

## CLINICAL REPORT

# Ten-year Audit of Melanoma in a Central England Population\*

Joseph HARDWICKE<sup>1</sup>, A. Murray BRUNT<sup>2</sup>, Gwen RYLANDS<sup>3</sup> and Sukh RAYATT<sup>1</sup>

<sup>1</sup>Department of Plastic Surgery, <sup>2</sup>Department of Oncology, and <sup>3</sup>Clinical Nurse Specialist for Skin Cancer, University Hospitals of North Staffordshire NHS Trust, Stoke-on-Trent, UK

**The incidence of melanoma in the North Staffordshire region has more than doubled over the last 10 years, and nearly tripled in the “thin” melanoma group ( $\leq 1$  mm). A retrospective audit was performed to investigate the overall management of melanoma, with a focus on thin melanomas. A total of 507 patients was identified between 1999 and 2009. The incidence of melanoma is increasing in the older age groups ( $>50$  years), although the thin melanomas were diagnosed at a significantly younger age than the cohort as a whole ( $p < 0.001$ ). The anatomical distribution was similar in both groups. More females were affected by thin melanomas (65%) compared with all melanomas (55%). This audit provides a unique insight into the incidence and characteristics of melanoma in a Central England population. The incidence of melanoma is increasing, but more so in the thin group. Thick ( $>4$  mm) and intermediate (1.01–4 mm) melanomas are increasing at a slower rate. *Key words: melanoma; incidence; trends; UK***

(Accepted November 18, 2010.)

Acta Derm Venereol 2011; 91: 440–443.

Joseph Hardwicke, The Old School House, 6, Church Street, Netherseal, Derbyshire DE12 8DF, UK. E-mail: hardwickej@doctors.org.uk

North Staffordshire describes an area in Staffordshire, in the West Midlands region of England. It contains the borough of Newcastle-under-Lyme, Staffordshire Moorlands and the city of Stoke-on-Trent. The total population of the area in 2001 was 457,165 and comprised a majority white population (96.6%) (1). In 2006, this population had been estimated at 458,766, indicating a relatively static population with only 0.3% estimated increase over 5 years (2). This area is served by the University Hospitals of North Staffordshire National Health Service (NHS) Trust.

Management of patients with malignant melanoma is coordinated by a skin cancer multi-disciplinary team (MDT). In the North Staffordshire region this has evolved to consist of plastic surgeons, dermatologists,

histopathologists, radiologists, specialist nursing staff and oncologists (3).

Studies from the UK and around the world (4–12) provide a description of melanoma within various differing cohorts, including epidemiological analysis, as well as clinical management and patient outcome data. There are no recent studies of a central England cohort of patients diagnosed with malignant melanoma, and few studies detail patient management data; the main focus is generally on incidence and outcome measures (13–15).

One of the authors (SR) noted an apparent increase in the number of patients diagnosed with thin melanomas (i.e.  $\leq 1$  mm Breslow thickness), presenting to the Department of Plastic Surgery. In response, a retrospective audit was performed to investigate the changing patterns of melanoma diagnosis in North Staffordshire, as well as demographic, pathological and clinical data associated with these patients. An increase in incidence of thin melanomas has been reported (4, 5). Additional aims of this audit were to ensure patients are managed in accordance with UK guidelines (3), as well as producing a local database for future analysis of trends in diagnosis. A separate analysis of patients with thin melanomas was also performed to identify any trends in this subgroup.

## MATERIALS AND METHODS

Patients who had been diagnosed with malignant melanoma between 1 August 1999 and 31 July 2009 were identified from hospital coding. Histopathological and radiological reports, as well as baseline patient identification details, were retrieved from respective databases. Enhanced patient details were obtained for the cohort diagnosed between 1 August 2004 and 31 July 2009 due to a conformational change in the medical record keeping after 1 August 2004.

