OR, 4.6; 95% CI 4.6–1.5, $P < 0.001$), ear (unadjusted OR, 1.9; 95% CI 1.2–3.1, $P = 0.01$), preauricular (unadjusted OR, 2.0; 95% CI 1.0–3.9, $P = 0.05$), perioral (unadjusted OR, 3.2; 95% CI 1.4–7.4, $P = 0.006$), hand ungual (unadjusted OR, 4.6; 95% CI 1.7–12.3, $P = 0.003$) and foot ungual (unadjusted OR, 3.6; 95% CI 1.6–7.7, $P = 0.001$) areas. The preauricular area became nonsignificant in the model following adjustment for age group and gender, while the perioral, foot ungual and plantar areas became nonsignificant in the model following additional adjustment for subtype. Acral lentiginous melanomas constituted just 2.6% of all invasive lesions, but comprised 83.3% and 87.2% of those in the ungual and plantar sites, respectively.

In situ tumours

To assess the distribution of in situ tumours ($n = 1228$), the upper back was selected as the reference area given that it had >100 lesions, as well as a proportion of in situ disease (20%) comparable to that in the overall cohort (24%). The majority of in situ tumours were of lentigo maligna (53.1%) or superficial spreading subtype (38.8%), and their anatomic distribution reflected these underlying histopathologic subtypes. In univariable analysis, a number of subsites had increased odds of in situ disease relative to the upper back (Table S4). These were mainly head and neck sites such as the forehead, nose, cheek, periocular, perioral as well as lateral neck. Facial sites such as the nose (unadjusted OR, 8.2; 95% CI 5.4–12.4, $P < 0.001$), cheek (unadjusted OR, 4.6; 95% CI 3.5–5.9, $P < 0.001$), periocular (unadjusted OR, 4.0; 95% CI 1.7–9.4, $P = 0.002$) and forehead (unadjusted OR, 2.5; 95% CI 1.6–3.8, $P < 0.001$) had the highest odds of in situ disease. However, when adjusted for subtype, the nose was the only

Table 2 Differences in anatomic distribution of melanoma for men and women across 50 body sites, with incidence adjusted for surface area

