



Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:

Xie, C;Pan, Y;McLean, C;Mar, V;Wolfe, R;Kelly, JW

Title:

Scalp melanoma: Distinctive high risk clinical and histological features

Date:

2017-08-01

Citation:

Xie, C., Pan, Y., McLean, C., Mar, V., Wolfe, R. & Kelly, J. W. (2017). Scalp melanoma: Distinctive high risk clinical and histological features. *Australasian Journal of Dermatology*, 58 (3), pp.181-188. <https://doi.org/10.1111/ajd.12437>.

Persistent Link:

<https://hdl.handle.net/11343/290828>

Title page

Manuscript title

Scalp melanoma – distinctive high risk clinical and histological features

Author names and affiliations

Charles Xie^{1,2}, Yan Pan¹, Catriona McLean¹, Victoria Mar¹, Rory Wolfe², John W. Kelly¹

¹ Victorian Melanoma Service, Alfred Hospital, Melbourne, Australia

² School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia

Corresponding author details

Dr Charles Xie, School of Public Health and Preventive Medicine, Level 6, The Alfred Centre,
99 Commercial Road, Melbourne VIC 3004 Australia

Phone: +61421891796 or +61399030107

Email: chencharlesxie@gmail.com

Acknowledgements

This work was supported by the School of Public Health and Preventive Medicine, Monash University.

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/ajd.12437](https://doi.org/10.1111/ajd.12437)

This article is protected by copyright. All rights reserved

Received Date : 16-Sep-2015

Revised Date : 06-Nov-2015

Accepted Date : 08-Nov-2015

Article type : Original Research

Abstract

Background/Objectives: Scalp melanoma has a worse prognosis than melanoma elsewhere, though the reasons for this are poorly understood. Current literature describing the clinicopathologic associations of scalp melanoma is limited. This study aims to compare clinical and histological features of scalp melanoma with other cutaneous head and neck melanoma (CHNM).

Methods: A cross-sectional study was performed of all primary CHNM cases seen at the Victorian Melanoma Service between 1994 and 2014, using prospectively recorded clinical data. Invasive and in-situ melanomas were compared separately.

Results: There were 306 scalp melanomas and 1163 other CHNM. Invasive scalp melanoma was associated with male sex (OR, 2.7; 95% CI, 1.9-3.9), increasing age (OR, 1.02 per year increase in age; 95% CI, 1.01-1.03), being first noticed by a person other than self, spouse/relative or doctor (OR, 2.9; 95% CI, 1.5-5.7), amelanosis (OR, 1.6; 95% CI, 1.1-2.3), and increased growth rate (OR, 1.14 per 1 millimetre [mm]/month growth rate increase; 95% CI, 1.04-1.26). Compared to other CHNM, scalp melanoma had greater median Breslow thickness (2.8mm versus 1.2mm), and it was independently associated with satellite metastases (OR, 4.7; 95% CI, 1.9-11.5) and nodular subtype (OR, 1.8; 95% CI, 1.1-3.1). In-situ scalp melanoma was associated with male sex, increasing age and presence of solar keratoses.

Conclusion: Scalp melanoma tends to occur in older men, is frequently rapidly growing, amelanotic, and is associated with high risk histological features. As it is more likely to be overlooked, increased recognition of the atypical presentations of scalp melanoma is required.

Keywords

melanoma; scalp; head and neck; epidemiology; clinical presentation; histopathology.

Introduction

There has been much interest in the influence of a melanoma's anatomic location on tumour characteristics and prognosis, with cutaneous head and neck melanoma (CHNM) described to have different clinical and histological features compared to melanoma elsewhere.¹⁻³ Scalp melanoma comprises 3-5% of all cutaneous melanomas in large cohorts,^{2,4} and has higher recurrence and mortality rates than other CHNM.⁵

The current literature describing scalp melanoma is limited, often with relatively small case series, or a predominant focus on recurrence and survival rates. We aim to describe the clinical and histological features of scalp melanoma, and to identify any differences between it and other CHNM. This will facilitate better understanding of the presentation of scalp melanoma, aid in its earlier detection and shed light on potential reasons for its poor prognosis.

Materials and methods

Institutional ethics approval was obtained from the Alfred Hospital for a cross-sectional study of all primary CHNM cases seen at the Victorian Melanoma Service (VMS) from its inception in October 1994 to February 2014. The VMS is a state-wide multidisciplinary tertiary referral clinic based at the Alfred Hospital in Melbourne, seeing approximately one-quarter of new melanoma cases across the state of Victoria, Australia. All patients presenting to the VMS were entered into a prospectively maintained melanoma database. This data was further correlated with patient medical records for the purposes of this study. Histology review of each melanoma specimen was conducted by experienced dermatopathologists at the VMS following the initial histological diagnosis and referral.