Exclusion criteria were: (i) *in situ* disease; (ii) primary diagnosis outside of date range; (iii) metastatic disease at presentation; (iv) no primary skin lesion identified; (v) histopathology specimen/report unavailable; (vi) no medical records available; (vii) non-NHS patients or NHS patients diagnosed outside of the North Staffordshire region. If the disease was upstaged within the study period, the highest American Joint Committee on Cancer (AJCC) stage was used for classification.

Statistical analyses were undertaken using GraphPad Prism version 4.00 (GraphPad Software, San Diego, CA, USA). Data were tested for a normal distribution by the Shapiro-Wilk test. Parametric data were compared using a two-tailed Student's *t*-test and a one-way analysis of variance (ANOVA) with a Bon-

\*This paper has been presented as a poster at the 6<sup>th</sup> European Association of Dermato-Oncology (EADO) Congress, 2010.

ferroni post-test for group analysis. Non-parametric data were compared with the Mann–Whitney test. Results are expressed as a mean and standard deviation (SD). Statistical significance was considered at a probability of  $p < 0.05$ .

RESULTS

A total of 746 individuals was identified from hospital coding for the 10-year study period. A total of 239 (32%) individuals was excluded due to non-fulfilment of the inclusion criteria (e.g. *in situ* disease, see above). The remaining 507 patient records were examined. Enhanced patient data was retrieved for the cohort diagnosed from the 5-year study period from 1 August 2004 to 31 July 2009 ( $n = 312$ ). The mean incidence of malignant melanoma over the 10-year study period was 51 cases/year, equating to a population-adjusted incidence of 11/100,000. The incidence of thin melanomas increased relative intermediate (1.01–4 mm) and thick (>4 mm) melanomas (Fig. 1).

Between 1 August 2004 and 31 July 2009, 314 melanomas were diagnosed in 312 individuals (163 thin melanomas). For the whole cohort, the mean age at diagnosis was 60.6 years. Over this 5-year study period, there was a greater increase in the incidence of malignant melanoma in the older age groups (50–70 years, >70 years) compared with the younger age groups (<30 years, 30–50 years) (Fig. 2). Malignant melanoma was more common in females (54.5%) than males (45.5%) with a female:male ratio of 1.2:1. Females were diagnosed at a significantly younger age (58.6 years) than males (62.5 years) ( $p < 0.05$ ). Ethnicity, as recorded in the patient record consisted of a majority White British population (92.3%).

The melanoma histological subtype was most commonly superficial spreading (56.1%), then nodular (26.8%), lentigo maligna melanoma (11.1%) and acral lentiginous in 0.6% (Fig. 3). Other subtypes including desmoplastic melanoma and unrecorded subtypes were seen in 5.6% of cases. The mean Breslow thickness of each of these subtypes is shown in Table I. The mean

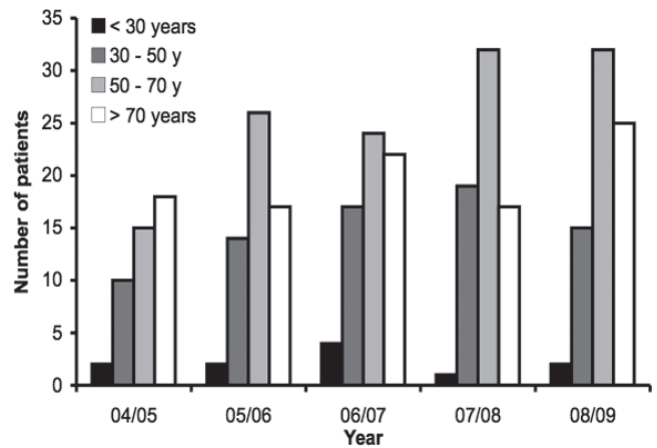


Fig. 2. Incidence of malignant melanoma amongst different age groups between 2004 and 2009 in North Staffordshire.

