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Iris Melanoma Outcomes Based on the American Joint Committee on Cancer Classification (Eighth Edition) in 432 Patients

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Purpose: The American Joint Committee on Cancer (AJCC) classification was updated to the eighth edition in January 2017, providing staging for iris melanoma. This study evaluated outcomes of iris melanoma per the AJCC classification, eighth edition.

Design: Retrospective case series.

Participants: Four hundred thirty-two patients with iris melanoma.

Methods: Management including tumor resection, plaque radiotherapy, or enucleation.

Main Outcome Measures: Local tumor recurrence, melanoma-related systemic metastasis, and melanoma-related death.

Results: Of 432 patients with iris melanoma, AJCC classification was category T1 (n = 324 [75%]), T2 (n = 83 [19%]), T3 (n = 2 [<1%]), and T4 (n = 23 [5%]). There was no difference in age, race, gender, eye, or iris color among T categories. Overall, Kaplan-Meier analysis of outcomes (at 5 and 10 years) revealed visual acuity reduction by 3 lines or more (42% and 54%, respectively), secondary glaucoma (29% and 33%, respectively), local recurrence (8% and 17%, respectively), secondary enucleation (12% and 19%, respectively), lymph node metastasis (1% and 1%, respectively), melanoma-related systemic metastasis (5% and 10%, respectively), and melanoma-related death (3% and 4%, respectively). Compared with T1 category, the hazard ratio (HR) for local recurrence in nonenucleated eyes was 1.31 for T2, not evaluable (NE) for T3 (because of small cohort), and 6.61 for T4; the HR for metastasis was 3.41 for T2, NE for T3 (because of small cohort), and 25.6 for T4; the HR for death was 7.51 for T2, NE for T3 (because of small cohort), and 26.5 for T4; and the odds ratio for enucleation was 1.23 for T2, 3.63 for T3, and 4.72 for T4. Features predictive of melanoma-related metastasis (multivariate analysis) included secondary glaucoma ($P < 0.001$; HR, 4.51), T2 category (vs. T1; $P = 0.01$; HR, 4.09), and T4 category (vs. T1; $P < 0.001$; HR, 30.8). Features predictive of melanoma-related death (multivariate analysis) included older age ($P = 0.008$; HR, 2.16 per 10-year increase), T2 category (vs. T1; $P = 0.005$; HR, 8.07), and T4 category (vs. T1; $P < 0.001$; HR, 20.3).

Conclusions: The AJCC eighth edition classification provides prognostic stratification of iris melanoma. By multivariate analysis, the ratio for melanoma-related metastasis was 4 times greater in category T2 and 31 times greater in T4 compared with T1. The ratio for melanoma-related death was 8 times greater in category T2 and 20 times greater in T4 compared with T1. The cohort size for T3 was too small to provide useful information. *Ophthalmology 2017;■:1–11 © 2017 by the American Academy of Ophthalmology*

The American Joint Committee on Cancer (AJCC) published an updated eighth edition manual of cancer classification in January 2017, applicable for several systemic and ocular cancers and designed to predict patient survival.[1] Regarding cancers of the eye, the AJCC provides classifications for eyelid carcinoma; conjunctival carcinoma; conjunctival melanoma; iris, ciliary body, and choroidal melanoma; retinoblastoma; lacrimal gland carcinoma; orbital sarcoma; and ocular adnexal lymphoma. This system serves as a guideline for ocular oncology tumor classification, patient management, and prognostication of patient outcomes.

There are approximately 7000 new cases of uveal melanoma worldwide each year, most occurring in white persons in North America and Europe.[2–4] Iris melanoma represents only a minority of cases of uveal melanoma.[4–7] In an analysis of 8033 consecutive cases of uveal melanoma, iris melanoma represented only 4%, compared with ciliary body (6%) and choroidal (90%) locations.[3]

The prognosis of iris melanoma generally is favorable, especially with small tumors that lack tumor seeding, secondary glaucoma, and extrascleral extension.[5–9] In a single-center analysis of 317 consecutive patients with iris melanoma, metastatic disease was discovered in 5% at 5 years, 9% at 10 years, and 11% at 20 years.[6] Multivariate analysis documented that the highest risk for metastasis included those with elevated intraocular pressure and extraocular extension.[6] In another multicenter analysis of 131 cases of iris melanoma classified according to the

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Table 1. American Joint Cancer Committee on Cancer Classification, Eighth Edition, of Iris Melanoma in 432 Patients

Primary Tumor (T) Category	Definition	No. (%)
T1	Tumor limited to the iris	324 (75)
T1a	Tumor limited to the iris ≤3 clock hours in size	193 (45)
T1b	Tumor limited to the iris >3 clock hours in size	66 (15)
T1c	Tumor limited to the iris with secondary glaucoma	65 (15)
T2	Tumor confluent with or extending into the ciliary body, choroid, or both	83 (19)
T2a	Tumor confluent with or extending into the ciliary body, without secondary glaucoma	51 (12)
T2b	Tumor confluent with or extending into the ciliary body and choroid, without secondary glaucoma	2 (<1)
T2c	Tumor confluent with or extending into the ciliary body, choroid, or both, with secondary glaucoma	30 (7)
T3	Tumor confluent with or extending into the ciliary body, choroid, or both, with scleral extension	2 (<1)
T4	Tumor with extrascleral extension	23 (5)
T4a	Tumor with extrascleral extension ≤5 mm in diameter	23 (5)
T4b	Tumor with extrascleral extension >5 mm in diameter	0 (0)