Data collected from each patient at the time of their initial outpatient appointment included: age, sex, phenotypic features (eye colour, hair colour, skin phenotype), historical features (number of blistering sunburns, solar keratoses, non-melanoma skin cancers, previous melanoma), clinical features (total naevus count, presence of dysplastic naevi, number of lentigines and freckles recorded as few, moderate or many) and tumour presentation (body site coded numerically including 132 head and neck sites, amelanosis, first observer, time from initial observation of change to histological diagnosis). Clinical features were assessed by a dermatologist or dermatology resident. Amelanotic tumours were those that appeared to the patient or doctor to be without pigmentation. We used a previously described historical estimation of growth rate of a tumour, derived by dividing its Breslow thickness, in millimetres (mm), by number of months from the initial observation of change in the lesion to time of histological diagnosis.⁶

Histological features assessed for all invasive melanomas were: tumour subtype, Breslow thickness, Clark level, ulceration, mitotic rate per square millimetre, neurotropism, lymphovascular invasion, satellite metastases and desmoplasia. For in-situ melanomas, only tumour subtype was assessed. Tumour subtype was classified, according to World Health Organization guidelines,⁷ as superficial spreading, lentigo maligna, nodular or desmoplastic, with less common tumour types grouped as other. Desmoplastic subtype was defined as melanoma with >80% of invasive tumour being associated with stromal fibrosis, i.e. “pure”

desmoplastic tumours;^{8,9} other tumours with focal desmoplasia were classified into other histological types. Mitotic rate values were categorised into <1, 1-4, 5-10, >10 per square millimetre for analysis.¹⁰ Regression, tumour infiltrating lymphocytes and pre-existing naevus were not routinely reported prior to the introduction of structured synoptic reports in 2005, thus only invasive melanomas diagnosed after 1st January 2005 were assessed for these features.

Mucosal and ocular melanomas were excluded, as well as cases where patient records were unobtainable, or where histology was not reviewed by a VMS dermatopathologist.

Melanoma cases were grouped into four anatomic sites – scalp, face (which included the forehead, nose, lips and cheeks), neck and ear. The scalp was defined as the maximal hair bearing area in a person's lifetime, extending from the hairline at age 20 years anteriorly to the superior nuchal line posteriorly, to the mastoid and zygomas laterally.

Comparisons were made between scalp and other CHNM, as well as between the individual head and neck sites. Invasive melanoma and in-situ melanoma were compared separately. All statistical analyses were performed using Stata version 13 (StataCorp LP, College Station, Texas, USA) statistical software. Statistical significance was assessed using a chi-square test, Wilcoxon rank-sum test or Kruskal Wallis test, as appropriate to the characteristic being compared between scalp and other sites in univariable analysis. Logistic regression was used to adjust the comparison of a characteristic between scalp and other CHNM for age and sex, as well as for more extensive multivariable analyses.

Results

6400 melanomas were managed at the VMS over the study period, from which 1617 CHNM were identified. After applying exclusion criteria, there were 1469 melanomas from 1402 patients, including 306 cases located on the scalp (20.8%) from 292 patients.

There were 244 invasive scalp melanomas identified from 238 patients, comprising 26.5% of all invasive CHNM. A higher proportion of scalp melanoma was invasive when compared to other CHNM (79.7% versus 58.3%, $p < 0.001$), although proportions of invasive melanoma were similar between scalp, neck (78.5%) and ear (78.4%) sites, with the face having a lower proportion of invasive melanoma (49.2%).

Invasive melanoma – associations of patient characteristics with tumour location

Scalp site was significantly associated with male sex (odds ratio [OR], 2.7; 95% confidence interval [CI], 1.9-3.9) and increasing age (OR, 1.02 per year of age; 95% CI, 1.01-1.03). While there were strong univariate associations between scalp site and a history of solar keratoses, history of non-melanoma skin cancer and past history of melanoma, the strength of these associations was reduced after adjusting for age and sex (Table 1). There was no evidence of an association between scalp melanoma and any of the phenotypic characteristics, namely hair colour, eye colour, skin type, and degree of freckling (data not shown).

Invasive melanoma – associations of clinical presentation with tumour location

After adjusting for age and sex, scalp site was strongly associated with increased growth rate (OR, 1.14 per 1mm/month increase in growth rate; 95% CI, 1.04-1.26), amelanosis (OR, 1.6; 95% CI, 1.1-2.3) and being first noticed by a person other than self, spouse/relative or doctor (OR, 2.9; 95% CI, 1.5-5.7) (Table 1). Of the 19 scalp melanomas noticed by a person other than self, spouse/relative or doctor, 13 (68.4%) were first noticed by a hairdresser.

