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### ORIGINAL ARTICLE

## Melanoma, Altitude, and UV-B Radiation

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#### KEYWORDS

Melanoma incidence;  
Altitude;  
UVB radiation

#### Abstract

*Background and objectives:* UV radiation is the main modifiable risk factor for the development of cutaneous melanoma. Many people in the Spanish province of Granada live at high altitudes and, therefore, receive high doses of UV-B radiation. The aims of this study were to assess the possible association between melanoma and altitude and to measure the daily erythemal dose at different altitudes.

*Material and methods:* An epidemiological study was carried out between 1982 and 2007 to assess the relationship between altitude, daily erythemal dose, and the prevalence of melanoma. We calculated the prevalence of melanoma in patients with a clinical and histological diagnosis of melanoma at Hospital Clínico Universitario San Cecilio in Granada, Spain. All individuals were required to be residents of the province of Granada in order to be included in the study. The prevalence of melanoma was calculated for altitude intervals of 100 m. Daily erythemal dose was estimated using measures of UV-B radiation obtained with pyranometers at altitudes of 0, 680, 1200, and 3398 m above sea level during the Evaluation of the Effects of Elevation and Aerosols on UV Radiation (VELETA) 2002 field campaign.

*Results:* The highest prevalence of melanoma was found between 1400 and 1499 m above sea level (the interval at which the highest settlements are found), with a rate of 2.36 cases per 1000 inhabitants (95% confidence interval, 0.64-6.03). Above 700 m, the daily erythemal dose increased exponentially with increasing altitude.

*Conclusions:* We observed a tendency toward increased prevalence of melanoma at higher altitude, with higher prevalences observed beyond 700 m above sea level.

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**PALABRAS CLAVE**

Incidencia melanoma;  
Altitud;  
Radiación UVB

**Melanoma, altitud y radiación UVB****Resumen**

*Introducción:* La radiación ultravioleta (UV) es el principal factor de riesgo ambiental modificable en el desarrollo del melanoma cutáneo. Muchas de las poblaciones de nuestra provincia están situadas a gran altitud, recibiendo elevadas dosis de radiación UVB. Nuestro objetivo es analizar una posible asociación entre melanoma y altitud y medir la dosis eritemática diaria a diferentes altitudes.

*Material y métodos:* Realizamos un estudio ecológico, en el que se trató de relacionar la prevalencia de melanoma, la altitud y la dosis eritemática diaria. El periodo de estudio comprendió los últimos 25 años (1982-2007). Calculamos la prevalencia de melanoma con aquellos pacientes diagnosticados clínicamente e histológicamente de melanoma, procedentes del Hospital Clínico Universitario "San Cecilio". Los individuos del estudio debían tener su lugar de residencia en la provincia de Granada. Calculamos la prevalencia de melanoma a intervalos de 100 m de altitud y estimamos la dosis eritemática diaria a partir de las medidas de radiación UVB realizadas con piranómetros situados a 0, 680, 1.200, 2.100 y 3.398 m de altitud durante la campaña VELETA-2002.

*Resultados:* La prevalencia de melanoma más alta está situada en el intervalo comprendido entre los 1.400-1.499 m a.s.l (intervalo con núcleos de población situados a mayor altitud) con 2,36 por 1.000 habitantes IC al 95% (0,64-6,03) por 1.000 habitantes. A partir de los 700 m de altura la dosis eritemática diaria aumenta de forma exponencial a medida que ascendemos en altitud.

*Conclusiones:* Este estudio encuentra una tendencia al aumento en la prevalencia de melanoma al ascender en altitud, siendo más intenso a partir de los 700 m a.s.l.

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**Introduction**

The incidence of cutaneous melanoma is on the rise worldwide, particularly in industrialized countries and among white populations.<sup>1,2</sup> Incidence has also increased in Spain in recent decades.<sup>3</sup> It is known that the main modifiable environmental risk factor for the development of melanoma is exposure to UV radiation.<sup>4,5</sup>

Switzerland and the Austrian province of Tyrol have a higher incidence of melanoma than other central European countries located at a similar latitude.<sup>6</sup> The differences are even greater for melanoma of the head, which is the type of melanoma most closely associated with cumulative UV radiation exposure.<sup>7</sup> This increased incidence of cutaneous melanoma in Austria and Switzerland may be related to the association between erythemal dose and altitude as the dose received increases as one ascends. Few studies have investigated the possible relationship between melanoma and altitude, however, and those that have produced conflicting results.<sup>8,9</sup>

