Uveal Melanoma: pathological aspects

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International Agency for Research on Cancer

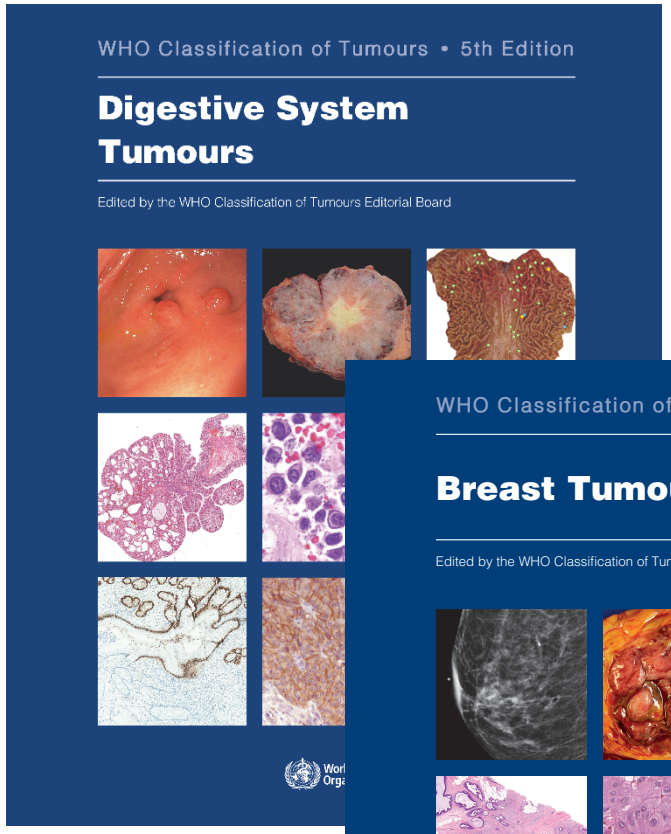
World Health Organization

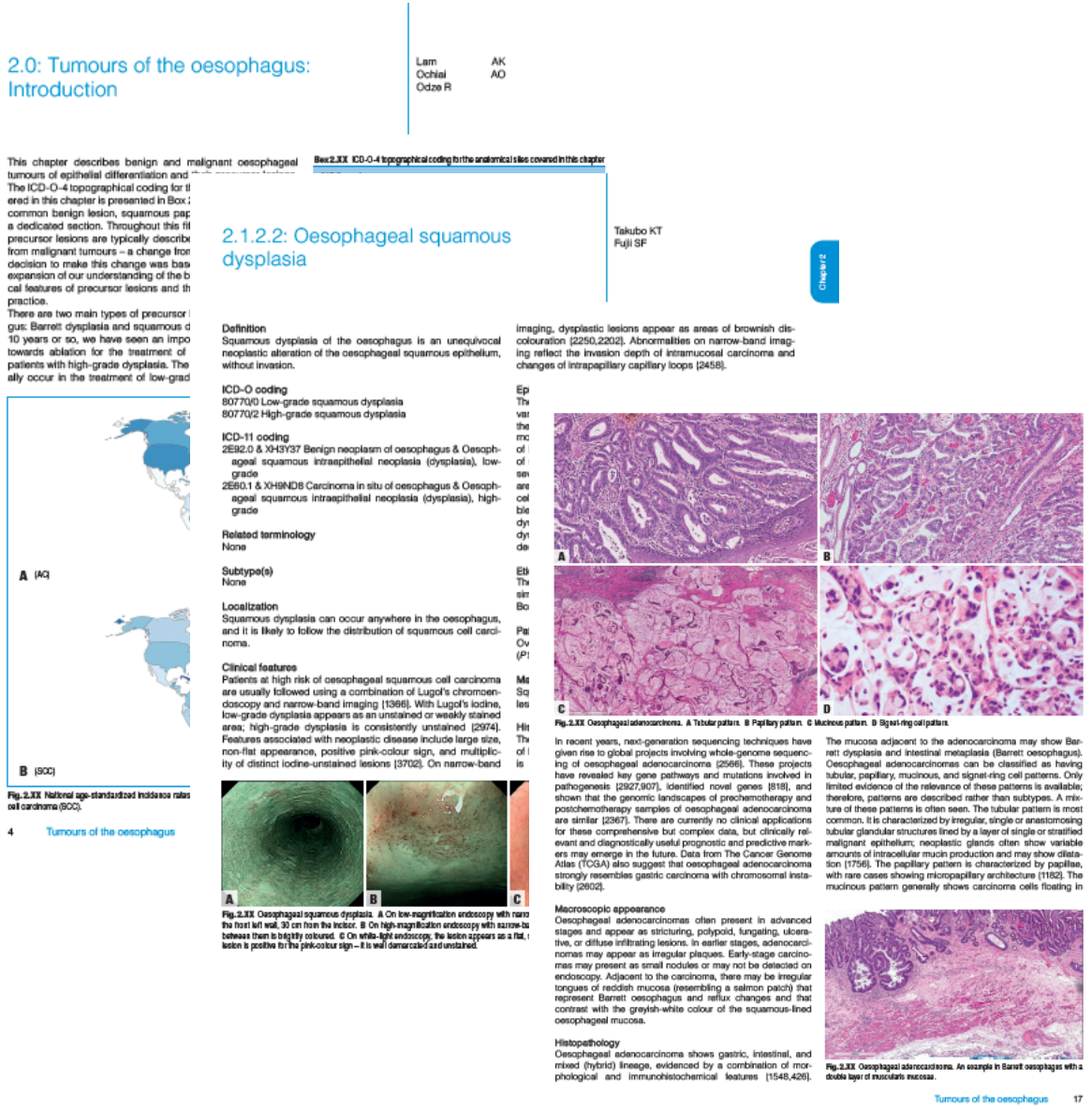
Declaration of Interests

- World Health Organisation
- Previously at U.K. NHS in Coventry. Previously a member of the ThermoFisher OncoNetwork Collaboration

- All opinions expressed are personal, and not those of any of the organisations above.