Invasive melanoma – associations of histological features with tumour location

Univariable analysis demonstrated that scalp site was strongly associated with nodular or desmoplastic tumour subtypes, increasing Breslow thickness, higher mitotic rate, neurotropism, lymphovascular invasion and satellite metastases (Table 2). After the histological features, age and sex were entered into a multivariable logistic regression model, there remained evidence of associations between scalp site and each of: satellite metastases (OR, 4.7; 95% CI, 1.9-11.5), nodular tumour subtype (OR, 1.8; 95% CI, 1.1-3.1) and desmoplastic tumour subtype (OR, 2.0; 95% CI, 1.0-4.0). Desmoplasia and other minor histological features were not included in the multivariable model due to high numbers of missing values.

Scalp site was associated with a lower likelihood of ulceration in the multivariable model (OR, 0.5; 95% CI, 0.3-0.9), representing a reversal of the direction of association upon adjusting for other characteristics. For three Breslow thickness categories (1.01-2mm, 2.01-4mm, >4mm), scalp melanoma had a lower proportion of ulcerated tumours compared to other CHNM (data not shown), in particular for tumours 1.01-2mm thickness (9.5% versus 22.3%, $p=0.07$) and tumours 2.01-4mm (25.0% vs 38.3%, $p=0.07$).

When satellite metastasis was excluded from the multivariable model, increasing Breslow thickness became strongly associated with scalp melanoma (OR, 1.10 per millimetre; 95% CI, 1.01-1.19). When lentigo maligna melanomas were compared, a higher proportion on the scalp were found to exhibit focal desmoplasia than elsewhere in the head and neck (32.5% versus 11.8%, $p<0.001$), although those on the scalp were also thicker (median Breslow thickness 1.7mm versus 0.8mm, $p<0.001$). Focal desmoplasia was present in 5.6% of all nodular CHNM.

In-situ melanoma – associations with tumour location

Scalp site showed univariate associations with male sex, increasing age, history of solar keratoses and non-melanoma skin cancer, being first noticed by the doctor, and superficial spreading tumour subtype on univariate analysis (Table 3). The associations of in-situ scalp

melanoma with solar keratoses (OR, 2.4; 95% CI, 1.3-4.5) and superficial spreading subtype (OR, 4.5; 95% CI, 1.8-11.2) remained after adjusting for age and sex.

Author Manuscript

Discussion

We have described the largest reported series of scalp melanomas and their clinicopathologic associations compared to other CHNM. Whereas melanomas on the trunk and limbs occur in a younger population and are associated with large numbers of naevi, CHNM occurs in an older and predominantly male population, and is associated with presence of solar keratoses.^{1-3, 11} Our scalp melanoma group's average age of 69 years was older than other CHNM, and slightly older than other scalp melanoma cohorts with average ages ranging from 50 to 67 years.^{2, 12, 13} In addition, our scalp melanoma group was more predominantly male, consistent with other reports of scalp melanoma being up to six times more common in men than women.^{1, 2, 12, 13} Our scalp melanoma patients had more evidence of solar field damage than patients with other CHNM, although this can be accounted for by age and sex for invasive melanoma cases.

As well as chronic solar damage, scalp melanoma has been found to be related to alopecia.¹⁴ By the age of 55 years, at least 62% of Australian men have some form of androgenic alopecia, and its prevalence and extent increases with age.¹⁵ On the other hand, the majority of Australian women do not experience hair loss until over 70 years of age.¹⁶ The hair shaft provides important physical scalp protection from ultraviolet damage.¹⁷ Although there was no data on hair loss for our patient cohort, it was likely that androgenic alopecia in many older men would have led to higher amounts of scalp ultraviolet exposure.

In our cohort, 13 scalp melanomas were first noted by the patients' hairdressers. There have been other reports of hairdressers discovering melanoma on the scalp.¹⁸ Given that many hairdressers already examine their clients' scalps for suspicious lesions, refer patients on to a doctor upon seeing a suspicious lesion, and are willing to undergo further skin cancer awareness training,¹⁹ it may be beneficial to implement a campaign educating hairdressers about recognizing melanomas and other skin cancers on the scalp. Interestingly, the majority of in-situ scalp melanomas were first noticed by the doctor, suggesting that in-situ scalp melanoma did not arouse the suspicion of patients by feel or touch, or non-medical observers from inspection.