Data from Kivelä T, Simpson RE, Grossniklaus HE, et al. Uveal melanoma. In: AJCC Cancer Staging Manual, 8th ed. New York: Springer; 2017:805–817. All patients were classified as N0 (no regional lymph node metastases) and M0 (no distant metastases) at date first seen.

seventh edition of the AJCC classification, tumor category was T1 (n = 73 [56%]), T2 (n = 44 [34%]), T3 (n = 3 [2%]), and T4 (n = 1 [<1%]), with 9 cases deemed not classifiable as Tx (7%).[9] In that group, the 5-year Kaplan-Meier estimate for metastasis was 11% overall. In the present study, we evaluated a larger cohort of 432 patients using the new eighth edition of the AJCC classification of iris melanoma[1,10] to provide outcomes analysis of visual acuity loss, tumor recurrence, enucleation, melanoma-related metastasis, and melanoma-related death.

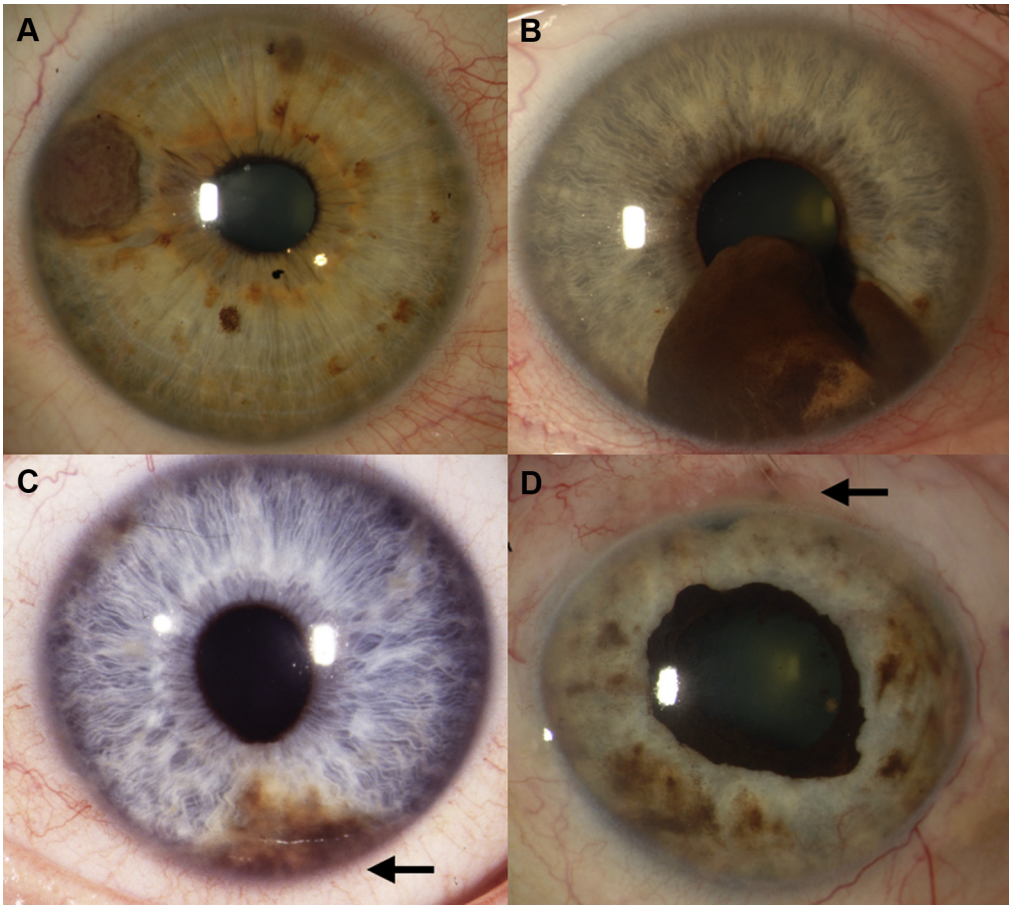

Figure 1. The American Joint Committee on Cancer classification, eighth edition, of iris melanoma based on tumor (T) category. **A**, T1 iris melanoma with darkly pigmented, circumscribed tumor with no iris or angle seeding and measuring 3 clock hours or less. **B**, T2 iris melanoma with darkly pigmented, circumscribed tumor and ciliary body invasion. **C**, T3 iris melanoma with pigmented tumor and local invasion into sclera (arrow), documented on gonioscopy and ultrasound biomicroscopy. **D**, T4 iris melanoma with diffuse, extensive iris involvement with pigmented and nonpigmented melanoma for the entire iris, causing iris ectropion, sentinel vessels, and subtle nonpigmented extraocular extension (arrow).