The province of Granada, in southeastern Spain, receives over 3000 hours of sunlight a year. It has 71 km of coastline along the Mediterranean Sea and is also home to the Sierra Nevada mountain range. Accordingly, over 50% of the land area is over 1000 m above sea level<sup>10</sup> and many of Granada's municipalities are located at high altitudes. The altitude of Granada's villages and towns ranges between 5 and 1476 m. Theoretically, UV radiation increases with altitude, mainly because at greater heights, UV radiation travels along a shorter path through the atmosphere and is therefore less subject to extinction (absorption and scattering) by

atmospheric particulates. Consequently, the prevalence of melanoma should increase with altitude.

The aim of this study was to analyze the possible association between melanoma prevalence, altitude, and daily erythemal dose by studying the prevalence of melanoma according to the altitude of the places of residence of the patients analyzed.

**Material and Methods**

We performed an ecological study of all the residents of the province of Granada who were histologically and clinically diagnosed with melanoma at Hospital Clínico Universitario San Cecilio over a period of 25 years (1982-2007). The patients were divided into groups according to their place of residence. For this purpose, all municipalities from sea level to the altitude of Trévez, the highest village in Granada, were grouped by intervals of 100-m altitude. The prevalence of melanoma for the period 1982 to 2007 was then analyzed for each of the groups, considering only cases of melanoma diagnosed and under treatment during this period and using the population at the midpoint of this time interval for the calculation of the prevalence.<sup>11</sup> The altitude of each municipality and its number of inhabitants was obtained from the Andalusian Institute of Statistics<sup>12</sup> and the National Institute of Statistics,<sup>13</sup> respectively.

Erythemal dose was estimated on the basis of continuous measurements of UV-B radiation by broadband pyranometers (Robertson-Berger YES UVB-1 model) during the Evaluation

**Table 1** Location of Pyranometers at Measurement Stations: Latitude, Longitude, and Altitude Above Sea Level

Station	Latitude, Longitude	Altitude
Motril	36° 45' N, 3° 31' W	10
Armillá	37° 09' N, 3° 37' W	680
Pitres	36° 56' N, 3° 19' W	1.252
Las Sabinas	37° 05' N, 3° 23' W	2.173
Pico Veleta	37° 03' N, 3° 21' W	3.398

of the Effects of Elevation and Aerosols on UV Radiation (VELETA) 2002 field campaign<sup>14-16</sup> (Table 1). The voltages recorded by these meters were converted to erythemal irradiance using an appropriate calibration factor. This factor was calculated for each pyranometer by comparison with the reference standard used on the days of the campaign devoted to instrument intercomparison.<sup>14-16</sup> The calibration method recommended by the World Meteorological Organization was used. The UV-B radiation data employed in the present study correspond to cloud-free conditions.

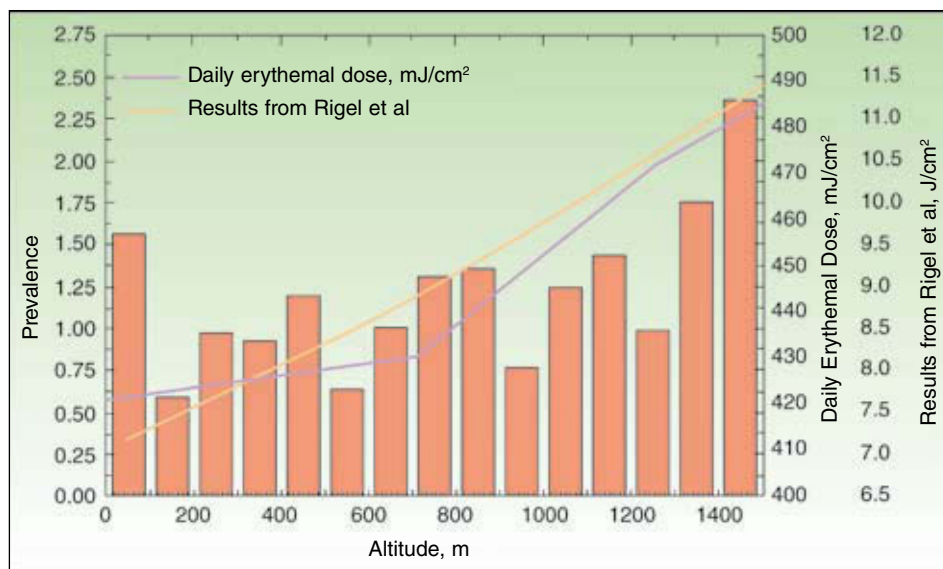
Analyzing the results of the VELETA-2002 field campaign,<sup>14-16</sup> we chose July 18, 2002 as a reference point for analyzing daily variations in UV-B radiation between the different measuring stations and for calculating daily erythemal dose and variations with altitude. An analysis of the meteorological conditions on that day showed a synoptic situation governed by a thermal low over the Iberian Peninsula. The wind was weak, mainly ageostrophic and influenced by the geography of the area. The Light Detection and Ranging system used during the campaign detected the arrival of air masses rich in mineral dust from Africa at an altitude of between 3 and 4 km; this air mixed with the planetary boundary layer at night. Back-trajectory analysis showed a continental air mass associated with