Scalp melanoma was associated with greater Breslow thickness, a finding reflected in other reports.^{1-3, 5, 13} Delayed detection may have contributed, and several authors propose that some melanomas may remain hidden behind hair.²⁰ The high prevalence of alopecia in our patient demographic would likely have diminished the importance of concealment by hair. Richard et al found rapid tumour growth to be a stronger influence on tumour thickness than diagnostic delay, although melanoma location was not recorded in that study.²¹ Therefore, increased thickness of scalp melanoma may be attributable partly to the rapid growth that we identified for scalp melanoma, and to a lesser extent to delayed diagnosis.

Rapid tumour growth may be explained by higher proportions of desmoplastic and nodular melanomas on the scalp, subtypes known to be associated with greater Breslow thickness, increasing age and solar damage.^{7, 9, 22} These subtypes are more frequently amelanotic and often rapidly growing,^{6, 7} characteristics that were strongly represented in our series of scalp melanomas. Melanomas exhibiting rapid growth have previously been associated with amelanosis, as well as other atypical clinical features such as symmetry, border regularity and elevation.⁶ The diagnosis of amelanotic melanoma is often delayed, with initial clinical misdiagnosis as basal cell carcinoma or benign skin lesion, and incorrect management.²³ Increased awareness of the potential significance of firm, rapidly growing non-pigmented lesions on the scalp (see Figures), among both clinicians and the general public, would be expected to facilitate early detection of scalp melanoma.

While there have been reports of nodular melanoma occurring more commonly on the scalp,^{1, 3} the predilection of desmoplastic melanoma for the scalp has not been previously described. The proportion of scalp melanomas being of desmoplastic subtype has only been described by three other reports, with a range from 0% to 8%,^{12, 13, 24} compared to 13% in our cohort. Desmoplastic melanoma more often shows neurotropism, and has a tendency to occur in the head and neck, often in older men, with a low incidence of *BRAF* mutations, suggesting that its pathogenesis is related to chronic sun exposure.⁷⁻⁹ In addition to “pure” desmoplastic melanomas, 32.5% of our scalp lentigo maligna melanoma had focal desmoplasia. While desmoplasia has the tendency to occur in lentigo maligna melanoma,^{8, 9} our findings suggest that this tendency is stronger on the scalp, although it is unclear whether this is related to their increased Breslow thickness or intrinsic properties of the scalp.

Of all the histological features, satellite metastases had the strongest association with scalp melanoma. Satellitosis may be microsattelites or clinically detectable satellites, are a feature associated with thicker tumours and other high-risk histological features.^{25, 26} They are also associated with shorter disease-free survival and high rates of nodal metastases,²⁶ and have been placed in the same prognostic category as in-transit metastases.²⁷ It appeared to confound the association between increasing Breslow thickness and scalp melanoma in our cohort, thus this high rate of satellitosis of scalp melanoma may at least in part be attributed to their increased thickness. Satellite metastases may also account for high rates of scalp melanoma local recurrence following wide local excision.¹²

Compared to other CHNM, a greater proportion of scalp melanoma had high mitotic rates, neurotropism and lymphovascular invasion, histological features known to be associated with thicker tumours and poorer prognosis.^{10, 28-30} Therefore, it was not surprising that these associations were weakened after multivariable analysis. Although a higher proportion of scalp melanoma was ulcerated, scalp melanoma was less likely to be ulcerated than other CHNM when comparison was focused on equal Breslow thickness. Hypoxia stimulates melanoma angiogenesis, which is one of the drivers behind ulceration.³¹ It is unclear if increased vascularity of the scalp reduces tumour hypoxia and angiogenesis, or if there is an alternative explanation for our findings.

When individual head and neck sites were analysed, we found that neck melanoma was distinct from other head melanoma, occurring in younger people, having stronger associations with high total naevi count and dysplastic naevi rather than markers of chronic sun damage, and a predominance of superficial spreading instead of lentigo maligna subtype. Similar findings have been reported previously,¹ suggesting that the pathogenesis of neck melanoma is more closely related to trunk melanoma than head melanoma.¹¹ Our findings suggest that melanomas on different anatomic sites in the head and neck tend to have different clinical presentations.

A limitation of this study is that it involves the retrospective analysis of a prospectively maintained general melanoma patient database. Therefore, the data collected did not include some clinical features, for example the presence and extent of alopecia which would have allowed us to better understand the impact of hair loss on melanoma pathogenesis. In

addition, we were unable to assess sentinel lymph node or BRAF mutation status, as the majority of our patient cohort did not have these tests performed. As the VMS does not routinely follow-up patients, melanoma recurrence or survival was unable to be assessed.

