Asymmetric lateral distribution of melanoma and Merkel cell carcinoma in the United States

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Background: A recent report suggested a trend toward more ultraviolet-linked skin cancers arising on the left rather than the right side of the body in the United States.

Objective: We sought to test whether the reported incidences of two ultraviolet-linked skin cancers, malignant melanoma (MM) and Merkel cell carcinoma (MCC), are statistically significantly greater on the left than the right in the United States.

Methods: MMs (n = 82,587) and MCCs (n = 2384) occurring on the left or right side of the face, arm, or leg that were reported in the Surveillance, Epidemiology, and End Results registry between 1986 and 2006 were included for analysis.

Results: MM and MCC were significantly more likely to present on the left than the right ($P < .01$ for both MM and MCC). In all, 53% of arm melanomas, 51% of facial melanomas, and 52% of leg melanomas presented on the left. A total of 55% of arm MCCs and 52% of facial MCCs presented on the left, whereas leg MCCs were equally distributed.

Limitations: National registry data did not provide information regarding sun exposure or driving habits. No equivalent registry data were available for basal or squamous cell carcinoma.

Conclusions: Both melanoma and MCC are significantly more likely to arise on the left than the right, and this effect was most prominent on the arm. Driver-side automobile ultraviolet exposure (approximately 5-fold stronger on the left than right arm) is a likely contributing factor. It may be prudent to remind individuals prone to skin cancer to take appropriate sun precautions when driving in an automobile. (J Am Acad Dermatol 2011;65:35-9.)

Key words: asymmetric; automobile; melanoma; Merkel cell carcinoma; presentation; ultraviolet.

Ultraviolet (UV) light is a well-characterized risk factor for most skin cancers, including melanoma[1] and Merkel cell carcinoma (MCC).[2,3] One source of environmental UV exposure is driving or riding in automobiles. Actinic keratoses have been reported to occur more frequently on the right side of the body in Australian drivers, where drivers sit on the right side of the car.[4] Conversely, in a recent case series from the United States, where drivers sit on the left side of the car, a trend toward left-sided bias in skin cancer was observed.[5] In this series of 890 cases, skin cancers (mostly basal cell carcinomas) were more frequently detected on the left side of the body (53% vs 47%), although the trend did not reach statistical significance.

A recent study by Moehrle et al[6] carefully examined the pattern of UV exposure received by a driver

Abbreviations used:

MCC:	Merkel cell carcinoma
MM:	malignant melanoma
SEER:	Surveillance, Epidemiology, and End Results
UV:	ultraviolet

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sitting on the left side of an automobile. Moehrle et al[6] reported that approximately 25% to 31% of ambient UV radiation is transmitted through an open car window (the remainder is blocked by the vehicle body). In contrast, a closed car window that only transmits UVA rays allows approximately 3% to 4% of environmental UV radiation to be transmitted.[6] For the driver, this radiation more strongly affects the left side of the body. In particular, a driver sitting on the left next to a closed car window receives many times more UV on the left arm and face than the right, with the highest total dose being on the left arm. In contrast, UV exposure to the leg is relatively evenly distributed, with only slightly more exposure on the right than the left leg.

As noted above, a nonsignificant trend toward left-sided skin cancer bias has recently been suggested in the US population.[5] To build on this study, we used national registry data from the Surveillance, Epidemiology, and End Results (SEER) database to test in a large number of cases whether there are significantly more left- than right-sided UV-associated cancers reported in the United States. Specifically, we focused on two skin cancers—malignant melanoma (MM) and MCC—because these are captured in the SEER database. We hypothesized that both MM and MCC would display a left-sided bias. Furthermore, we hypothesized this bias might be a result of driving and thus particularly affect the face and left arm, but not the leg.

CAPSULE SUMMARY

- More ultraviolet-associated skin cancers (melanomas and Merkel cell carcinomas) occur on the left side of the body than the right in the United States.
- The left arm is most prominently affected by this asymmetry for both cancer types.
- It may be appropriate to remind individuals prone to skin cancer that ultraviolet exposure from automobile driving is a common and established source of ultraviolet that preferentially affects the left arm.

METHODS

Patient inclusion

Information was obtained from the SEER registry database.[7] We considered all melanoma (*International Classification of Diseases for Oncology, Third Edition* code 8270-8774) and MCC (*International Classification of Diseases for Oncology, Third Edition* code 8247) cases that met the following criteria: diagnosed between 1986 and 2006; lateralized cancer (as opposed to midline) with known side, known age, known gender. Cancers that presented on one of 3 body sites were considered for analysis: skin of face and scalp (C44.3, C44.4), upper limb (C44.6), and lower limb (C44.7). A total of 82,587 melanoma and 2384 MCC cases were included in the analysis.