WHO Classification of Tumours





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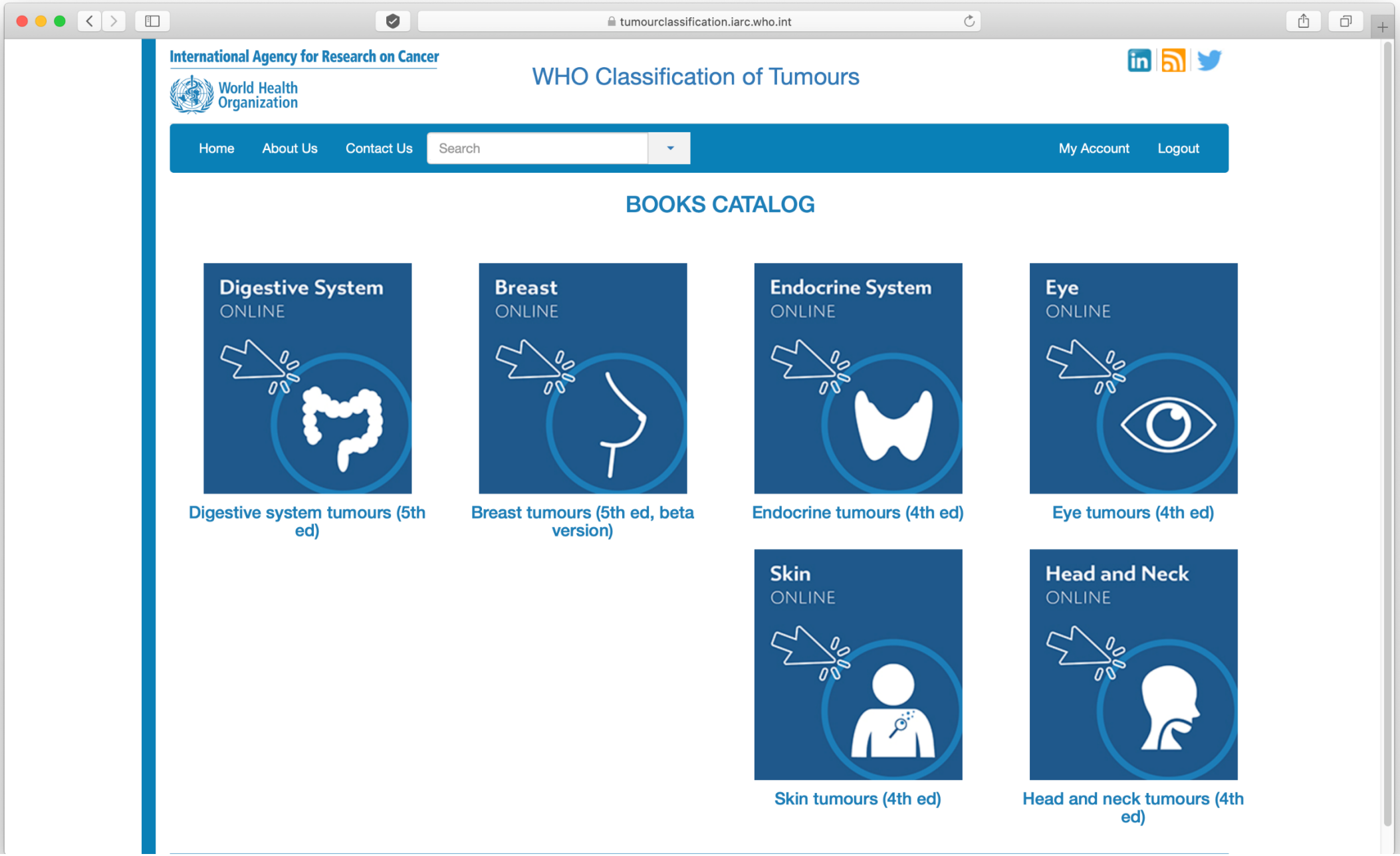
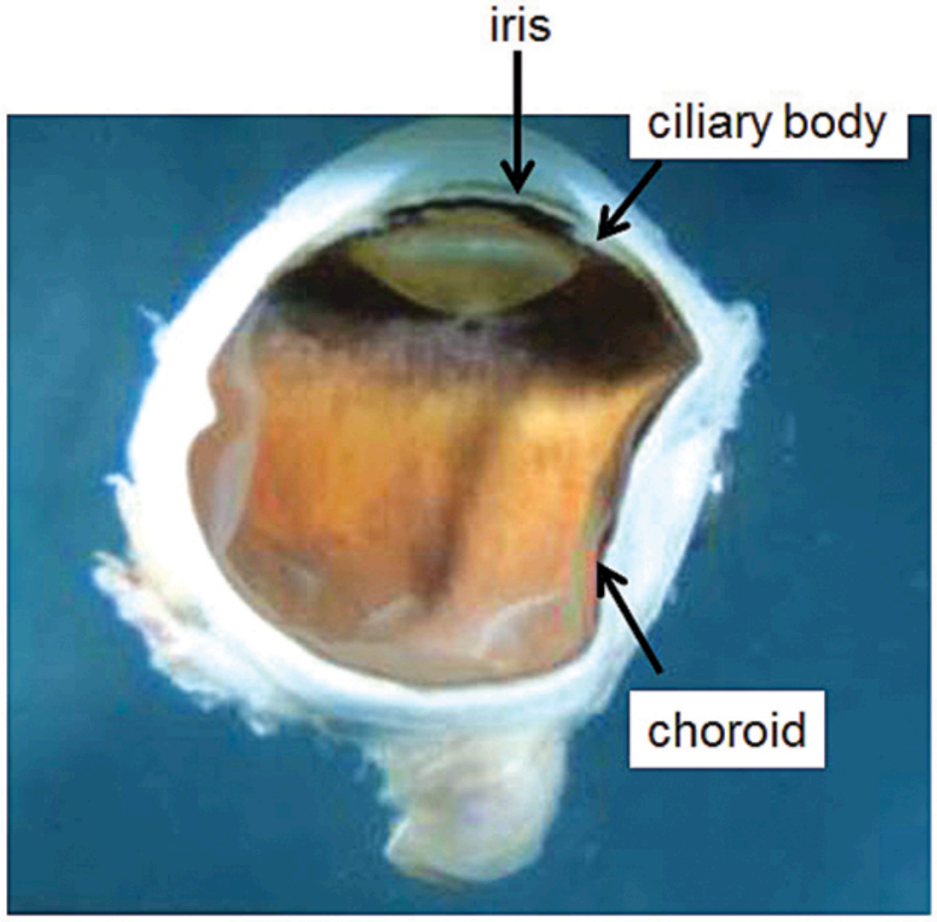
tumourclassification.iarc.who.int