In conclusion, a distinctive clinicopathologic spectrum of melanoma presents on the scalp compared to other head and neck sites. Scalp melanomas are more likely to be rapidly growing, amelanotic, and nodular in subtype. They tend to occur in older men, and by inference, it is likely that male pattern alopecia and chronic solar damage play a role in causation. Not only should clinicians routinely examine the scalp for melanoma, they should also adjust their diagnostic criteria to accommodate this distinctive spectrum of clinical presentation. High risk histological features such as increased Breslow thickness and satellite metastases may explain the poor prognosis of scalp melanoma. Associations with desmoplasia, neurotropism and satellitosis indicate careful histological assessment of melanoma excision specimens from the scalp, with consideration given to wider surgical margins if these features are found.

References

1. Fisher SR. Cutaneous malignant melanoma of the head and neck. *Laryngoscope*. 1989;99(8 Pt 1):822-36.
2. Hoersch B, Leiter U, Garbe C. Is head and neck melanoma a distinct entity? A clinical registry-based comparative study in 5702 patients with melanoma. *Br J Dermatol*. 2006;155(4):771-7.
3. de Giorgi V, Rossari S, Gori A, et al. The prognostic impact of the anatomical sites in the 'head and neck melanoma': scalp versus face and neck. *Melanoma Res*. 2012;22(5):402-5.
4. Garbe C, Buttner P, Bertz J, et al. Primary cutaneous melanoma. Prognostic classification of anatomic location. *Cancer*. 1995;75(10):2492-8.
5. Parrett BM, Kashani-Sabet M, Singer MI, et al. Long-term prognosis and significance of the sentinel lymph node in head and neck melanoma. *Otolaryngol Head Neck Surg*. 2012;147(4):699-706.
6. Liu W, Dowling JP, Murray WK, et al. Rate of growth in melanomas: characteristics and associations of rapidly growing melanomas. *Arch Dermatol*. 2006;142(12):1551-8.
7. LeBoit P.E. BG, Weedon D, Sarasain A. (Eds.): World Health Organization. Classification of Tumours. Pathology and Genetics of Skin Tumours. Lyon: IARC Press, 2006.
8. Busam KJ, Mujumdar U, Hummer AJ, et al. Cutaneous desmoplastic melanoma: reappraisal of morphologic heterogeneity and prognostic factors. *Am J Surg Pathol*. 2004;28(11):1518-25.
9. de Almeida LS, Requena L, Rutten A, et al. Desmoplastic malignant melanoma: a clinicopathologic analysis of 113 cases. *Am J Dermatopathol*. 2008;30(3):207-15.
10. Azzola MF, Shaw HM, Thompson JF, et al. Tumor mitotic rate is a more powerful prognostic indicator than ulceration in patients with primary cutaneous melanoma: an analysis of 3661 patients from a single center. *Cancer*. 2003;97(6):1488-98.
11. Whiteman DC, Pavan WJ, Bastian BC. The melanomas: a synthesis of epidemiological, clinical, histopathological, genetic, and biological aspects, supporting distinct subtypes, causal pathways, and cells of origin. *Pigment Cell Melanoma Res*. 2011;24(5):879-97.

12. Terakedis BE, Anker CJ, Leachman SA, et al. Patterns of failure and predictors of outcome in cutaneous malignant melanoma of the scalp. *J Am Acad Dermatol*. 2014;70(3):435-42.
13. Cappello ZJ, Augenstein AC, Potts KL, et al. Sentinel lymph node status is the most important prognostic factor in patients with melanoma of the scalp. *Laryngoscope*. 2013;123(6):1411-5.
14. Stanganelli I, Argenziano G, Sera F, et al. Dermoscopy of scalp tumours: a multi-centre study conducted by the international dermoscopy society. *J Eur Acad Dermatol Venereol*. 2012;26(8):953-63.
15. Severi G, Sinclair R, Hopper JL, et al. Androgenetic alopecia in men aged 40-69 years: prevalence and risk factors. *Br J Dermatol*. 2003;149(6):1207-13.
16. Gan DCC, Sinclair RD. Prevalence of male and female pattern hair loss in Maryborough. *J Investig Dermatol Symp Proc*. 2005;10(3):184-9.
17. Otberg N, Shapiro J. Chapter 88: Hair Growth Disorders. In: Goldsmith LA, Katz SI, Gilchrist BA, et al., editors. *Fitzpatrick's Dermatology in General Medicine*, 8e. New York, NY: The McGraw-Hill Companies, 2012.
18. Pillemer BBL, Pugliano-Mauro MA, Ferris LK, et al. Three cases of scalp melanomas discovered by hairdressers. *J Clin Aesthet Dermatol*. 2013;6(8):32-4.
19. Roosta N, Black DS, Wong MK, et al. Assessing hairdressers' knowledge of scalp and neck melanoma and their willingness to detect lesions and make referrals to dermatologists. *J Am Acad Dermatol*. 2013;68(1):183-5.
20. Benmeir P, Baruchin A, Lusthaus S, et al. Melanoma of the scalp: the invisible killer. *Plast Reconstr Surg*. 1995;95(3):496-500.
21. Richard MA, Grob JJ, Avril MF, et al. Melanoma and tumor thickness: challenges of early diagnosis. *Arch Dermatol*. 1999;135(3):269-74.
22. Chamberlain AJ, Fritschi L, Giles GG, et al. Nodular type and older age as the most significant associations of thick melanoma in Victoria, Australia. *Arch Dermatol*. 2002;138(5):609-14.
23. McClain SE, Mayo KB, Shada AL, et al. Amelanotic melanomas presenting as red skin lesions: a diagnostic challenge with potentially lethal consequences. *Int J Dermatol*. 2012;51(4):420-6.