	Males[‡] (n = 2660)			Females[§] (n = 2481)			Analysis of difference[¶]
Anatomic location[†]	No. of lesions	IRR (95% CI)	P Value	No. of lesions	IRR (95% CI)	P Value	P Value (For ratio of IRRs)
Scalp							
Posterior scalp	50	0.6 (0.4–0.9)	0.004	10	0.1 (0.05–0.2)	<0.001	**<0.001**
Anterior scalp	110	1.7 (1.3–2.3)	<0.001	33	0.4 (0.3–0.7)	<0.001	**<0.001**
Lateral scalp	45	1.6 (1.1–2.3)	0.008	11	0.3 (0.2–0.6)	0.001	**<0.001**
Postauricular scalp	30	3.8 (2.5–5.7)	<0.001	3	0.3 (0.1–1.0)	0.05	**<0.001**
Face							
Preauricular	38	4.8 (3.3–7.0)	<0.001	17	1.8 (1.1–3.1)	0.02	**0.003**
Forehead	71	1.4 (1.0–1.9)	0.04	46	0.8 (0.5–1.1)	0.13	**0.01**
Nose/Perinasal	58	4.9 (3.5–6.8)	<0.001	67	4.8 (3.5–6.6)	<0.001	0.95
Cheek	185	4.3 (3.3–5.5)	<0.001	244	4.8 (3.8–6.0)	<0.001	0.50
Perioral/Chin	20	1.3 (0.8–2.1)	0.34	19	1.0 (0.6–1.7)	0.92	0.55
Periocular	7	0.4 (0.2–1.0)	0.04	15	0.8 (0.5–1.4)	0.44	0.21
Ear	104	5.3 (3.4–7.0)	<0.001	33	1.4 (1.0–2.1)	0.08	**<0.001**
Neck							
Anterior neck	19	0.4 (0.2–0.6)	<0.001	14	0.2 (0.1–0.4)	<0.001	0.22
Lateral neck	32	1.3 (0.9–2.0)	0.15	26	0.9 (0.6–1.4)	0.76	0.22
Posterior superior neck	23	0.6 (0.4–1.0)	0.06	10	0.2 (0.1–0.5)	<0.001	**0.02**
Posterior inferior neck	59	1.2 (0.9–1.7)	0.20	26	0.5 (0.3–0.7)	0.001	**<0.001**
Supra-clavicular	13	0.4 (0.2–0.7)	0.001	7	0.2 (0.07–0.4)	<0.001	0.11
Trunk							
Upper back	481	3.7 (2.9–4.6)	<0.001	252	1.6 (1.3–2.1)	<0.001	**<0.001**
Mid back	159	1.2 (0.9–1.6)	0.14	76	0.5 (0.4–0.7)	<0.001	**<0.001**
Lower back	111	1.1 (0.8–1.5)	0.42	34	0.3 (0.2–0.4)	<0.001	**<0.001**
Buttocks	13	0.06 (0.03–0.1)	<0.001	22	0.09 (0.05–0.1)	<0.001	0.33
Sternum	25	0.9 (0.6–1.4)	0.65	22	0.7 (0.4–1.1)	0.10	0.38
Supramammary chest	50	0.8 (0.6–1.2)	0.34	27	0.4 (0.3–0.6)	<0.001	**0.006**
Mammary	41	0.5 (0.3–0.7)	<0.001	16	0.3 (0.2–0.6)	<0.001	0.21
Upper abdominal	55	0.4 (0.3–0.5)	<0.001	29	0.2 (0.1–0.2)	<0.001	**0.003**
Lower abdominal	29	0.3 (0.2–0.4)	<0.001	17	0.1 (0.08–0.2)	<0.001	**0.04**
Inguinal	1	0.05 (0.01–0.4)	0.003	5	0.1 (0.04–0.3)	<0.001	0.49
Axillary	2	0.1 (0.02–0.4)	0.001	2	0.04 (0.01–0.2)	<0.001	0.40
Upper limb							
Anterior arm	97	0.6 (0.5–0.9)	0.003	123	0.7 (0.5–0.9)	0.007	0.69
Posterior arm	133	0.9 (0.7–1.2)	0.38	191	1.1 (0.9–1.4)	0.51	0.27
Cubital	4	0.3 (0.1–0.8)	0.02	16	0.5 (0.3–0.8)	0.009	0.36
Elbow	16	0.6 (0.4–1.0)	0.04	20	0.6 (0.4–1.0)	0.05	0.86
Anterior forearm	49	0.6 (0.4–0.8)	0.001	63	0.6 (0.5–0.8)	0.003	0.70
Posterior forearm	87	1 (Reference)		102	1 (Reference)		(Reference)
Anterior wrist	1	0.1 (0.02–0.9)	0.04	0	NA		NA
Posterior wrist	3	0.2 (0.05–0.6)	0.005	8	0.4 (0.2–0.9)	0.02	0.24
Dorsal hand	7	0.1 (0.05–0.2)	<0.001	15	0.2 (0.1–0.3)	<0.001	0.21
Palm	2	0.06 (0.01–0.2)	<0.001	2	0.02 (0.01–0.1)	<0.001	0.40
Ungual hand	13	1.6 (0.9–2.9)	0.10	10	1.1 (0.6–2.1)	0.82	0.34
Lower limb							
Anterior thigh	83	0.3 (0.2–0.4)	<0.001	167	0.5 (0.4–0.7)	<0.001	**0.006**
Posterior thigh	36	0.1 (0.1–0.2)	<0.001	55	0.2 (0.1–0.2)	<0.001	0.31
Medial thigh	10	0.08 (0.04–0.2)	<0.001	20	0.1 (0.04–0.2)	<0.001	0.20
Knee	25	0.3 (0.2–0.4)	<0.001	43	0.4 (0.2–0.4)	<0.001	0.20
Popliteal	20	0.2 (0.1–0.3)	<0.001	25	0.2 (0.1–0.3)	<0.001	0.85
Anterior leg	73	0.5 (0.4–0.7)	<0.001	169	1.0 (0.8–1.3)	0.91	**0.001**
Posterior leg	99	0.7 (0.5–0.9)	0.008	238	1.4 (1.1–1.7)	0.006	**<0.001**
Lateral ankle	4	0.1 (0.04–0.3)	<0.001	9	0.2 (0.1–0.4)	<0.001	0.29
Medial ankle	6	0.3 (0.1–0.7)	0.005	13	0.3 (0.2–0.5)	<0.001	0.88
Dorsal foot/heel	21	0.1 (0.07–0.2)	<0.001	62	0.3 (0.2–0.4)	<0.001	**0.002**
Plantar foot	26	0.3 (0.2–0.4)	<0.001	30	0.2 (0.2–0.4)	<0.001	0.96
Ungual foot	14	1.8 (1.0–3.1)	0.05	17	1.8 (1.1–3.1)	0.02	0.93