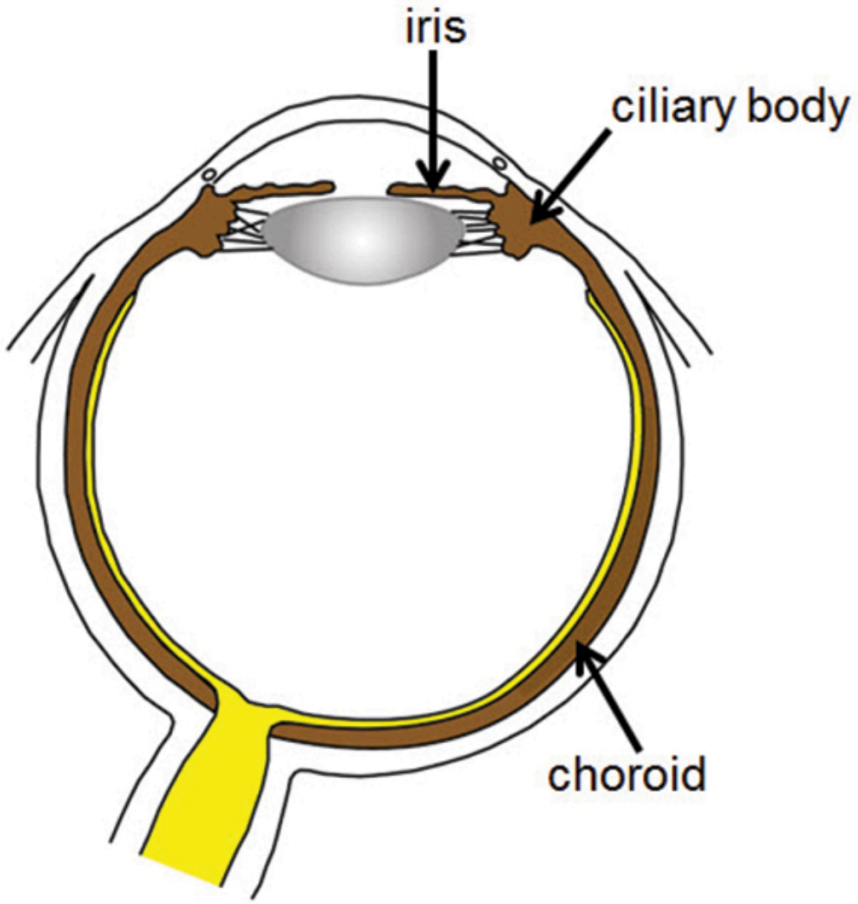


Uveal Melanoma

- Definition: Primary malignant melanocytic tumours of the uveal tract: Choroid, Ciliary Body (CB) and Iris.
- Diagnosis: Usually clinical by ophthalmoscopy during routine eye exam – only 25% have symptoms.
- Circumscribed and nodular – may hide behind iris.
- CB melanoma may cause glaucoma by anterior displacement of the lens-iris diaphragm, tumour seeding, iris neovascularization, or rarely by pigment dispersion.
- Choroidal lesions domes-shaped (75%), mushroom shaped (with retinal detachment, of diffuse (5%).
- Pigmented in 55%, but non-pigmented in 15%.

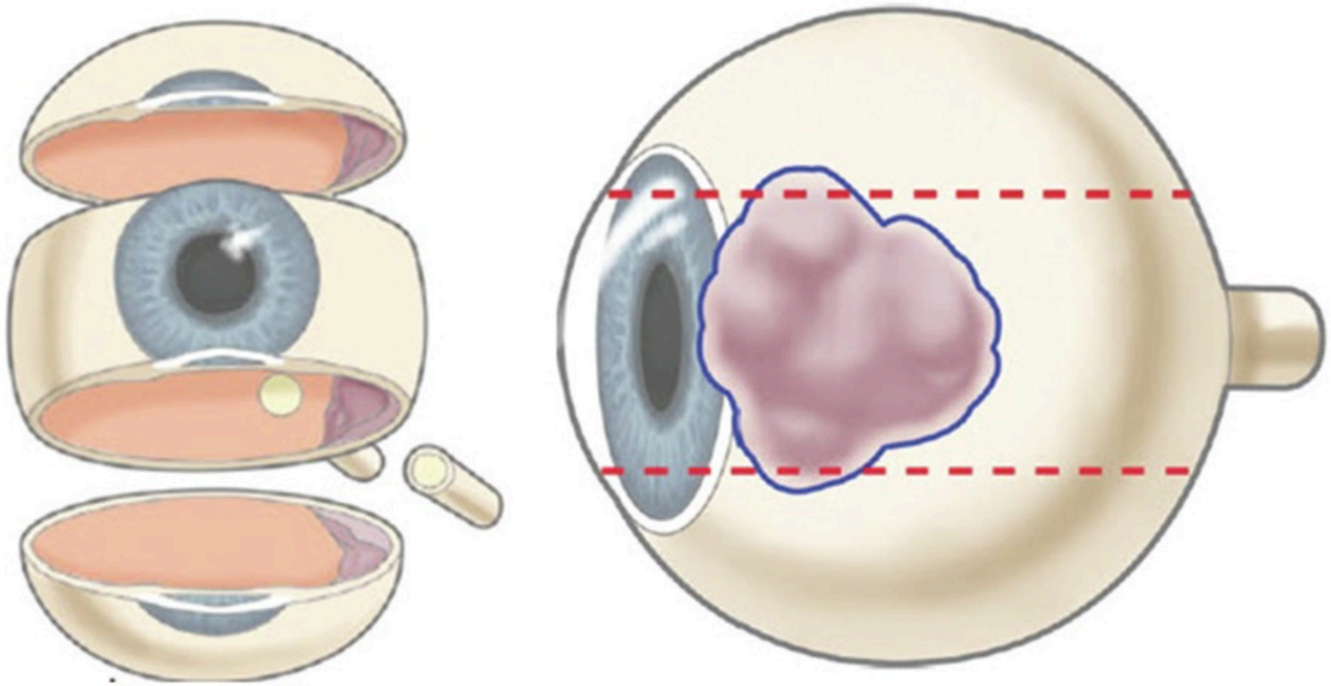
Anatomy





uveal tract

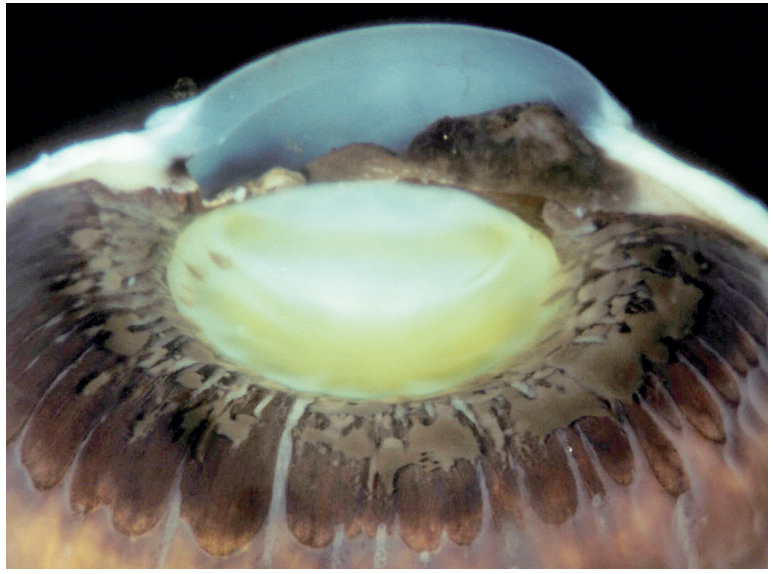
Macroscopic dissection



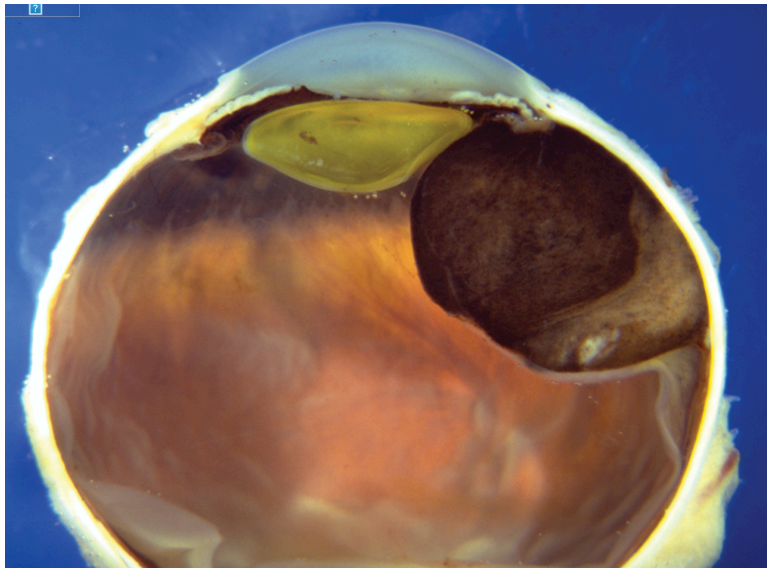
- Observe
- Transilluminate
- Cut culottes either side of tumour
- Embed on best side, and culottes
- Cut levels!