24. Ettl T, Irga S, Muller S, et al. Value of anatomic site, histology and clinicopathological parameters for prediction of lymph node metastasis and overall survival in head and neck melanomas. *J Craniomaxillofac Surg*. 2014;42(5):e252-8.
25. Bartlett EK, Gupta M, Datta J, et al. Prognosis of patients with melanoma and microsatellitosis undergoing sentinel lymph node biopsy. *Ann Surg Oncol*. 2014;21(3):1016-23.
26. Shaikh L, Sagebiel RW, Ferreira CMM, et al. The role of microsatellites as a prognostic factor in primary malignant melanoma. *Arch Dermatol*. 2005;141(6):739-42.
27. Balch CM, Gershenwald JE, Soong S-j, et al. Final Version of 2009 AJCC Melanoma Staging and Classification. *J Clin Oncol*. 2009;27(36):6199-206.
28. Shen S, Wolfe R, McLean CA, et al. Characteristics and associations of high-mitotic-rate melanoma. *JAMA Dermatol*. 2014;150(10):1048-55.
29. Kashani-Sabet M, Sagebiel RW, Ferreira CM, et al. Vascular involvement in the prognosis of primary cutaneous melanoma. *Arch Dermatol*. 2001;137(9):1169-73.
30. Baer SC, Schultz D, Synnestvedt M, et al. Desmoplasia and neurotropism. Prognostic variables in patients with stage I melanoma. *Cancer*. 1995;76(11):2242-7.
31. Bezrookove V, De Semir D, Nosrati M, et al. Prognostic impact of PHIP copy number in melanoma: linkage to ulceration. *J Invest Dermatol*. 2014;134(3):783-90.

Tables

Table 1: Patient characteristics and clinical presentation of invasive melanoma – scalp vs other head and neck sites

Patient characteristics	Scalp (n=244)	Total other head & neck (n=678)	p-value ^a	OR (CI) ^b	p-value ^b	Face (n=394)	Neck (n=179)	Ear (n=105)	p-value ^c
% male	79.9	58.0	<0.001	2.7 (1.9-3.9)	<0.001	51.5	63.1	73.3	<0.001
Median age (IQR)	69.3 (56.6-80.3)	62.3 (47.0-73.7)	<0.001	1.02 (1.01-1.03) ^d	<0.001	65.9 (50.7-76.0)	56.3 (39.3-69.5)	57.6 (46.2-70.9)	<0.001
% >5 blistering sunburns ^f	19.4	16.7	0.35	1.1 (0.7-1.6)	0.69	15.6	19.1	16.7	0.59
% solar keratoses	51.2	41.2	0.007	1.0 (0.7-1.4)	0.81	42.9	36.9	41.9	0.03
% history of NMSC ^f	48.5	36.5	0.001	1.1 (0.8-1.6)	0.46	40.6	32.2	28.9	0.001
% history of another melanoma	21.7	15.9	0.04	1.2 (0.8-1.8)	0.32	16.5	16.8	12.4	0.15
% moderate/many lentigines ^f	57.7	55.5	0.61	1.0 (0.7-1.4)	0.83	54.7	59.2	52.3	0.68
% total naevi >100 ^f	20.4	24.5	0.23	1.0 (0.6-1.5)	0.90	20.4	34.2	22.8	0.004
% dysplastic naevi ^f	22.8	23.8	0.76	1.2 (0.8-1.8)	0.38	18.9	35.3	21.8	0.001
Melanoma clinical presentation									
% amelanotic	31.2	19.3	<0.001	1.6 (1.1-2.3)	0.006	20.6	15.1	21.9	0.001
Median growth rate in mm/month (IQR) ^f	0.75 (0.24-2.00)	0.31 (0.08-0.90)	<0.001	1.14 (1.04-1.26) ^e	0.006	0.31 (0.07-0.95)	0.30 (0.10-0.82)	0.33 (0.09-0.83)	<0.001
% first noticed by ^f			0.02						0.002
Self	38.6	48.1		1 (reference)		50.0	44.4	47.6	
Spouse/relative	18.2	17.9		1.2 (0.8-1.8)	0.45	13.7	21.4	27.2	