[†]Anatomic subsites are illustrated in Figure 1; ocular, mucosal and genital melanomas were excluded.

[‡]Poisson regression was used to assess the unadjusted incidence rate ratio of melanoma per unit area at 50 anatomic sites, with reference to the posterior forearm, for males.

[§]Poisson regression was used to assess the unadjusted incidence rate ratio of melanoma per unit area at 50 anatomic sites, with reference to the posterior forearm, for females.

[¶]The difference in IRRs between males or females at each subsite was evaluated by assessing the interaction between sex and site using poisson regression. IRR, incidence rate ratio.

Bold values indicate a site with a statistically significant ($P < 0.05$) difference in melanoma incidence per unit area between the two groups.

Table 3 Differences in anatomic distribution of melanoma for patients age ≤60 or >60 years across 50 body sites, with incidence adjusted for surface area

Anatomic location[†]	≤60 years[‡] (*n* = 2820)			>60 years[§] (*n* = 2321)			Analysis of difference[¶] *P* value (For ratio of IRRs)
	No. of lesions	IRR (95% CI)	*P* value	No. of lesions	IRR (95% CI)	*P* value	
Scalp							
Posterior scalp	17	0.2 (0.1–0.3)	<0.001	43	0.5 (0.4–0.7)	<0.001	**0.001**
Anterior scalp	41	0.6 (0.4–0.8)	0.002	102	1.6 (1.2–2.1)	0.001	**<0.001**
Lateral scalp	21	0.7 (0.4–1.0)	0.08	35	1.3 (0.8–1.8)	0.26	**0.04**
Postauricular scalp	11	1.2 (0.6–2.2)	0.57	22	2.8 (1.7–4.4)	<0.001	**0.04**
Face							
Preauricular	26	2.8 (1.8–4.4)	<0.001	29	3.6 (2.4–5.5)	<0.001	0.42
Forehead	34	0.6 (0.4–0.8)	0.005	83	1.6 (1.2–2.2)	0.002	**<0.001**
Nose/Perinasal	46	3.3 (2.4–4.7)	<0.001	79	6.6 (4.9–8.9)	<0.001	**0.004**
Cheek	153	3.0 (2.4–3.9)	<0.001	276	6.3 (4.9–8.0)	<0.001	**<0.001**
Perioral/Chin	18	1.0 (0.6–1.6)	0.94	21	1.3 (0.8–2.1)	0.26	0.41
Periocular	6	0.3 (0.1–0.7)	0.008	16	1.0 (0.6–1.7)	1.0	**0.03**
Ear	68	3.0 (2.2–4.0)	<0.001	69	3.5 (2.5–4.7)	<0.001	0.50
Neck							
Anterior neck	18	0.3 (0.2–0.5)	<0.001	15	0.3 (0.2–0.5)	<0.001	0.91
Lateral neck	34	1.2 (0.8–1.8)	0.29	24	1.0 (0.6–1.6)	1.0	0.49
Posterior superior neck	15	0.4 (0.2–0.6)	<0.001	18	0.5 (0.3–0.8)	0.007	0.40
Posterior inferior neck	46	0.8 (0.6–1.2)	0.31	39	0.8 (0.6–1.2)	0.28	0.91
Supra-clavicular	11	0.3 (0.2–0.5)	<0.001	9	0.3 (0.1–0.5)	<0.001	0.89