Macroscopic appearance

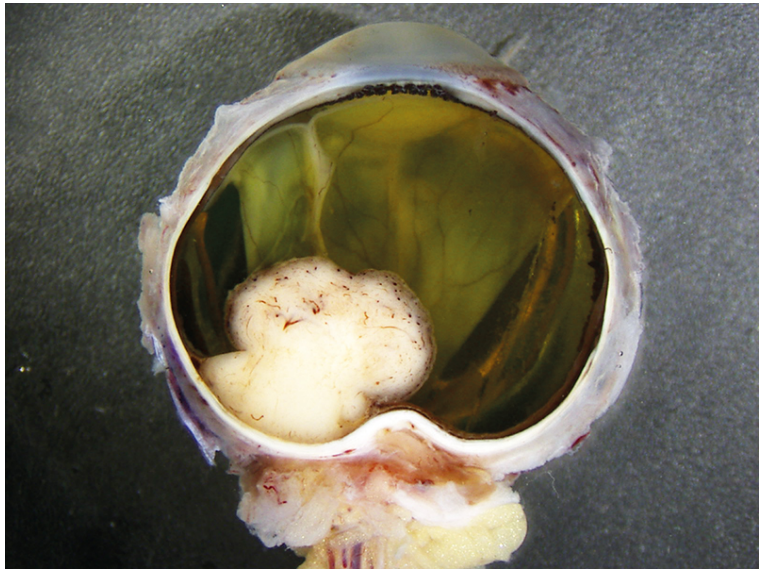
Iris Melanoma



CB Melanoma



Choroidal Melanoma



Sources: Bechrakis N.E.,

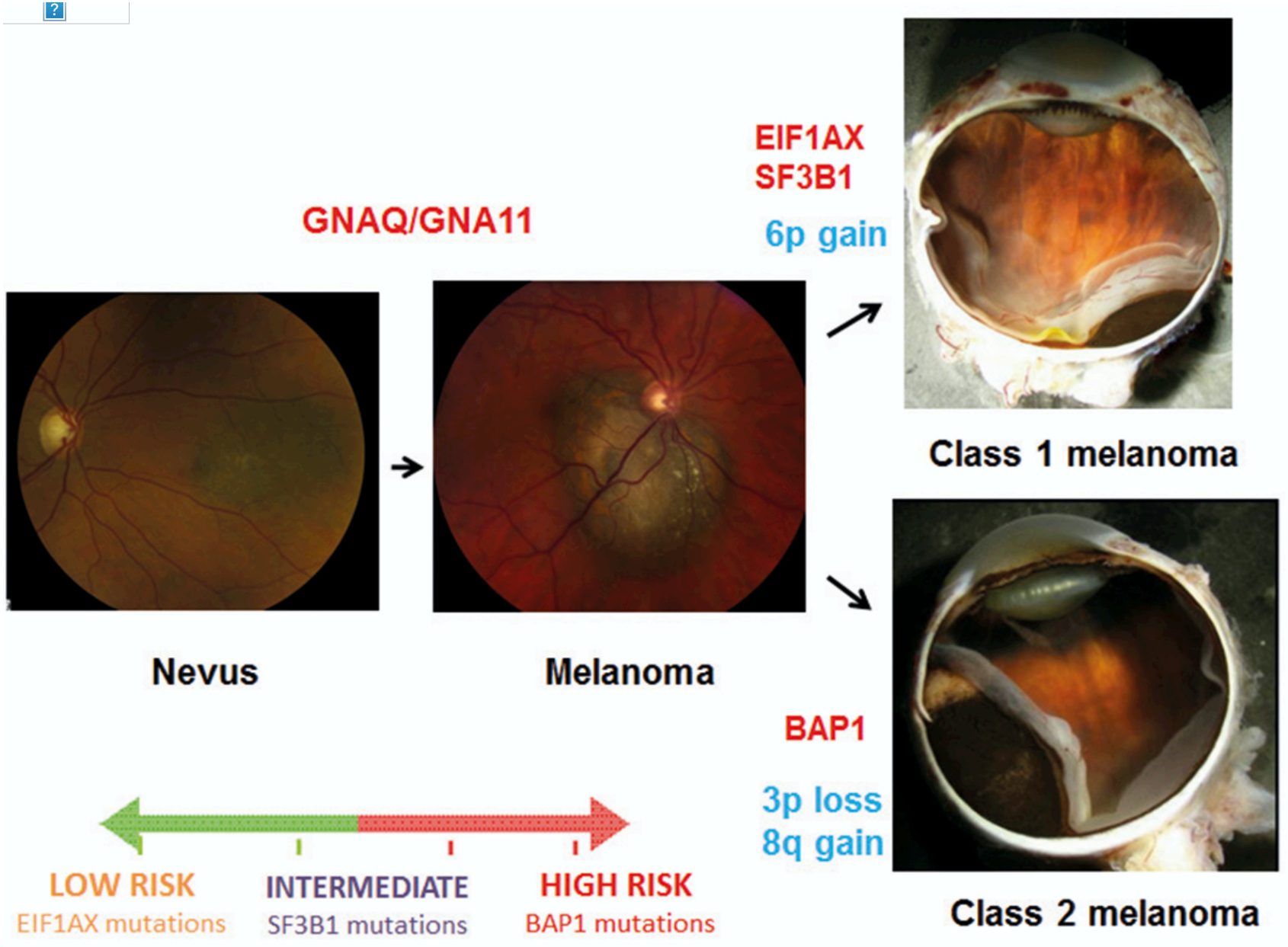
Epidemiology

- Worldwide, the incidence rate is about 2–8 cases per 1 million person-years – lower at lower latitudes (1.3–2.9 cases per 1 million person-years) and increasing with latitude (to 6.1–8.6 cases per 1 million person-years)

- Risk factors include uveal naevus (1 in 400), light skin pigmentation, blonde or red hair, dysplastic naevus syndrome, or BAP1 tumour syndrome.

