

EVERY MILLIMETER COUNTS FOR NEVUS TRANSFORMATION INTO MALIGNANT MELANOMA



A summary of my 2019 Wendell L. Hughes Lecture.

BY CAROL L. SHIELDS, MD

The prevalence of choroidal nevus located within two 45° screening fields centered on the foveola and optic disc was 4.7% in the 2005 to 2008 National Health and Nutrition Examination Survey (NHANES).¹ Because the NHANES evaluated only a small region in the posterior segment, however, it likely underestimated the true prevalence of choroidal nevus.

The most serious risk carried by choroidal nevus is its potential transformation into malignant melanoma. This risk is highest in the elderly population; a lifetime risk for a patient living beyond 80 years of age potentially approaches 1%.^{2,3} The aging of the US population has prompted researchers to attempt to identify clinical clues to the likelihood of transformation so as to promote the earliest possible detection of melanoma. Recent studies have identified multimodal imaging factors that predict this transformation. In particular, tumor thickness (> 2 mm) has repeatedly been found to be one of the most powerful predictive factors for transformation.⁴ More important, a combination of tumor thickness and other features has been found to compound the risk of transformation.⁵

In a recent retrospective analysis, my colleagues and I explored the risk of nevus transformation into melanoma per millimeter increment.⁶

TABLE. CHOROIDAL NEVUS TRANSFORMATION INTO MELANOMA BASED ON NEVUS THICKNESS

Nevus thickness	Hazard ratio for transformation into melanoma relative to flat nevus (0-1.0 mm)	P value
0-1.0 mm	1.0	-
1.1-2.0 mm	4.7	$P = 0.01$
2.1-3.0 mm	35.7	$P < 0.0001$
> 3.0 mm	52.0	$P < 0.0001$

METHODOLOGY

We reviewed the charts of all patients with a clinical diagnosis of choroidal nevus who were seen on the Ocular Oncology Service at Wills Eye Hospital in Philadelphia between 2007 and 2017. We analyzed each nevus per incremental increase in millimeter thickness and categorized them as flat (≤ 1.0 mm), thin (1.1–2.0 mm), thicker (2.1–3.0 mm), and thickest (> 3.0 mm).

We then followed these independent categories longitudinally with regard to the clinical outcome of growth into melanoma (Table), which we defined as enlargement in basal dimension or thickness by at least 0.5 mm in 2 years or less.

RESULTS

In all, our study included 3,806 choroidal nevi, and there was follow-up for

2,355 of these. Over the 10-year period, only 90 (3.8%) of the 2,355 nevi transformed into melanoma.

Increasing nevus thickness posed a greater risk of transformation into melanoma. Each millimeter of increased thickness posed a threat. Compared with completely flat nevi, thin nevi had a 4.7 times greater risk, thicker nevi a 35.7 times greater risk, and thickest nevi a 52.0 times greater risk of growth into melanoma. Perhaps in more relevant terms, Kaplan-Meier 10-year rate of growth was 2.2% for flat, 10.9% for thin, 40.2% for thicker nevi. The most striking increased risk occurred at transition from 2.0 mm or less to greater than 2.0 mm. This cutoff was also associated with a substantial increase in OCT evidence of subretinal fluid, overlying drusen, and overlying atrophy of the retinal pigment epithelium.

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INCREASING NEVUS THICKNESS POSED A GREATER RISK OF TRANSFORMATION INTO MELANOMA. EACH MILLIMETER OF INCREASED THICKNESS POSED A THREAT.

Multivariable analysis showed that, as a group, there were six important factors in the transformation of a nevus into melanoma: thickness greater than 2 mm on ultrasonography, subretinal fluid detected with spectral-domain OCT, a decrease in VA to 20/50 or worse, orange pigment on fundus autofluorescence, melanoma acoustic hollowness by ultrasonography, and a tumor diameter greater than 5 mm.

A limitation of our study was the number of patients lost to follow-up.

CONCLUSION

Ocular oncologists consider the importance of thickness of choroidal nevi when making decisions on management. Our study is the first to specifically evaluate each millimeter incremental risk of choroidal nevus for transformation into melanoma. We found that increasing nevus thickness is associated with an increased risk of transformation, but it is important to recognize that not all enlargement signals a transformation to melanoma. That said, we identified a major increase in the transformation rate for nevi that were more than 2.0 mm thick. Continuing advances in imaging technology could further elucidate the impact of submillimeter change. ■

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CAROL L. SHIELDS, MD

- Director, Ocular Oncology Service, Wills Eye Hospital, Thomas Jefferson University, Philadelphia
- Editorial Advisory Board Member, *Retina Today*
- carolshields@gmail.com
- Financial disclosure: None