Solar Elastosis in Cutaneous Melanoma

Robin T. Vollmer, MD

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Abstract

By studying more than 1,200 patients with cutaneous melanoma and long-term follow-up, I examined the relationship between solar elastosis and age at diagnosis of melanoma, key features of melanoma, and the outcome of overall survival in melanoma. I found that melanomas with elastosis were diagnosed significantly later than those without elastosis ($P < 0.05$; log-rank test). This result may be because elastosis is positively related to age. However, I also found that melanomas of head and neck areas, which tend to have more elastosis, were diagnosed at later ages than melanomas of other body sites ($P = 1.2 \times 10^{-5}$; log-rank test). Thus, a second explanation for the results favors a protective effect of elastosis on the development of cutaneous melanoma, possibly related to increased levels of vitamin D. I also found that once melanoma develops, cases with elastosis demonstrated no differences in thickness, mitotic rate, ulceration, or overall survival time from cases without elastosis.

One important cause of cutaneous melanoma is solar radiation, particularly UV radiation in the 290- to 320-nm energy range. Although other risk factors are important and include cutaneous phenotype, genetic and family history, numbers and types of nevi, and the status of the immune system, herein I concentrate on some issues involving UV radiation. Concepts from radiation biology suggest that the effect of UV radiation on the skin can be understood in terms of the incident dose, $I_o$, and the absorbed dose, $I$; it is the absorbed dose that relates most closely to biologic effects. This approach leads to a mathematical model that may be applicable to UV radiation–induced melanoma. Specifically, the absorbed dose depends on the incident dose as follows:

$$I = I_o \times \exp(-\mu \times d)$$

where $d$ is the depth from the surface of the skin and $\mu$ is an absorption coefficient related to how well the skin filters UV radiation. This equation implies that at the surface of the skin, where $d = 0$, the absorbed dose is the same as the incident dose. The equation also implies that as the depth from the surface, $d$, increases, the absorbed dose decreases in an exponential manner as has been observed. Because the absorption coefficient, $\mu$, is directly related to the filtering ability of the skin, $\mu$ is highest for dark-skinned persons and lowest for fair-skinned persons. Furthermore, $\mu$ also seems related to the wavelength of incident light with higher values for UV-B than for UV-A. For example, Figure 1 shows the expected fraction of incident dose absorbed (ie, $I/I_o$) as a function of depth in millimeters of skin using the preceding model and previously published results for UV-B (300 nm) and UV-A (350 nm). Whereas 90% of UV-B is absorbed by 0.1 mm, 90% of UV-A is absorbed by 0.6 mm.
Thus, elastosis may represent a good surrogate for the cumulative dose of absorbed UV radiation. Related to the potential protective effect of long-term exposure to UV radiation, some have found that elastosis is a favorable prognostic marker for cutaneous melanoma, a result that suggests that melanomas developing after higher cumulative absorbed doses of UV radiation are different from those that develop at lower doses. In this study, I studied more than 1,200 patients and their specimens to further explore relationships between elastosis, as a surrogate for I, and several key attributes of cutaneous melanoma, including age at diagnosis, tumor thickness, and survival time.

Materials and Methods

Study Patients

The study patients comprised 1,234 referred to the Duke Melanoma Clinic, Durham, NC, during the 1980s and early 1990s, and I evaluated all of their primary cutaneous melanomas. Elastosis in the superficial dermis is readily recognized with the routine H&E stain as an increase in and coalescence of light blue to gray elastin fibers, and in sun-damaged skin, the accumulation of elastin (ie, elastosis) displaces ordinary collagen and other stromal structures. For example, Image 1 shows melanoma in situ overlying dermis without elastosis, Image 2 shows melanoma in situ overlying dermis with mild elastosis, and Image 3 shows melanoma in situ overlying dermis with heavy elastosis. In general, I evaluated and graded the elastosis using the skin immediately adjacent to the dermal portion of the tumors. Although I graded elastosis as 0 (absent) to 3 (heavy), for

![Figure 1](https://academic.oup.com/ajcp/article-abstract/128/2/260/1760197)

**Figure 1** Plot of fraction of incident dose of light absorbed ($I/I_o$) vs depth in the skin in millimeters using previously published results and the model of Equation 1. The upper curve is for UV-A at a wavelength of 350 nm, and the lower curve is for UV-B at a wavelength of 300 nm.

Assuming that any biologic effects of UV radiation are directly related to the absorbed dose, I, then the preceding model suggests that the incidence of those effects is positively related to incident UV radiation, inversely related to the absorption coefficient, and inversely related to the depth of the biologic effect from the skin surface. These are relationships observed in cutaneous melanoma. For example, increasing geographic latitude decreases $I_o$ and also decreases the incidence of melanoma after controlling for skin phenotype. Melanomas are common on the head and neck where values of $I_o$ are high. People with fair skin and blond or red hair have the lowest values of $\mu$ and the greatest chance of developing melanoma.

Finally, the proximity of junctional melanocytes to the surface of the skin emphasizes the importance of small values of $d$ for the development of melanoma in situ, especially for UV-B, for which 90% of incident light is absorbed by 0.1 mm.