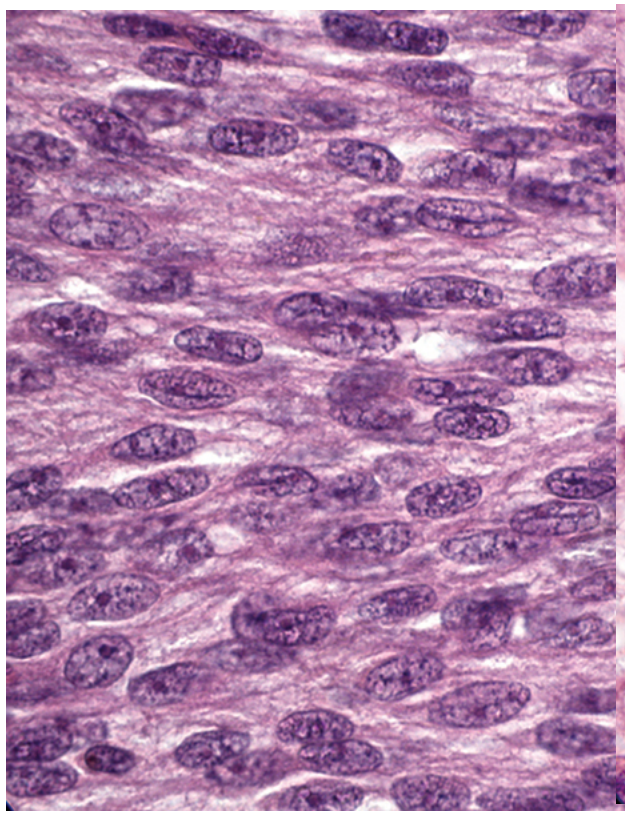
- UV has no definite role. There is an association with welding.

Genomics of Uveal Melanoma

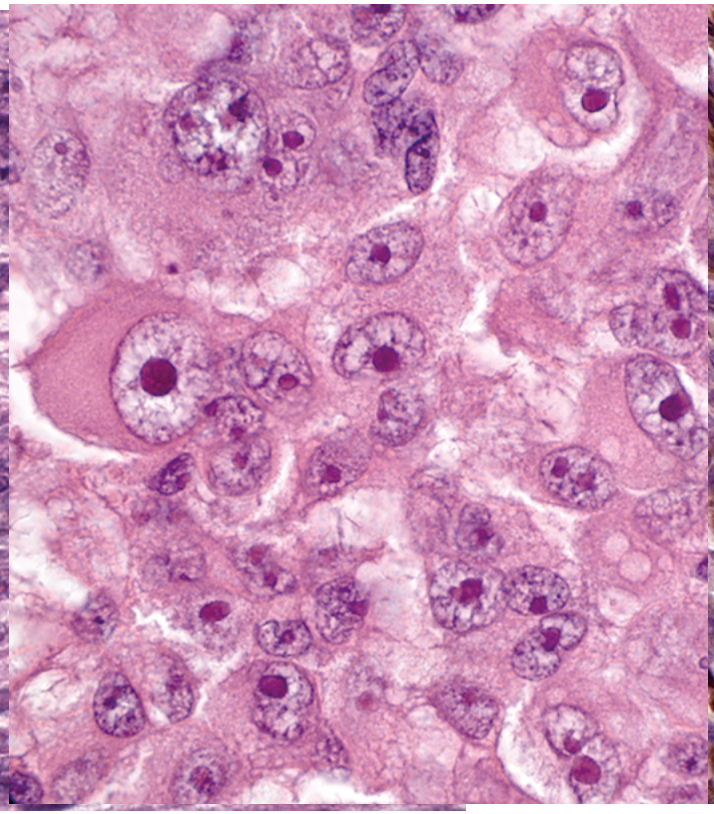


Grossniklaus H.E.