Breslow thickness, overall, was 2.3 mm (median 0.9 mm), with a median Clark level of 3. Nodular melanomas were significantly thicker than superficial spreading or lentigo maligna melanomas ( $p < 0.001$ ). Ulceration was seen in 36.9% of nodular melanomas, but was less than 8.5% in superficial spreading or lentigo maligna melanoma.

In the thin melanoma subgroup, age at diagnosis was significantly less when compared with melanomas >1 mm (56 vs. 64.8 years;  $p < 0.001$ ). The incidence of thin melanoma showed a marked increase in female:male ratio when compared with the overall incidence (female:male ratio of 1.9:1). There was no significant difference in age at diagnosis between the sexes ( $p = 0.36$ ). Superficial spreading subtype again, was most common, but significantly more so in the

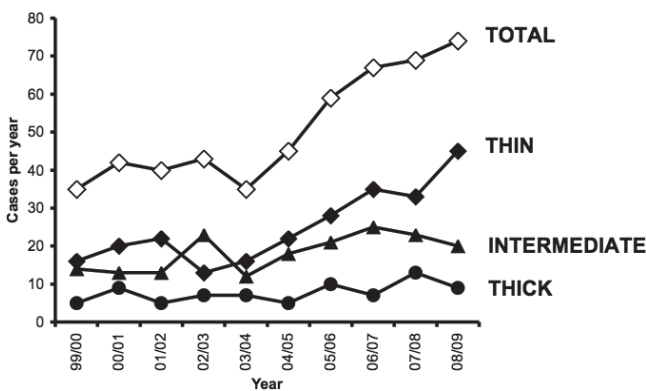


Fig. 1. Incidence of thin, intermediate and thick malignant melanoma in North Staffordshire.

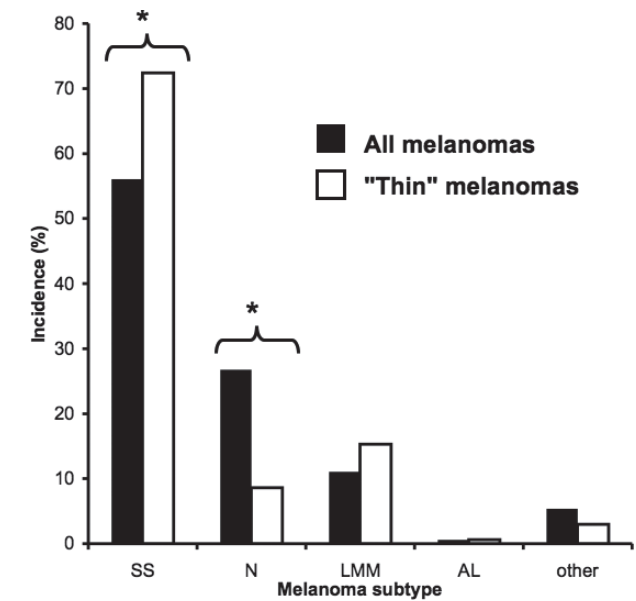


Fig. 3. Distribution of melanoma subtype in North Staffordshire. A comparison between all melanomas and thin melanomas. SS: superficial spreading; N: nodular; LMM: lentigo maligna melanoma; AL: acral lentiginous.

Table 1. Overall distribution of melanoma pathological subtype (2004 to 2009). Nodular melanomas are significantly thicker than superficial spreading (SS) or lentigo maligna melanoma. \* $p < 0.001$ . The majority of thin melanomas were of SS subtype

Subtype	Mean Breslow thickness, mm	Range, mm
Superficial spreading	1.2	0.1–10.2
Nodular	4.8*	0.4–25
Lentigo maligna melanoma	1	0.1–4.1
Acral lentiginous	3.1	0.6–5.5

thin melanoma cohort (72.4% vs. 56.1%;  $p < 0.001$ ) (Fig. 3).