Trunk							
Upper back	408	2.7 (2.2–3.3)	<0.001	325	2.5 (1.9–3.1)	<0.001	0.58
Mid back	149	1.0 (0.8–1.3)	0.90	86	0.7 (0.5–0.9)	0.005	**0.04**
Lower back	98	0.9 (0.6–1.1)	0.27	47	0.5 (0.3–0.7)	<0.001	**0.009**
Buttocks	28	0.1 (0.07–0.2)	<0.001	7	0.03 (0.01–0.1)	<0.001	**0.005**
Sternum	31	1.0 (0.6–1.4)	0.86	16	0.6 (0.3–1.0)	0.04	0.12
Supramammary chest	45	0.7 (0.5–0.9)	0.02	32	0.5 (0.4–0.8)	0.002	0.46
Mammary	39	0.4 (0.3–0.6)	<0.001	18	0.4 (0.3–0.7)	0.001	0.86
Upper abdominal	58	0.3 (0.2–0.4)	<0.001	26	0.2 (0.1–0.3)	<0.001	**0.02**
Lower abdominal	38	0.3 (0.2–0.4)	<0.001	8	0.07 (0.03–0.1)	<0.001	**0.001**
Inguinal	2	0.09 (0.02–0.4)	0.001	4	0.1 (0.03–0.3)	<0.001	0.88
Axillary	3	0.07 (0.02–0.2)	<0.001	1	0.05 (0.01–0.4)	0.003	0.82
Upper Limb							
Anterior arm	138	0.8 (0.6–1.0)	0.07	82	0.5 (0.4–0.7)	<0.001	0.06
Posterior arm	189	1.1 (0.9–1.4)	0.52	135	0.9 (0.6–1.2)	0.39	0.28
Cubital	9	0.6 (0.3–1.1)	0.10	11	0.4 (0.2–0.7)	0.003	0.45
Elbow	16	0.5 (0.3–0.8)	0.01	20	0.7 (0.4–1.2)	0.17	0.32
Anterior forearm	70	0.7 (0.5–0.9)	0.02	42	0.5 (0.3–0.7)	<0.001	0.13
Posterior forearm	101	1 (Reference)		88	1 (Reference)		(Reference)
Anterior wrist	0	NA	NA	1	0.1 (0.01–0.9)	0.04	NA
Posterior wrist	7	0.4 (0.2–0.8)	0.01	4	0.3 (0.09–0.7)	0.007	0.51
Dorsal hand	11	0.1 (0.07–0.2)	<0.001	11	0.2 (0.08–0.3)	<0.001	0.76
Palm	3	0.04 (0.01–0.1)	<0.001	1	0.03 (0.00–0.2)	<0.001	0.82
Ungual hand	12	1.3 (0.7–2.4)	0.38	11	1.4 (0.7–2.6)	0.32	0.91
Lower Limb							
Anterior thigh	178	0.6 (0.4–0.7)	<0.001	72	0.3 (0.2–0.4)	<0.001	**<0.001**
Posterior thigh	64	0.2 (0.1–0.3)	<0.001	27	0.09 (0.06–0.1)	<0.001	**0.008**
Medial thigh	23	0.2 (0.1–0.3)	<0.001	7	0.06 (0.02–0.1)	<0.001	**0.02**
Knee	44	0.4 (0.3–0.6)	<0.001	24	0.3 (0.2–0.4)	<0.001	0.11
Popliteal	27	0.2 (0.2–0.4)	<0.001	18	0.2 (0.1–0.3)	<0.001	0.43
Anterior leg	143	0.8 (0.7–1.1)	0.19	99	0.7 (0.5–0.9)	0.006	0.24
Posterior leg	210	1.2 (1.0–1.6)	0.08	127	0.9 (0.7–1.1)	0.27	**0.05**
Lateral ankle	9	0.2 (0.1–0.4)	<0.001	4	0.1 (0.04–0.3)	<0.001	0.28
Medial ankle	13	0.3 (0.2–0.5)	<0.001	6	0.3 (0.1–0.7)	0.004	0.91
Dorsal foot/heel	58	0.3 (0.2–0.4)	<0.001	25	0.1 (0.08–0.2)	<0.001	**0.01**
Plantar foot	22	0.2 (0.1–0.3)	<0.001	34	0.3 (0.2–0.5)	<0.001	0.07
Ungual foot	9	1.0 (0.5–1.9)	0.95	22	2.8 (1.7–4.4)	<0.001	**0.02**