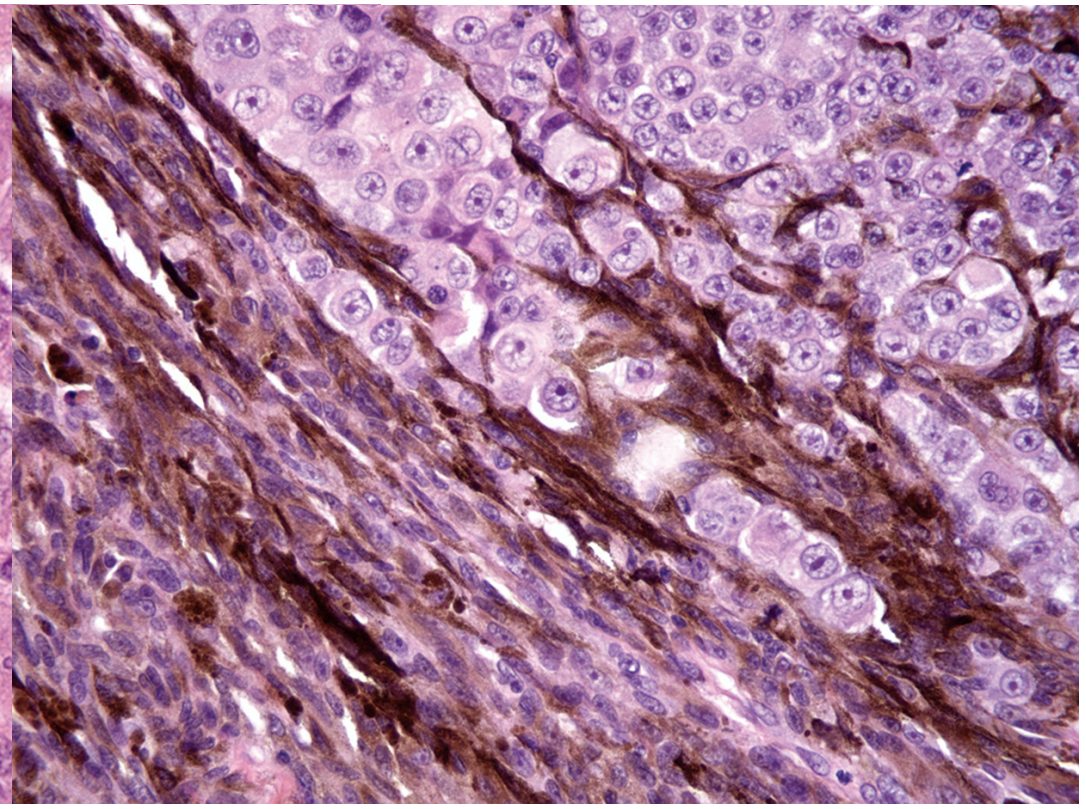
Histopathology – Choroid



Spindle B cells

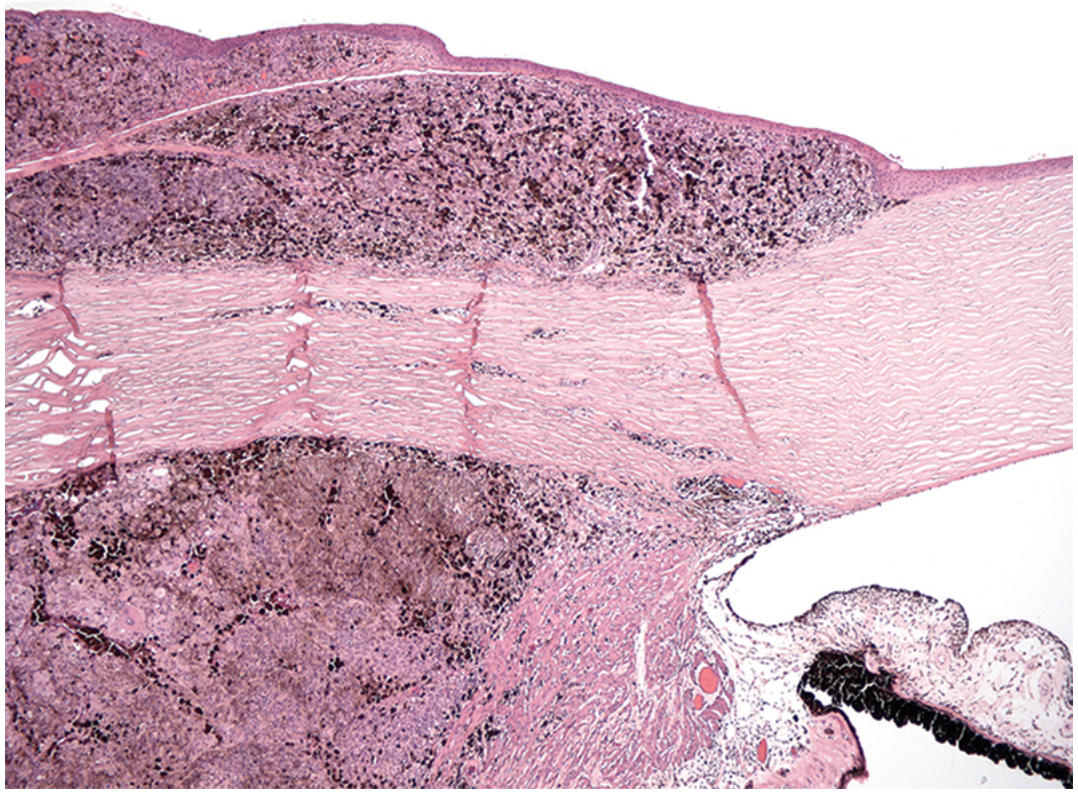


Epithelioid cells

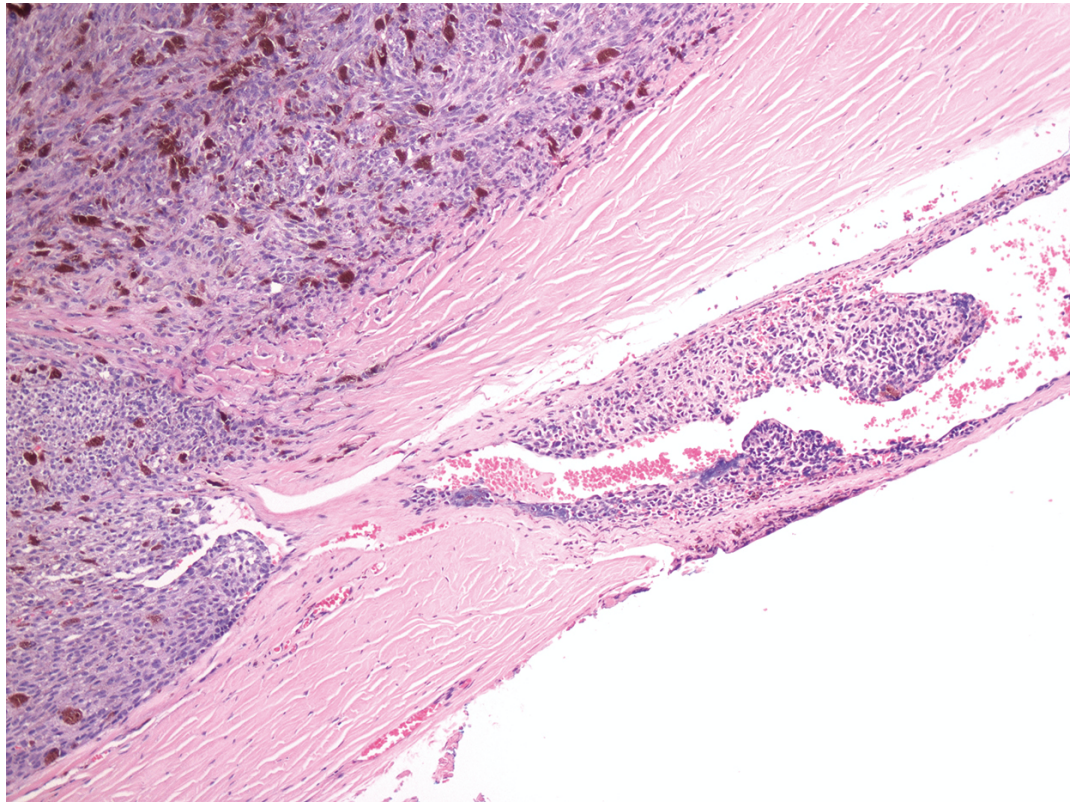


Mixed cells

Histopathology – Local spread

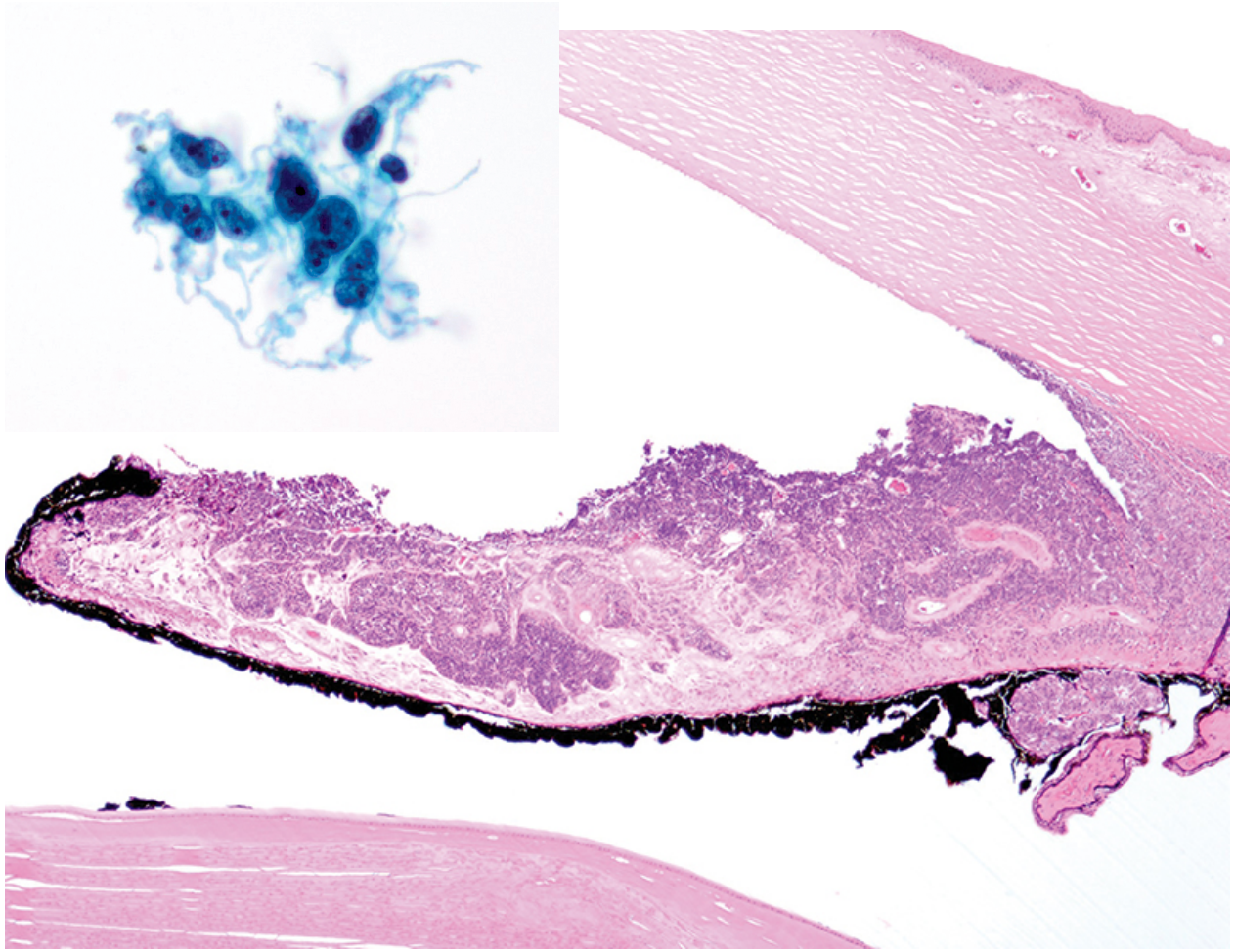


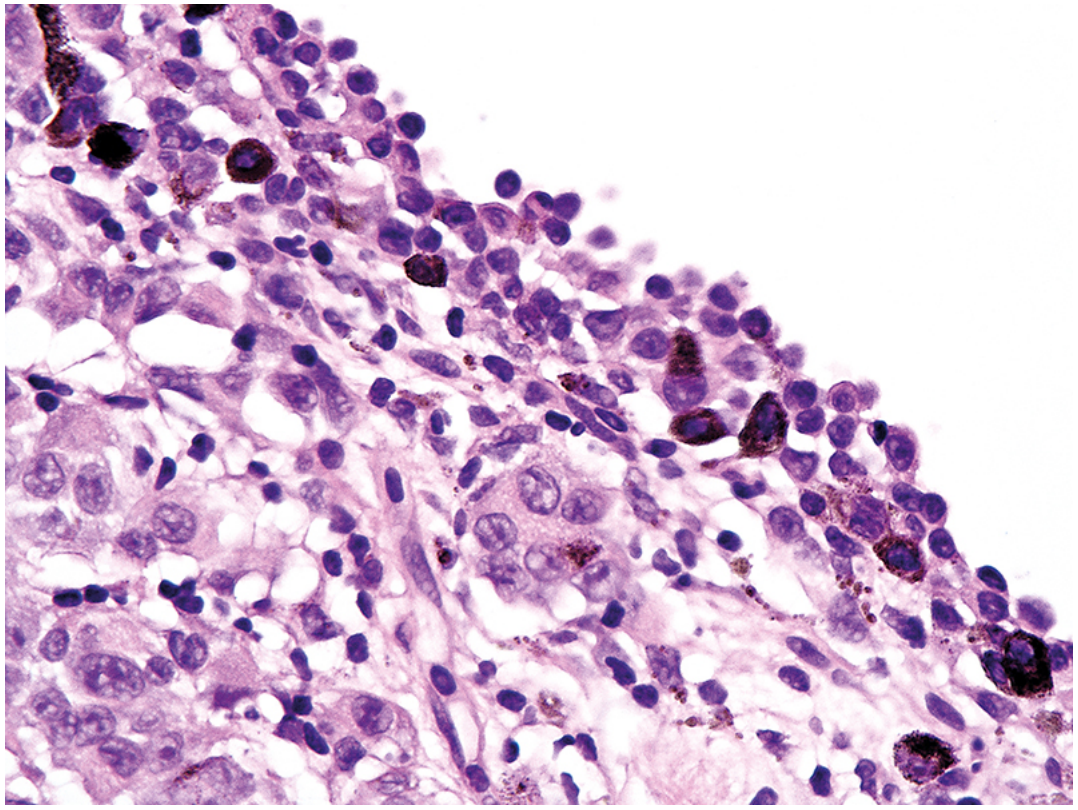
Collecting duct involvement



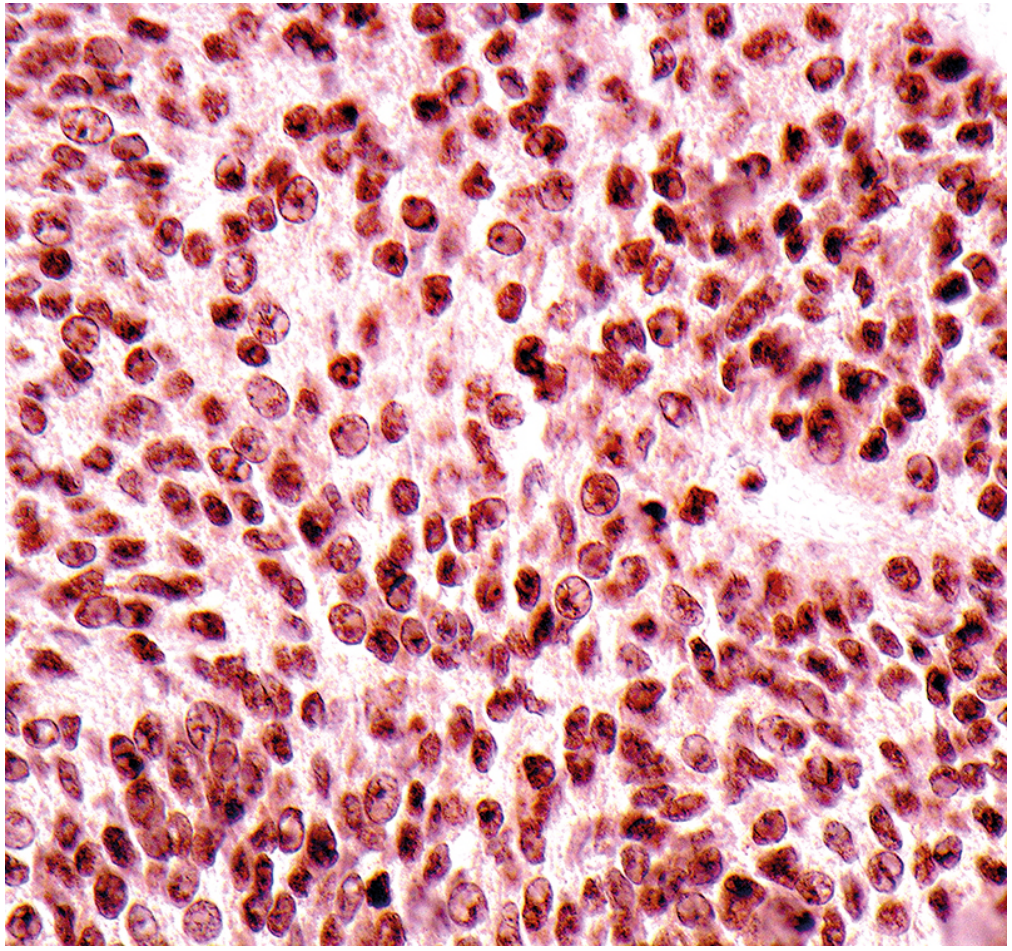
Vortex vein involvement

Histopathology – Iris melanoma