a Saharan dust event. This atmospheric situation meant that July 18 was the day on which altitude exerted the greatest effect on the variables measured at midday at the lowest and highest stations, with a difference of almost 3 between the UV index measured at these stations. We also analyzed the effects of sloped surfaces on UV-B radiation measurements during the campaign. The results showed no significant shifts from measurements taken on horizontal surfaces. The horizontal proximity of the measurement stations allows us to confidently state that the main differences detected in UV-B radiation levels were due to differences in altitude.

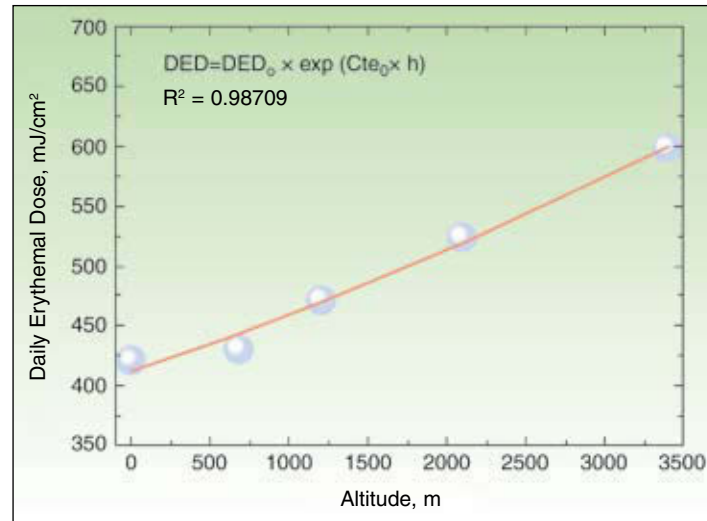
The following variables were analyzed for the study:

1. Daily erythemal dose (mJ/cm<sup>2</sup>) as a function of altitude
2. Altitude of place of residence (m)
3. Prevalence of melanoma between 1982 and 2007 in municipalities at different altitudes (intervals of 100 m)

Considering the fundamental law of extinction (Beer-Bouguer-Lambert law),<sup>17</sup> which describes the exponential decay of solar radiation based on the path along which it travels and the processes of scattering and absorption due to different atmospheric particulates, in the current study, we used a first-order exponential decay function to correlate the study variables with altitude. We analyzed, separately, the relationship between altitude (independent variable) and both daily erythemal dose and melanoma prevalence (dependent variables). We used the coefficient of determination (R<sup>2</sup>) to evaluate the correlations and the proportion of variance in the experimental data explained by the model. In the iterative process, to fit the exponential model, no constraints were placed on any of the parameters.



**Figure 1** Prevalence of melanoma during study period (1982-2007) at altitudes above sea level divided by intervals of 100 m and daily erythemal dose in the province of Granada. Also shown are the daily erythemal dose measurements estimated by altitude by Rigel et al<sup>9</sup> in Vail, Colorado and New York in the United States.



**Figure 2** Exponential regression curve for altitude above sea level and daily erythemal dose in the province of Granada on July 18, 2001. DED indicates daily erythemal dose;  $DED_0$ , daily erythemal dose at sea level; exp, exponential; Cte, constant; h, height.

## Results

We observed a strong correlation between altitude and daily erythemal dose. Specifically, this dose increased with altitude and did so exponentially above 700 m (Figures 1 and 2).