[†]Anatomic subsites are illustrated in Figure 1; ocular, mucosal and genital melanomas were excluded

[‡]Poisson regression was used to assess the unadjusted incidence rate ratio of melanoma per unit area at 50 anatomic sites, with reference to the posterior forearm, for patients diagnosed age ≤60 years.

[§]Poisson regression was used to assess the unadjusted incidence rate ratio of melanoma per unit area at 50 anatomic sites, with reference to the posterior forearm, for patients diagnosed age >60 years.

[¶]The difference in IRRs for patients ≤60 or >60 years at each subsite was evaluated by assessing the interaction between age group and site using poisson regression. IRR, incidence rate ratio.

Bold values indicate a site with a statistically significant ($P < 0.05$) difference in melanoma incidence per unit area between the two groups.

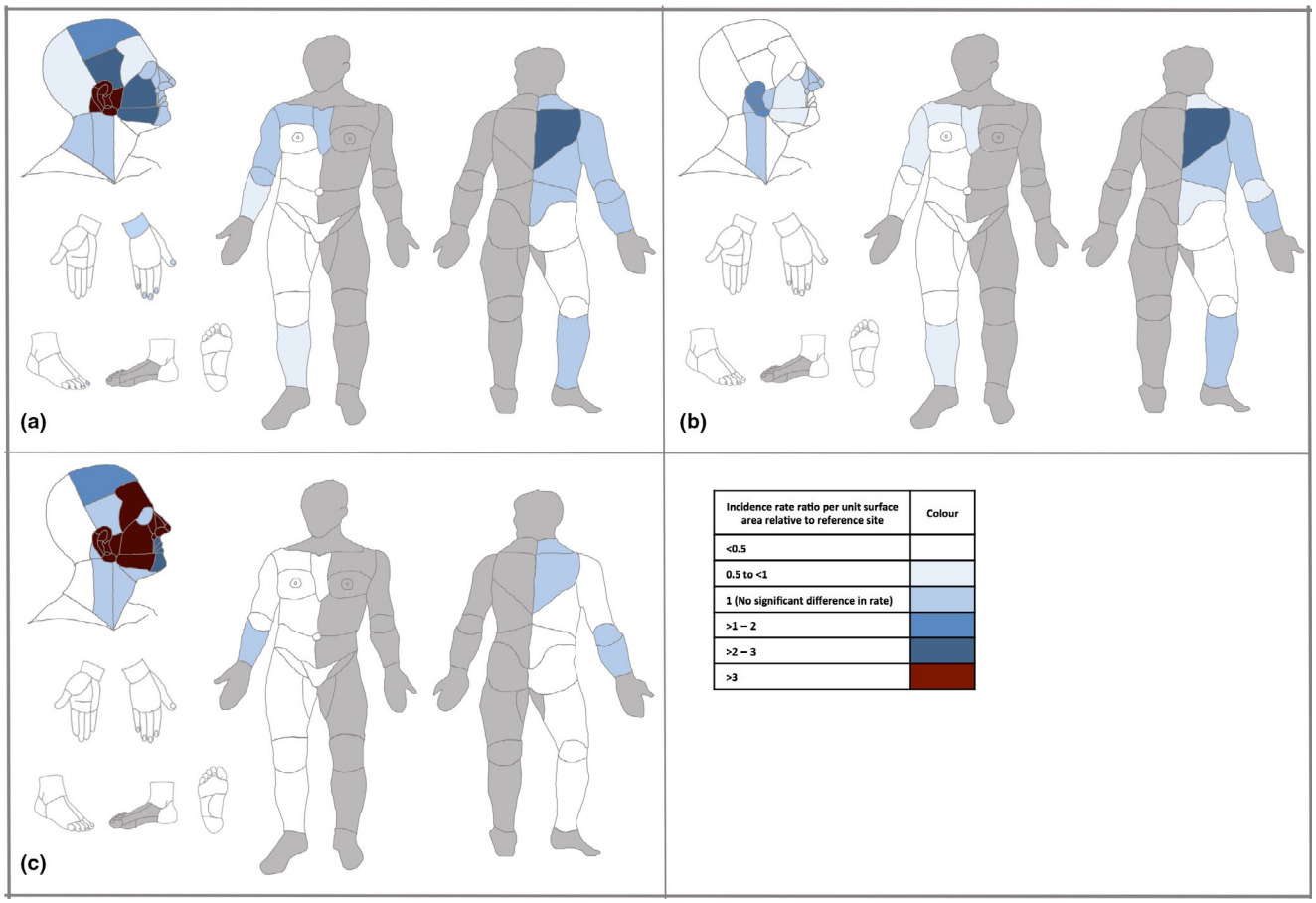

Figure 2 The anatomic distribution of melanoma for nodular (a), superficial spreading (b) and lentigo maligna (c) subtypes. Colours indicate the unadjusted ratio of incidence rate per unit area, relative to the reference site. The reference site for superficial spreading and nodular subtypes was the posterior arm, while the reference site for lentigo maligna was the posterior forearm; these sites had similar proportions of melanoma per unit surface area. Laterality was not assessed and mucosal, ocular as well as genital melanomas were excluded (shaded in grey).

area with increased odds of in situ disease (adjusted OR, 2.0; 95% CI 1.2–3.3, $P = 0.009$).

DISCUSSION

In this study, we examined the detailed anatomic distribution of cutaneous melanoma in a large Australian cohort with prospectively collected site data. Our results corroborated known associations of melanoma site distribution with age, sex, histologic subtype and patterns of sun exposure.[8–14] The association of increased melanoma thickness with male gender and older age in our cohort was comparable to previous reports.[19,20,24] Increased Breslow thickness was also associated with the hair-bearing scalp, ear, preauricular, perioral, subungual and plantar areas.