Data extraction

Data were extracted using SEERstat software (National Cancer Institute, Bethesda, MD).

Statistical analysis

Melanoma and MCC were analyzed separately. Statistical analysis was performed with GraphPad Prism software (GraphPad Software, La Jolla, CA). The χ^2 test was used to test whether the observed left-right distribution differed significantly from 50% on the left and 50% on the right.

RESULTS

Malignant melanoma

Among 82,587 melanomas analyzed, 52.3% presented on the left side and 47.7% on the right. This left bias was statistically significant ($P < .001$).

Appreciably more tumors were observed on the left side of the face and the left arm as compared with the right (Fig 1). In all, 51% of face and scalp melanomas (7787 of 15,185, $P = .002$) and 53% of arm melanomas (19,791 of 37,588, $P < .001$) presented on the left side. However, melanomas were also significantly more likely to present on the left leg than the right. A total of 52% of leg tumors (15,627 of 29,814, $P < .001$) presented on the left side.

Data were split out by age and sex to determine whether left-right biases were more pronounced in any particular group. Women older than 65 years trended toward less left-side bias in the head and neck as compared with older men, however, this difference between men and women was not significant ($P = .56$) (Table I).

Merkel cell carcinoma

A total of 2384 MCCs met inclusion criteria and were analyzed. Of these, 1256 (52.7%) presented on the left and 1128 (47.3%) on the right ($P = .046$) (Table II). Face, scalp, and upper limb cases were more likely to present on the left than the right, but cases on the leg were evenly distributed. Left side presentation occurred in 465 of 845 cases on the upper limb (55%, $P = .004$), 503 of 968 cases on the face and scalp (52%, $P = .22$), and 288 of 571 cases on the lower limb (50%, $P = .83$) (Fig 2).

DISCUSSION

It has previously been suggested by Butler and Fosko[5] that skin cancers in the United States,