Doctor	35.2	29.7		1.1 (0.8-1.6)	0.53	32.4	27.5	23.3	
Other person	8.1	4.4		2.9 (1.5-5.7)	0.001	4.0	6.7	1.9	

Abbreviations: OR, odds ratio; CI, confidence interval; IQR, interquartile range; NMSC, non-melanoma skin cancer; mm, millimetre.

^a statistical test comparing scalp and total other head and neck (unadjusted)

^b association between scalp and total other head and neck (adjusted for sex and age)

^c statistical test comparing scalp and the three other individual head and neck sites (unadjusted)

^d OR is per year increase in age

^e OR is per 1mm/month growth rate increase

^f missing values: blistering sunburns = 32, history of NMSC = 25, lentigines = 189, total naevi = 125, dysplastic naevi = 149, growth rate = 206, first noticed by = 25

Table 2: Histological features of invasive melanoma – scalp vs other head and neck sites

	Scalp (n=244)	Total other head & neck (n=678)	p-value ^a	OR (CI) ^b	p-value ^b	Face (n=394)	Neck (n=179)	Ear (n=105)	p-value ^c
% Tumour subtype			<0.001						<0.001
Lentigo maligna melanoma	35.7	43.1		1 (reference)		56.4	23.5	26.7	
Superficial spreading melanoma	23.8	33.9		1.1 (0.7-1.7)	0.68	21.8	55.9	41.9	
Nodular melanoma	26.6	15.6		1.8 (1.1-3.1)	0.02	13.5	15.1	24.8	
Desmoplastic melanoma	12.7	4.3		2.0 (1.0-4.0)	0.06	5.1	3.9	1.9	
Other	1.2	3.1		1.3 (0.3-5.3)	0.67	3.3	1.7	4.8	
Median Breslow thickness in mm (IQR) ^e	2.8 (1.3-5.3)	1.2 (0.5-2.7)	<0.001	1.06 (0.98-1.16) ^d	0.15	1.2 (0.5-2.6)	1.1 (0.5-2.5)	1.2 (0.7-3.0)	<0.001
% Breslow thickness ^e			<0.001						<0.001
≤1mm	20.5	44.5				44.0	49.2	38.1	
1.01-2mm	17.6	22.8				23.4	19.6	25.7	

2.01-4mm	27.5	18.3				18.6	17.9	18.1	
>4mm	34.4	14.5				14.0	13.4	18.1	
% Clarke level ^e			<0.001						<0.001
II	12.4	27.2				29.7	26.3	19.2	
III	11.5	17.4				15.5	21.8	17.3	
IV	41.6	43.3				41.4	42.5	51.9	
V	34.6	12.1				13.5	9.5	11.5	
% Ulceration ^e	28.6	23.5	0.12	0.5 (0.3-0.9)	0.01	22.6	22.2	29.9	0.20
% Satellite metastases ^e	11.3	2.1	<0.001	4.7 (1.9-11.5)	0.001	2.8	1.2	1.1	<0.001
% Mitotic rate/square mm ^e			<0.001						0.002
<1	24.0	39.2		1 (reference)		41.1	40.1	30.5	
1-4	36.9	33.7		1.3 (0.8-2.0)	0.28	31.8	32.7	42.1	
5-10	23.2	16.3		1.3 (0.8-2.3)	0.33	17.0	16.1	13.7	
>10	15.9	10.9		1.4 (0.7-2.6)	0.36	10.1	11.1	13.7	
% Neurotropism ^e	13.9	6.4	0.001	1.4 (0.7-2.6)	0.35	6.6	6.9	4.6	0.006
% Lymphovascular invasion ^e	7.7	4.6	0.07	0.7 (0.3-1.7)	0.38	3.9	5.5	5.4	0.27
% Desmoplasia ^{e, f}	29.3	11.5	<0.001			13.6	9.8	5.4	<0.001
% TIL (moderate/many) ^g	19.8	14.6	0.18			18.7	20.7	23.3	0.51
% Regression ^g	21.2	17.3	0.30			15.7	22.8	14.0	0.28
% Associated naevus ^g	13.9	14.8	0.79			9.0	24.5	23.4	0.001

Abbreviations: OR, odds ratio; CI, confidence interval; IQR, interquartile range; mm, millimetre; TIL, tumour infiltrating lymphocytes.