The anatomical distribution, on all but the upper limb showed marked variation between the sexes. Males had a predilection for disease affecting the trunk and head and neck, whilst in females it was the lower limb. The thin melanoma subgroup displayed similar distribution (Fig. 4). The average Breslow thickness amongst the male cohort (2.75 mm) was significantly greater than amongst females (1.84 mm;  $p = 0.015$ ). Nodular melanoma was more common in males (male:female = 1.9:1), whilst superficial spreading was more common in females (female:male = 1.4:1).

Control of local disease was performed to UK guidelines (3) in 96.4% of cases. The mean time between initial diagnostic excision biopsy and wide excision was 44.5 days. In the cases where wide excision was not performed (11 cases), 3 local recurrences were observed. Overall, metastatic nodal disease has occurred in 7.4% of patients, affecting the inguinal nodes in 10 cases, the axillary nodes in 7 and neck nodes in 6. The mean Breslow thickness of malignant melanoma in these cases was 7.2 mm, and 60.1% showed epidermal ulceration. These cases were diagnosed clinically at a mean of 339 days (range 7–1646 days) after initial diagnosis. All underwent cytological and radiological investigation prior to lymph node dissection. Four out of 23 cases of nodal disease arose from AJCC stage I

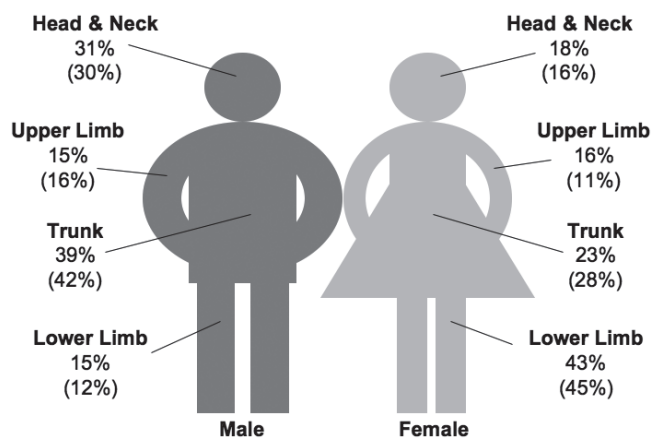


Fig. 4. Anatomical distribution of all malignant melanomas between the sexes in North Staffordshire. Distribution of thin melanomas shown in parentheses.

to IIA melanomas, and three of these from thin melanomas. The tumour mitotic rate (mitoses/mm<sup>2</sup>) was significantly higher in the melanoma nodal metastases group (mean = 17.7/mm<sup>2</sup>), compared with the localized melanomas (mean = 3.4/mm<sup>2</sup>;  $p < 0.0001$ ). There was no significant difference in mitotic rate when comparing metastatic thin melanoma with metastatic intermediate or thick melanoma. All cases of nodal metastasis were associated with a tumour mitotic rate of  $> 1/\text{mm}^2$ .

The incidence of melanoma more than doubled between 1999/2000 and 2008/2009, from 7.5/100,000 to 15.9/100,000 (an increase of 111%), although no statistical significant change was noted in Breslow thickness ( $1.81 \pm 2.87$  mm and  $1.87 \pm 1.53$  mm, respectively) or female:male ratio (both 1.1:1). The incidence of thin melanomas nearly tripled over this study period (181%), whilst intermediate (1.01–4 mm) and thick melanomas ( $> 4$  mm) increased more slowly (42% and 80%, respectively).

## DISCUSSION

The overall incidence of malignant melanoma found in North Staffordshire is comparable with that found in other UK studies (4–8). The increasing incidence, especially in the thin melanoma group is also similar. Our study looks at a more contemporary group than other published data, and hence the above-average incidence of all melanomas may be representative of the UK as a whole (in line with a predicted increase in incidence (16, 17)). The increase in the thin melanoma cohort may represent earlier diagnosis, indicating improved public and professional education in relation to melanoma.