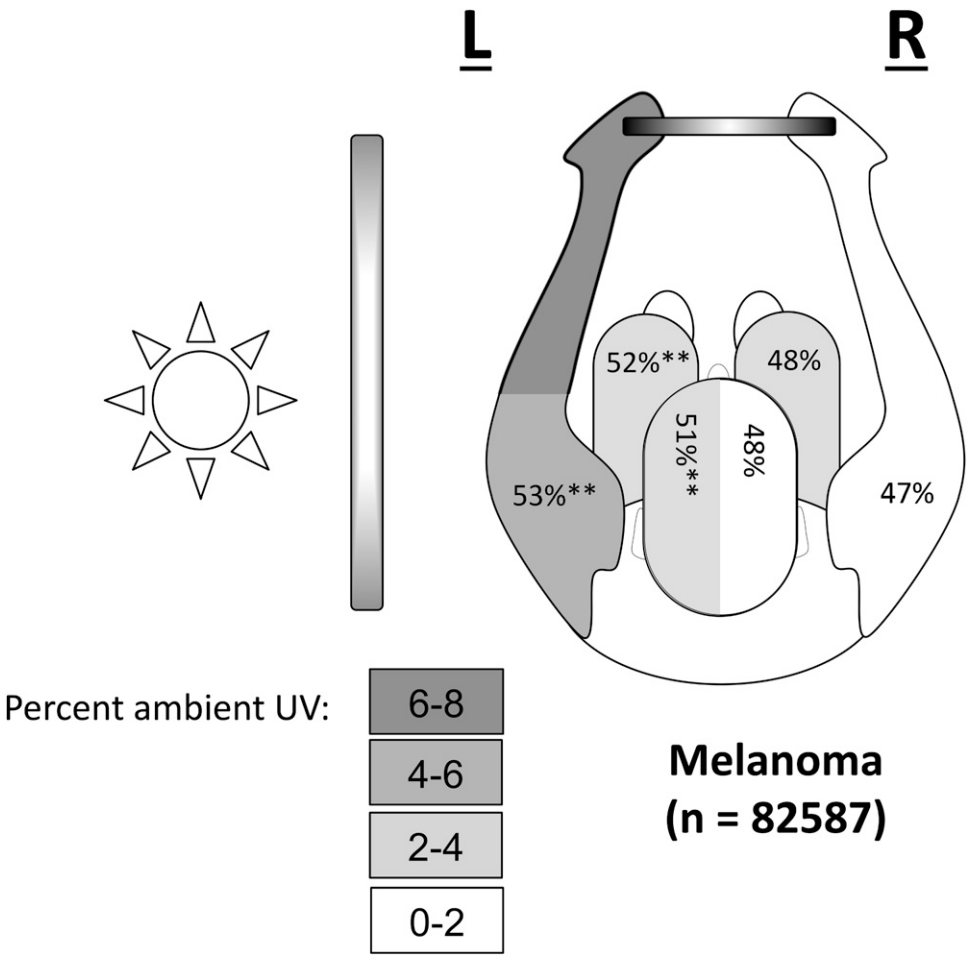

Fig 1. Fraction of non-midline melanomas that present on each side of body. Percentage of lateralized melanomas presenting on left and right sides are shown for face/scalp, arm, and leg. Statistical significance, ***P* less than .01. *Shaded areas* receive relatively more ultraviolet (*UV*). Body site shading reflects fraction of total ambient UV that reaches driver seated on left with windows and sunroof closed, as reported in Moehrle et al.[6] Open window increases UV dose by more than 5-fold with continued preferential exposure to left arm.

Table I. Percent of melanomas that present on left, broken down by age, sex, and body site

	MM: lateralized tumors presenting on left side			
	Scalp and face	**Upper limb**	**Lower limb**	**Total**
Men aged > 65 y	52%* (3080/5920)	53%* (4511/8514)	53%* (1339/2536)	53%* (8930/16,970)
Women aged > 65 y	51% (1786/3474)	51%† (3224/6262)	51%† (3065/5972)	51%* (8075/15,708)
Men aged < 65 y	50% (1826/3618)	53%* (5855/10,960)	53%* (3012/5703)	53%* (10,693/20,281)
Women aged < 65 y	50% (1095/2173)	52%* (6201/11,852)	53%* (8211/15,603)	52%* (15,507/29,628)
Total	51%* (7787/15,185)	53%* (19,791/37,588)	52%* (15,627/29,814)	52%* (43,205/82,587)

MM, Malignant melanoma.
Statistical significance: *$P < .01$; †$P < .05$.

particularly in men, are more likely to present on the left side of the body. Importantly, this contrasts with Australia, where a similarly sized study finds that actinic keratoses in men are significantly more likely to present on the right side of the body.[4] Both sets of authors suggest automobile UV exposure as a possible explanation, and the observed reversal in the asymmetrically involved side is consistent because drivers in the United States sit on the left side of the car whereas drivers in Australia sit on the right.

Table II. Percent of Merkel cell carcinomas that present on left, broken down by age, sex, and body site

	MCC: lateralized tumors presenting on left side			
	Scalp and face	Upper limb	Lower limb	Total
Men aged > 65 y	54% (266/493)	55%* (236/430)	52% (98/187)	54%† (600/1110)
Women aged > 65 y	49% (175/357)	58%* (133/230)	54% (131/244)	53% (439/831)
Men aged < 65 y	53% (31/59)	55% (58/106)	43% (43/100)	50% (132/265)
Women aged < 65 y	53% (31/59)	48% (38/79)	40% (16/40)	48% (85/178)
Total	52% (503/968)	55%† (465/845)	50% (288/571)	53%† (1256/2384)

MCC, Merkel cell carcinoma.
Statistical significance: *$P < .05$; †$P < .01$.