^a statistical test comparing scalp and total other head and neck (unadjusted)

^b multivariable model with following variables: age, sex, tumour subtype, Breslow thickness, mitotic rate, ulceration, neurotropism, lymphovascular invasion, satellite metastases (773 cases included in model)

^c statistical test comparing scalp and the three other individual head and neck sites (unadjusted)

^d OR is per mm increase in Breslow thickness

^e missing values: Breslow thickness = 1, Clarke level = 2, ulceration = 71, mitotic rate = 74, neurotropism = 97, lymphovascular invasion = 72, satellite metastases = 71, desmoplasia = 163

^f desmoplasia includes tumours of desmoplastic subtype and other tumours with focal desmoplasia

^g only cases diagnosed after 1st January 2005 were assessed for these features; missing values (out of 587): tumour infiltrating lymphocytes = 112, regression = 50, associated naevus = 72

Table 3: Patient characteristics, clinical presentation and histological features of in-situ melanoma – scalp vs other head and neck sites

	Scalp (n=62)	Total other head & neck (n=485)	p-value ^a	OR (CI) ^b	p-value ^b	Face (n=407)	Neck (n=49)	Ear (n=29)	p-value ^c
% male	79.0	48.3	<0.001	3.6 (1.9-6.8)	<0.001	44.5	63.3	75.9	<0.001
Median age (IQR)	72.6 (59.8-79.6)	63.8 (52.4-74.6)	<0.001	1.03 (1.01-1.05) ^d	0.01	64.1 (52.6-75.2)	62.9 (52.0-71.4)	63.4 (50.1-66.7)	0.003
% >5 blistering sunburns ^e	27.6	17.2	0.06	1.6 (0.9-3.1)	0.13	16.7	23.9	13.8	0.15
% solar keratoses	72.6	44.5	<0.001	2.4 (1.3-4.5)	0.004	42.8	57.1	48.3	<0.001
% history of NMSC ^e	50.0	36.1	0.04	1.2 (0.7-2.1)	0.59	35.0	46.8	34.5	0.08
% history of another melanoma	29.0	24.5	0.44	1.0 (0.6-1.9)	0.89	22.6	42.9	20.7	0.02
% moderate/many lentigines ^e	68.0	62.4	0.44	1.3 (0.7-2.5)	0.44	61.4	74.4	56.0	0.31
% total naevi >100 ^e	21.6	20.8	0.91	1.1 (0.5-2.4)	0.75	19.2	30.2	26.9	0.33
% dysplastic naevi ^e	7.8	14.0	0.22	0.5 (0.2-1.5)	0.24	12.4	26.2	16.0	0.05
% amelanotic	0	1.2	0.38	NA	NA	1.2	2.0	0	0.69

% first noticed by ^e			0.04						0.20
Self	18.3	36.3		1 (reference)		38.0	29.8	24.1	
Spouse/relative	16.7	14.2		1.6 (0.6-4.1)	0.30	13.4	19.2	17.2	
Doctor	58.3	42.9		1.6 (0.7-3.3)	0.26	42.3	44.7	48.3	
Other person	6.7	6.6		1.8 (0.5-6.3)	0.34	6.3	6.4	10.3	
Tumour subtype			0.04						<0.001
Lentigo maligna	85.5	92.8		1 (reference)		97.3	63.3	79.3	
Superficial spreading	14.5	6.2		4.5 (1.8-11.2)	0.001	2.2	30.6	20.7	
Other/unclassifiable	0	1.0		NA	NA	0.5	6.1	0	

Abbreviations: OR, odds ratio; CI, confidence interval; IQR, interquartile range; NA, not applicable; NMSC, non-melanoma skin cancer.

^a statistical test comparing scalp and total other head and neck (unadjusted)

^b association between scalp and total other head and neck (adjusted for sex and age)

^c statistical test comparing scalp and the three other individual head and neck sites (unadjusted)

^d OR is per year increase in age

^e missing values: blistering sunburns = 30, history of NMSC = 19, lentigines = 109, total naevi = 93, dysplastic naevi = 97, first noticed by = 16

Figure legends

Figure 1: This red nodule on a woman's scalp was a 2.02 millimetre thick nodular melanoma.

Figure 2: This 79 year old man presented with a scalp nodule, with excisional biopsy revealing 9 millimetre thick desmoplastic melanoma with neurotropism.



ajd_12437_f1.jpg



ajd_12437_f2.jpg