The patient demographic data is typical of that of malignant melanoma, with a greater incidence in the female population. The pathological and anatomical distribution is also typical. The rise in incidence of thin melanoma, and clinical outcome in this group has also been noted by other authors (18–21) who identified the prognostic relevance of tumour mitotic rate, which has led to amendments of the AJCC staging system (22). The mitotic rate in the present study was significantly higher in the nodal metastases group, compared with the localized melanomas. All cases of nodal metastasis were associated with a tumour mitotic rate of  $> 1/\text{mm}^2$ , confirming the relevance of mitotic rate in the staging of melanoma.

Thin melanomas that produce nodal metastases may potentially be detected at an earlier time with the provision of a sentinel lymph node biopsy (SLNB) service. Although the importance of SLNB in the staging of melanoma is well recognized, the impact on survival rate is yet to be established, as well as concerns over sensitivity and specificity (23, 24). The creation of a SLNB service is currently under review in the North Stafford-



shire region. Recent studies have advocated the use of SLNB in melanomas of Breslow thickness >0.76 mm (25–27) as a staging tool to identify regional node-negative patients who would not benefit from a complete nodal dissection. All of the cases of nodal metastasis in this study were >0.76 mm in thickness, with a tumour mitotic rate of >1 mm<sup>2</sup>. The appreciation of tumour mitotic rate may be a key selector in this cohort.

In summary, the present audit provides a picture of the contemporary incidence of malignant melanoma in a stable population in Central England. Whilst melanoma has more than doubled in incidence over the last 10 years in North Staffordshire, the incidence of thin melanoma has nearly tripled. This may be due to enhanced surveillance and increased patient education in the region, leading to earlier diagnosis.

#### ACKNOWLEDGEMENTS

The authors would like to thank Dr Thomas Hunter for his help with data collection and input, and Dr Mark Stephens for providing diagnostic information.