The anatomic distribution of melanoma in our study was generally consistent with the aetiological role of sun exposure. Similar to other large population studies,[8–14] melanoma incidence per unit area was highest in facial sites with the most cumulative sun exposure, such as the ear in men as well as the nose and cheek in women. There was a higher incidence of melanoma per unit area in sites with likely greater sun-exposure; the upper back had higher incidence than the lower back and buttocks, the supramammary chest had higher incidence than the abdomen, the posterior upper limb had higher incidence than the anterior upper limb and the lower leg had a higher incidence than the thigh. However, like others,[10–12] we found that the dorsal hand was a notable exception, with a low incidence of melanoma despite being a heavily sun-exposed site. Furthermore, although we did not identify an increased incidence of melanoma on the shoulder or upper arm relative to the forearm as previously reported,[8,10–12] this may reflect differences in site classification, including the distinction of anterior and posterior limb surfaces in our study. This may also relate to changes in relation to clothing trends with time[8,11] and geographic differences in the populations studied.[10,12]

Relative to women, men had a higher incidence of melanoma on the hair-bearing scalp, ears, peri-auricular, posterior neck and forehead, attributable to reduced protective hair coverage in these areas.[25,26] The greater

melanoma incidence amongst men was particularly pronounced in the anterior scalp of older patients, and this could be explained by the occurrence of androgenic alopecia.[27] When compared, men also had a higher incidence of melanoma on the supramammary chest, abdomen and back, while women had a higher incidence in lower limb areas such as the anterior thigh, lower leg and dorsal foot. Previous population studies have described similar findings with a predominance of melanoma on the back in men and the lower limb in women, and this is thought to be related to differences in clothing as well as occupational and recreational sun-exposure patterns.[10–12]