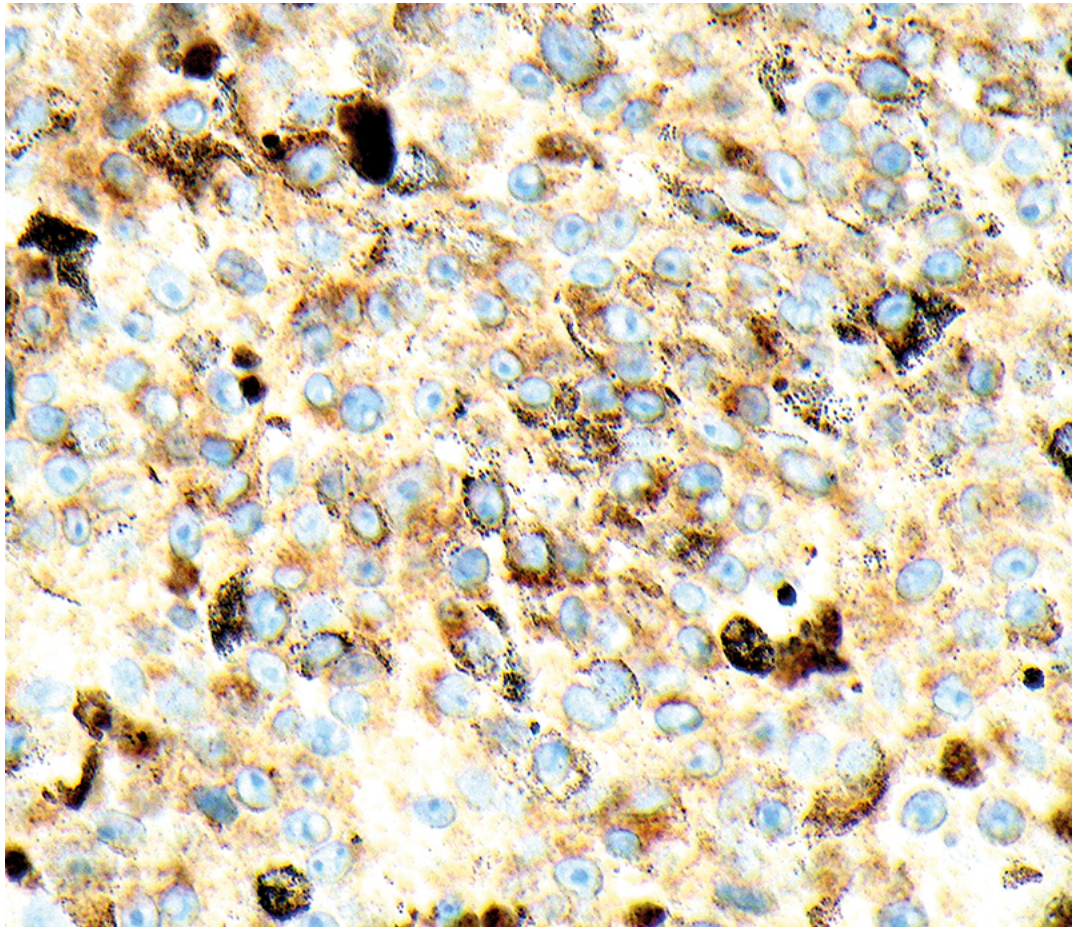




BAP1 immunohistochemistry

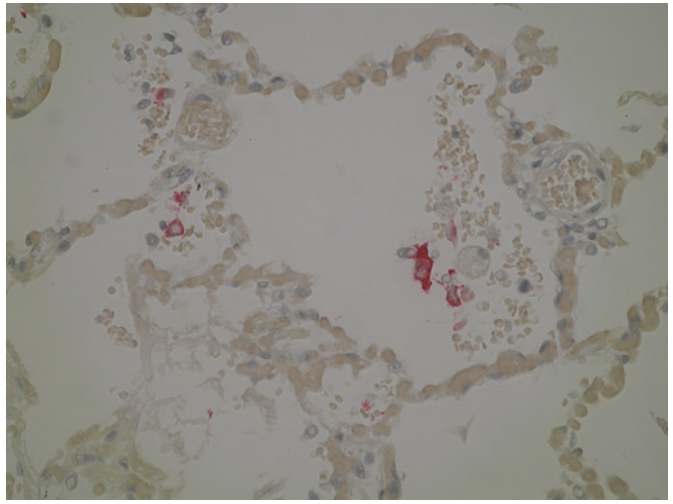


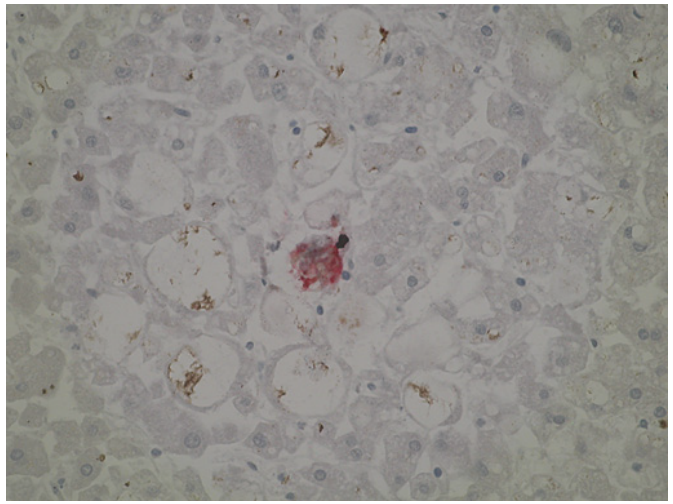
BAP1 is positive in the nuclei.



BAP1-negative choroidal melanoma.

Micrometastasis





Tumour latency:

- Immune control of metastatic cells
- Lack of angiogenesis
- Reduced cell turnover/growth.

No evidence of multicellular micrometastases, so option 3 most likely.

Conclusions

- Uveal melanomas may arise from the iris, ciliary body, or choroid.
- Anterior tumours may invade the collecting ducts and gain access to conjunctival lymphatics
- Posterior tumours may invade vortex veins leading to haematogenous spread, often to lungs or liver
- 50% of patients die from haematogenous spread: as well as size, cell type, and vascularity, identification of tumours with BAP1 loss has prognostic significance.

Thank you!

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