There was a tendency towards an increase in melanoma prevalence with altitude; this tendency was also stronger above 700 m. Interestingly, we also found a high prevalence in municipalities located near the coast (0-99 m). The highest prevalence of melanoma was detected in the highest municipalities (1400-1499 m), with a rate of 2.36 cases per 1000 inhabitants (95% confidence interval, 0.64-6.03) (Table 2, Figure 1). The correlation between altitude and melanoma prevalence was exponential (Figure 3).

## Discussion

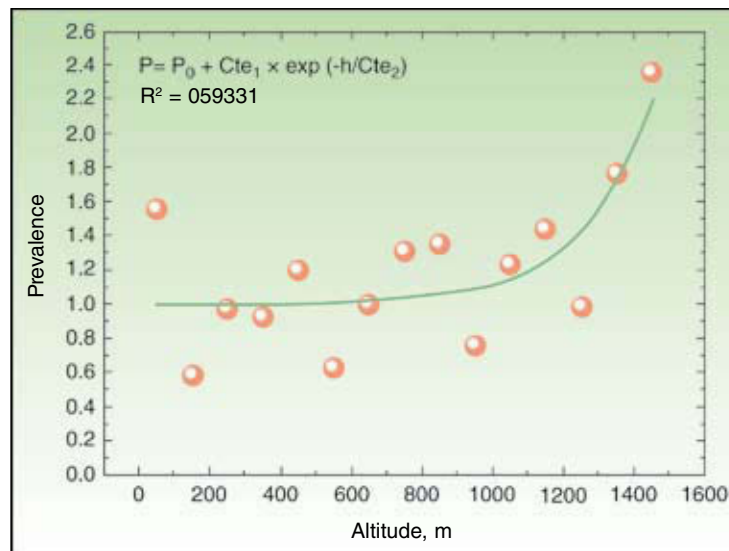
We observed a tendency towards an increase in the prevalence of melanoma with altitude, and this tendency was even more pronounced at altitudes above 700 m. According to our findings, daily erythemal dose also increased with altitude, with an exponential increase observed above 700 m. The highest prevalence of melanoma was found in the altitude interval of 1400 to 1499 m (there were no municipalities above this altitude), Nevertheless, prevalence was also high in coastal populations (in the lowest altitude range, 0-99 m) (Table 2, Figure 1).

The tendency towards increased melanoma prevalence at higher altitudes may be due to the higher daily erythemal doses also detected at these altitudes. The exponential

**Table 2** Total Number of Cases of Melanoma Shown by Altitude of Place of Residence, Number of Inhabitants per Altitude Interval, Prevalence of Melanoma per 1000 Inhabitants, and 95% Confidence Interval (CI) for Melanoma Prevalence

Altitude	No. of Cases	No. of Inhabitants <sup>a</sup>	Prevalence	95% CI
0-99	138	88 701	1.55	(1.29-1.82)
100-199	2	3442	0.58	(0.07-2.1)
200-299	8	8206	0.97	(0.24-1.71)
300-399	2	2160	0.92	(0.11-3.34)
400-499	40	33 350	1.20	(0.81-1.59)
500-599	35	55 459	0.63	(0.41-0.85)
600-699	81	81 197	1.00	(0.77-1.22)
700-799	431	329 453	1.31	(1.18-1.43)
800-899	87	64 103	1.36	(1.06-1.65)
900-999	37	48 309	0.76	(0.51-1.02)
1000-1099	17	13 690	1.24	(0.62-1.87)
1100-1199	14	9749	1.44	(0.63-2.24)
1200-1299	4	4066	0.98	(0.27-2.52)
1300-1399	3	1704	1.76	(0.36-5.14)
1400-1499	4	1696	2.36	(0.64-6.03)

<sup>a</sup>Population measured at midpoint of time interval (1982-2007).



**Figure 3** Exponential regression curve for altitude above sea level and prevalence of melanoma in the study period by altitude intervals of 100 m in the province of Granada. P indicates prevalence;  $P_0$ , prevalence at sea level; cte, constant; exp, exponential; h, height.

increase in daily erythemal dose detected above 700 m may be related to the position of the planetary boundary layer; this layer tends to lie at between 1000 and 1200 m above sea level, and in some cases, after solar midday, it can break up due to radiative heating of its surfaces. There are very few aerosol particles above this layer to absorb and scatter UV radiation, explaining the increase in daily erythemal doses found at higher altitudes. The high prevalence of melanoma observed in coastal populations may be related to the fact that people living close to the beach undertake more outdoor recreational activities and are thus more exposed to the sun.