Currently, many consider that intermittent, intense exposure to UV radiation is more likely to cause melanoma than long-term cumulative exposure, and in fact, long-term exposure may be protective owing to UV radiation–induced vitamin D. The question to ponder then concerns the relationship between long-term cumulative exposure to UV radiation and cutaneous melanoma.

Solar elastosis (hereafter referred to as elastosis) is the deposit of altered elastin in the highest levels of the dermis and is commonly thought due to absorbed sunlight. In my experience, elastosis is most intense at cutaneous depths from slightly less than 0.1 mm to approximately 1.0 mm, so that its location corresponds to the zones of maximally absorbed light in the UV spectrum (Figure 1). Furthermore, elastosis increases with age and is most common in fair-skinned persons.
statistical analyses, in this study, elastosis was scored as absent or present (ie, 0 vs >0). Other details about the patients and their melanomas are given in Table 1.

### Statistical Analysis

I used Kaplan-Meier plots, the log-rank test, and the Cox proportional hazards model to evaluate the relationships between elastosis, patient age and anatomic tumor site, tumor thickness, and mitotic rate; I used the same methods to study the relationship between elastosis and overall survival time. In the survival analysis, I used an exponential transformation of thickness \( T(\text{thick}) \) described previously and defined as follows:

\[
T(\text{thick}) = 1 - 0.966 \times \exp(-0.2016 \times \text{thickness})
\]

### Results

**Relationships Between Solar Elastosis and Patient Age, Anatomic Tumor Site, and Sex**

As expected, I found that the presence of elastosis was significantly related to patient age and anatomic tumor site, and this is illustrated by the Kaplan-Meier plots in Figure 2. Here, the probability of no elastosis is plotted against patient age, and the curves demonstrate that as age increases, the probability of an elastosis-free skin biopsy result decreases. The curves also demonstrate that the relationship between the elastosis-free state and patient age is different for different body sites (\( P < 0.05 \); log-rank test), so that acral sites remain without elastosis for longer times than do other sites. Head and neck sites develop elastosis sooner than the other body sites, and extremity and trunk sites had curves with intermediate times to elastosis. A Cox multivariate model analysis demonstrated that after controlling for the effects of anatomic site, female sex was also associated with longer times to elastosis (\( P = 0.03 \)). Figure 3 shows Kaplan-Meier plots demonstrating that the distribution of age at diagnosis is different for melanomas with elastosis (upper curve) from those without elastosis (lower curve) (\( P < 0.001 \); log-rank test). Specifically, melanomas with elastosis occur at later ages.
Solar Elastosis and Histologic Features of Melanoma

Figure 4 and Figure 5 demonstrate that the distributions of tumor thickness (Figure 4) and mitotic rate (Figure 5) were the same for melanomas with and without elastosis ($P > .7$; log-rank tests). Furthermore, the prevalence of tumor ulceration was the same for melanomas with and without elastosis ($P > .9$; $\chi^2$ test).

Analysis of Overall Survival Time

Figure 6 shows the Kaplan-Meier curves for overall survival probability vs the presence of elastosis. The curves are nearly identical, and a Cox proportional hazards model analysis of overall survival time demonstrated that after controlling for tumor thickness, body site, mitotic rate, and patient age, solar elastosis was not related to survival time ($P > .1$).

Discussion

There are at least 2 possible explanations for why melanomas with elastosis occur at later ages than melanomas without elastosis, and the data herein are not sufficient to decide between these 2 explanations. The first and simpler explanation is that elastosis is a just a surrogate for older age, and this is the only reason that melanomas with elastosis occur at older ages. This explanation is supported by Figure 2, which demonstrates that elastosis increases with age and depends on location. A secondary conclusion based on this explanation is that neither the cumulative dose of UV radiation nor its surrogate of elastosis relates to the onset of melanoma. Instead, and as many have suggested, it is intermittent, intense UV radiation that is important.
The second possible explanation for the results in Figure 3 is that melanomas with elastosis differ in some fundamental way from those without elastosis. Melanomas without elastosis develop earlier, because tumor-generating events other than UV radiation are active, and melanomas with elastosis develop later because they lack these non–UV radiation events and may benefit in a complex way from solar-enhanced levels of vitamin D. Support for this alternative explanation comes from the association I found between body site and onset of melanoma. Specifically, I found that melanomas of head and neck sites, which tend to have more elastosis, occurred at later ages than those of remaining body sites (P = 1.2 × 10−5; log-rank test). Those of the head occurred at a median age of 52 years, whereas those of other body sites occurred at a median age of 47 years.

Regardless of which of the preceding explanations applies to the results in Figure 3, my results suggest that once melanoma develops, its key morphologic features and subsequent behavior are the same regardless of elastosis. Specifically, I found no differences in thickness, mitotic rate, ulceration, or overall survival between tumors with and without elastosis.

From the Department of Pathology, Veterans Affairs and Duke University Medical Centers, Durham, NC.

Address reprint requests to Dr Vollmer: Laboratory Medicine 113, VA Medical Center, 508 Fulton St, Durham, NC 27705.

References