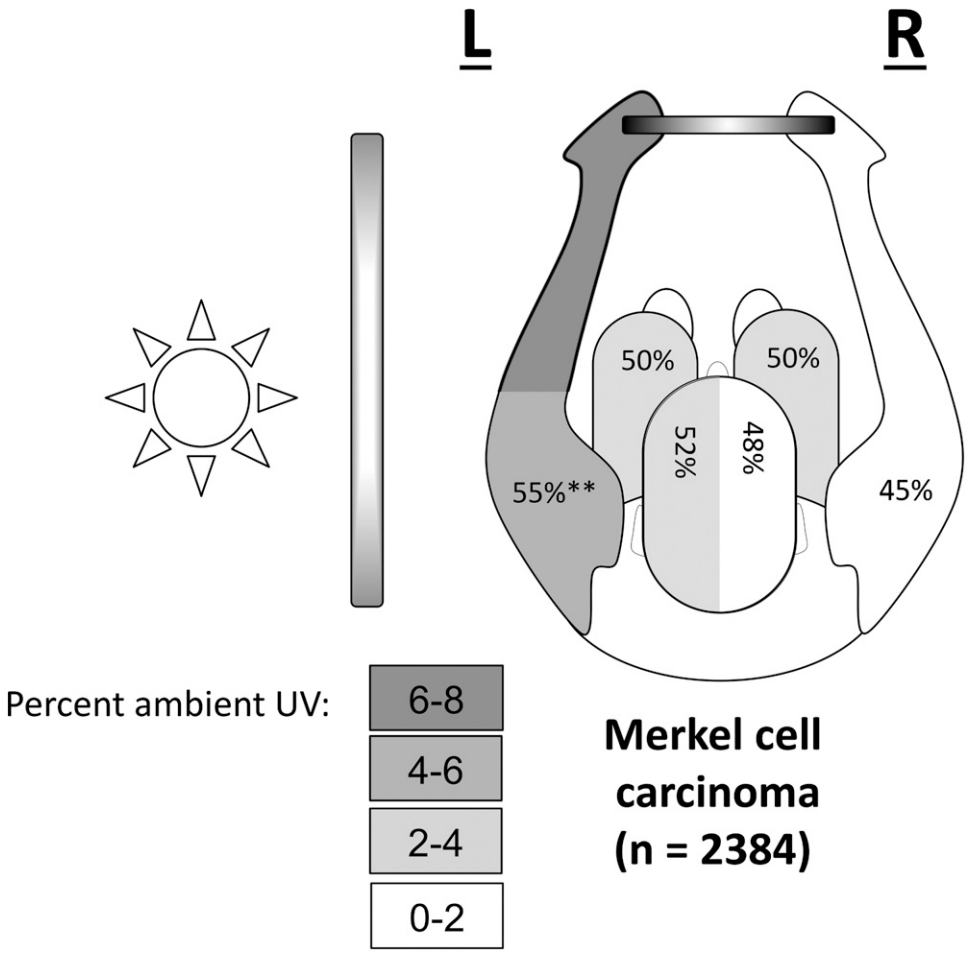

Fig 2. Fraction of non-midline Merkel cell carcinomas (MCC) that present on each side of body. Percentage of lateralized MCC presenting on left and right sides are shown for face/scalp, arm, and leg. Statistical significance, **P less than .01. *Shaded areas* receive relatively more ultraviolet (*UV*). Body site shading reflects fraction of total ambient UV that reaches driver seated on left with windows and sunroof closed, as reported in Moehrle et al.[6]

However, Butler and Fosko[5] only looked at a limited number of cases (890), and the observed left-sided trend in the United States was nonsignificant except in a few subgroups. To test for presence of left-sided bias in the United States, we analyzed the laterality of skin cancers reported in the SEER national registry database. MCC and MM were the focus, because these aggressive UV-linked cancers are captured by the SEER program. Indeed, both of these cancers showed a highly significant left-side bias in their primary location that was particularly pronounced on the arms.

The left-sided bias of melanoma can be partially but not perfectly explained by UV exposure while driving. The observed asymmetry for melanoma was most prominent for the left arm, which receives the largest UV exposure from driving and significantly more UV than the right arm (approximately 5-fold difference with windows closed).[6] Significant left-sided asymmetry was also detected for leg melanomas. For the leg, UV exposure in the automobile is more evenly distributed, with only an approximate 1.5-fold difference between sides and the expected UV exposure being greater on the right. Findings on the leg may be a result of alternate sources of asymmetric UV, however, population-wide asymmetric UV exposures that could account for this observed bias are elusive and no additional potential exposures were gleaned from a PubMed search of "asymmetrical ultraviolet." Regardless of cause, this left-sided association was statistically significant at all studied sites (arm, leg, and scalp/face) and is equivalent to approximately one in 20 melanomas that arise in excess on the left in the United States.

MCC is an increasingly common skin cancer that has been strongly linked to environmental UV.[2,3,8,9] We observed significantly more MCCs presenting on the left than the right. In particular, the arm demonstrated the most left-side bias, with 1.2 MCCs occurring on the left for each on the right. This observed pattern is consistent with excess left-sided UV exposure from automobile driving.[6,10] Therefore, automobile UV exposure may represent an appreciable risk factor for MCC. However, we cannot rule out other possible explanations.

Our study has several limitations. SEER does not provide information on whether the skin was sun exposed or not. Furthermore, we do not have information on individual driving or automobile riding habits, and cannot test the association of left bias with time in the driver's seat. To determine the importance of automobile UV exposure in this asymmetric distribution, further study is indicated in countries with opposite driving patterns and/or of sets of data annotated with driving habit information. Despite these limitations, these findings represent the largest study of asymmetry in skin cancer in the United States to date.

In summary, both MCC and MM are significantly more likely to present on the left side than the right in the United States. Automobile UV exposure is a well-characterized source of asymmetric UV exposure and likely contributes to the observed excess of melanoma and MCC presenting on the left arm. These excess left-sided cancers represent one of every 20 upper limb melanomas and a striking one of every 10 upper limb MCCs. Therefore, it may be prudent to recommend sunscreen application or other UV protective measures in individuals prone to skin cancer who spend significant time driving automobiles or trucks.

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