A clear increase in melanoma incidence has been detected with decreasing latitude in the United States and Australia.<sup>18-21</sup> This negative association, however, does not seem to hold true in Europe, where, in fact, the lowest melanoma incidence rates are found in countries closest to the equator, a phenomenon that has been attributed to the fact that people in the Mediterranean have darker skin than their northern neighbours.<sup>22-25</sup> Erythemal dose decreases with latitude as the solar zenith angle decreases.

In a study conducted in the USA, Rigel et al<sup>9</sup> measured the amount of UV radiation ( $J/cm^2$ ) at increasing altitudes. Based on their results, they established that UV-B radiation ( $mW/cm^2$ ) increased exponentially with altitude and concluded that regions located at higher altitudes would probably have a higher frequency of melanoma. Nonetheless, they had no clinical data to support this hypothesis. It is difficult to compare their results with those of similar studies as the authors did not include information on the integral used to calculate the erythemal dose, which they expressed in  $J/cm^2$ . To compare the results reported by Rigel et al for erythemal dose to our results, we analyzed rates of change in erythemal dose with altitude, and found them to be similar between the 2 studies. Our observation

of a tendency towards an increase in the prevalence of melanoma with altitude in the province of Granada supports the hypothesis of Rigel et al that melanoma is probably more common at higher altitudes.

In a study conducted in the province of Styria in Austria, Richtig et al<sup>8</sup> observed a lower incidence of melanoma in places that are located at higher altitudes and that receive a higher average number of hours of sunlight. However, it should be noted that the highest altitude analyzed in that study was 957 m, which is a height that can be considerably affected by the planetary boundary layer. Furthermore, the study only included places located at an altitude of between 285 and 957 m, making it difficult to establish a vertical gradient of change, as can be seen in Figure 1. In our study, we analyzed municipalities located at altitudes ranging from sea level to 1479 m, meaning that we included places above and below the boundary layer.

It is only in recent years that pyranometers have been used as a means of objectively measuring cumulative UV radiation<sup>4,26-30</sup>; prior to this, studies investigating the possible relationship between UV radiation and melanoma used retrospective surveys to estimate the amount of UV radiation exposure.

A meta-analysis conducted by Gandini et al<sup>31</sup> showed a positive association between total UV radiation exposure and melanoma incidence, and in an epidemiological study by Armstrong and Kricke,<sup>32</sup> mean erythemal dose ( $mJ/cm^2$ ) was positively correlated with melanoma incidence. In our study, we also found an increase in the prevalence of melanoma with daily erythemal dose.

Higher average UV-B radiation flux has been associated with a greater risk of developing melanoma in both sexes,<sup>29</sup> and a study in which place of residence and average time spent outdoors were used to calculate cumulative erythemal dose found that the risk of melanoma was elevated in women within the group with the greatest



history of sun exposure.<sup>33</sup> Recent studies have suggested a linear relationship between cumulative UV-B radiation exposure and the risk of melanoma.<sup>30</sup>

On analyzing the incidence of melanoma by relative body surface, Whiteman et al<sup>34</sup> showed that melanoma was most common on the head and neck, which is where cumulative UV exposure is greatest. Furthermore, women, in whom cumulative exposure to UV radiation on the legs is greater than in men, have been found to have a higher rate of melanoma of the legs.<sup>35</sup>

Our study has several limitations. Firstly, our estimates of daily erythemal dose were based on environmental measurements and not individual sun exposure. Secondly, we should ideally have collected data on possible changes of residence as the individuals analyzed may have lived in different places and therefore received different daily erythemal doses. Similarly, the possibility that people might have been living in one place but working in another was not considered. Thirdly, we did not analyze clinical or pathological variants of melanoma by altitude or daily erythemal dose. Finally, because this was an ecological study and we had access to limited information, we did not analyze the possible role of other risk factors for melanoma. The lack of statistical significance in the relationship between altitude and melanoma prevalence in our study might be due to the small number of melanoma cases detected at high altitudes, as this prevented us from calculating annual melanoma incidence.

In conclusion, we observed a tendency towards increased melanoma prevalence at higher altitudes, and particularly above 700 m. Further studies are needed to analyze other melanoma risk factors and markers (eg, individual sun exposure, patterns of exposure, and skin phototype) as well as histologic variants of melanoma to shed more light on the possible association between melanoma and altitude.

## Conflict of Interest

The authors declare that they have no conflict of interest.

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