Variations in melanoma distribution according to age and subtype are thought to reflect unique patterns of sun-exposure at different sites, and biological pathways with distinct somatic mutations are involved.[15] At younger ages, melanoma tends to occur in sites with intermittent sun-exposure such as the trunk and limbs and is commonly of the superficial spreading subtype.[8–14] In contrast, in older age melanoma is associated with areas of chronic cumulative sun exposure, such as the head and neck, and lentigo maligna is more common.[8–14] Consistent with this, we found that younger patients had a higher incidence of melanoma in many intermittently exposed sites on the trunk and lower limbs than older patients. Likewise, older patients had a higher incidence of melanoma on chronically exposed facial sites than younger patients. Furthermore, lentigo maligna predominantly involved chronically sun-exposed areas of the head and neck, particularly central facial sites such as the nose and cheek. Superficial spreading subtype was more common on intermittently sun-exposed trunk and limb sites. Interestingly, nodular and superficial spreading subtypes had a similar distribution on the trunk and limbs, with high incidence on the upper back. However, relative to superficial spreading subtype, nodular melanoma was more common in the hair-bearing scalp, peri-auricular, ear, cheek and perioral sites. The peri-auricular, ear and cheek had the highest incidence of nodular melanoma per unit area. Previous studies have similarly shown that nodular melanoma is more common in the head and neck, leading some to suggest that it may arise primarily as a result of chronic sun-exposure.[1–4,24]

In our study, several head and neck as well as acral areas were found to have increased odds of thicker melanomas; after adjustment for age and sex these were the hair-bearing scalp, ear, perioral, ungual and plantar sites. Melanomas of the scalp and ear were associated with increased thickness and this was independent of histopathologic subtype. These findings are consistent with previous reports of the scalp and ear having a predilection for thicker melanomas,[1–6] and delayed diagnosis due to concealment by hair,[28] as well as rapid growth,[5,29] may be important contributing factors. Notably, the nose had the highest incidence of in situ disease, independent of histologic subtype, possibly reflecting the high visibility of this area leading to earlier diagnosis.

Our study has several limitations. There may have been selection bias as the VMS is a statewide tertiary referral service to which patients with advanced or aggressive disease are more likely to have been referred. Nevertheless, overall findings on melanoma distribution were consistent with statewide cancer registry data, despite invasive melanoma being overrepresented (76.6% in our cohort vs 56.1% Victorian Cancer Registry).[30] Furthermore, like other population studies,[10] we found consistency in melanoma incidence rates between contiguous sites with similar sun exposure (e.g. upper and lower abdomen). The prognostic significance of anatomic location was not examined in survival analyses.

CONCLUSION

Our study corroborates earlier research on melanoma distribution, providing more detailed subsite information. Melanoma most commonly arises in sun-exposed areas such as the nose and cheek in women, as well as the ear in men. The upper back is the most common site for melanoma on the trunk and limbs. Intermittently exposed sites on the trunk and lower limbs have a higher incidence of melanoma amongst younger patients, while chronically exposed sites in the head and neck have a higher incidence of melanoma in older patients. Men have a higher incidence on the scalp, ear, posterior neck and trunk, while women have a higher incidence on the lower limbs. Relative to superficial spreading subtype, nodular melanoma is more likely to occur in head and neck sites, with the peri-auricular, ear and cheek having the highest incidence of nodular melanoma per unit area. Increased Breslow thickness is associated with the hair-bearing scalp, ear, perioral, subungual and plantar sites. Improved patient and physician awareness of the anatomic distribution of melanoma may lead to earlier diagnosis and better outcomes in future.

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Supporting Information

Additional Supporting Information may be found online in Supporting Information:

Table S1. Surface areas used to assess melanoma distribution for 50 body sites.
Table S2. Differences in anatomic distribution of superficial spreading and nodular melanoma subtypes with incidence adjusted for surface area across 50 body sites.
Table S3. Breslow thickness of invasive melanomas compared across 50 body sites.
Table S4. Odds of in situ melanoma compared across 50 body sites.
Figure S1. Lesion location form (developed by the Pigmented Lesion Study Group) used to determine the anatomic location of each cutaneous melanoma.