*The authors declare no conflict of interest.*

#### REFERENCES

1. Stoke on Trent City Council. [cited 2009 Dec 11] Available from: <http://www.stoke.gov.uk/ccm/navigation/council-and-democracy/statistics/north-staffordshireprofile/>.
2. Office for National Statistics. [cited 2009 Dec 11] Available from: <http://www.statistics.gov.uk/statbase/Product.asp?vlnk=13893>.
3. Marsden JR, Newton-Bishop JA, Burrows L, Cook M, Corrie PG, Cox NH, et al. Revised UK guidelines for the management of cutaneous melanoma 2010. *Br J Dermatol* 2010; 163: 238–256.
4. Mowbray M, Stockton DL, Doherty VR. Changes in the site distribution of malignant melanoma in South East Scotland (1979–2002). *Br J Cancer* 2007; 96: 832–835.
5. MacKie RM, Bray C, Vestey J, Doherty V, Evans A, Thomson D, et al. Melanoma incidence and mortality in Scotland 1979–2003. *Br J Cancer* 2007; 96: 1772–1777.
6. Neal RD, Cannings-John R, Hood K, Sowden J, Lawrence H, Jones C, et al. Excision of malignant melanomas in North Wales: effect of location and surgeon on time to diagnosis and quality of excision. *Fam Prat* 2008; 25: 221–227.
7. Harman KE, Fuller LC, Salisbury JR, Higgins EM, du Vivier AWP. Trends in the presentation of cutaneous malignant melanoma over three decades at King's College Hospital, London. *Clin Exp Dermatol* 2004; 29: 563–566.
8. Downing A, Newton-Bishop JA, Forman D. Recent trends in cutaneous malignant melanoma in the Yorkshire region of England; incidence, mortality and survival in relation to stage of disease, 1993–2003. *Br J Cancer* 2006; 95: 91–95.
9. Howlett AL, Dewar RAD, Morris SF. The epidemiology of cutaneous malignant melanoma in Nova Scotia. *Can J Plast Surg* 2006; 14: 211–214.
10. Lasithiotakis KG, Leiter U, Gorkiewicz R, Eigentler T, Breuninger H, Metzger G, et al. The incidence and mortality of cutaneous melanoma in Southern Germany. *Cancer* 2006; 107: 1331–1339.
11. Nagore E, Oliver V, Botella-Estrada R, Moreno-Picot S, Guillen C, Fortea JM. Clinicopathological analysis of 1571 cutaneous melanomas in Valencia, Spain: factors related to tumour thickness. *Acta Derm Venereol* 2006; 86: 50–56.
12. Amerio P, Manzoli L, Auremma M, Carbone A, Proietto G, Angelucci D, et al. Epidemiology and clinical and pathological characteristics of cutaneous melanoma in Abruzzo (Italy). *Int J Dermatol* 2009; 48: 718–722.
13. Ratchet B, Quinn MJ, Cooper N, Coleman MP. Survival from melanoma of the skin in England and Wales up to 2001. *Br J Cancer* 2008; 99: S47–S49.
14. McMullen EA, Kee F, Patterson CC, Gavin AT, Dolan OM. Improved survival for melanoma in Northern Ireland: a comparison of two 5-year periods (1984–1988 and 1994–1998). *Br J Dermatol* 2004; 151: 587–593.
15. Goodwin RG, Holme SA, Roberts DL. Variations in registration of skin cancer in the United Kingdom. *Clin Exp Dermatol* 2004; 29: 328–330.
16. MacKie RM, Hauschild A, Eggermont AMM. Epidemiology of invasive cutaneous melanoma. *Ann Surg Oncol* 2009; 20: vi1–vi7.
17. Diffey BL. The future incidence of cutaneous melanoma within the UK. *Br J Dermatol* 2004; 151: 868–872.
18. Gimotty PA, Elder DE, Fraker DL, Botbyl J, Sellers K, Elenitsas R, et al. Identification of high-risk patients among those diagnosed with thin cutaneous melanomas. *J Clin Oncol* 2007; 25: 1129–1134.
19. Wright BE, Scheri RP, Xing Ye MS, Faries M, Turner RR, Essner R, et al. The importance of sentinel node biopsy in patients with thin melanoma. *Arch Surg* 2008; 143: 892–900.
20. Cecchi R, Buralli L, Innocenti S, De Gaudio C. Sentinel node biopsy in patients with thin melanomas. *J Dermatol* 2007; 34: 512–515.
21. Wong SL, Brady MS, Busam KJ, Coit DG. Results of sentinel lymph node biopsy in patients with thin melanoma. *Ann Surg Oncol*; 2006; 13: 302–309.
22. Balch CM, Gershenwald JE, Soong S-J, Thompson JF, Atkins MB, Byrd DR, et al. Final version of 2009 AJCC melanoma staging and classification. *J Clin Oncol* 2009; 27: 6199–6206.
23. Meirion Thomas J. Prognostic false-positivity of the sentinel node in melanoma. *Nat Clin Pract Oncol* 2008; 5: 18–23.
24. Caraco C, Marone E, Celentano G, Botti G, Mozzillo N. Impact of false-negative sentinel lymph node biopsy on survival in patients with cutaneous melanoma. *Ann Surg Oncol* 2007; 14: 2662–2667.
25. Vermeeren L, Ent FV, Sastrowijoto P, Hulsewe K. Sentinel lymph node biopsy in patients with thin melanoma: occurrence of nodal metastases and its prognostic value. *Eur J Dermatol* 2010; 20: 30–34.
26. Andtbacka RH, Gershenwald JE. Role of sentinel lymph node biopsy in patients with thin melanoma. *J Natl Compr Canc Netw* 2009; 7: 308–317.
27. Phan GQ, Messina JL, Sondak VK, Zager JS. Sentinel lymph node biopsy for melanoma: indications and rationale. *Cancer Cont* 2009; 16: 234–239.