


# Ocular Melanoma



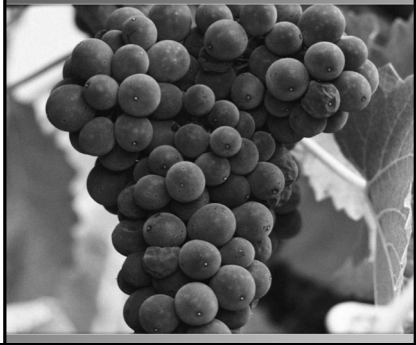
Michal Gutowski, MD  
March 8, 2019

## Uveal Melanoma

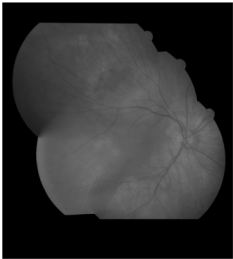
- Melanoma of the iris ciliary body and choroid
- Diagnostic and metastatic evaluation
- Major treatment modalities
- Fine needle aspirate biopsies

## Uveal Melanoma

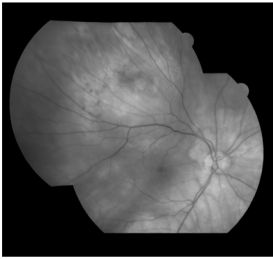
A brief review

The uveal tract	
Iris Ciliary body Choroid	

## Malignant Transformation



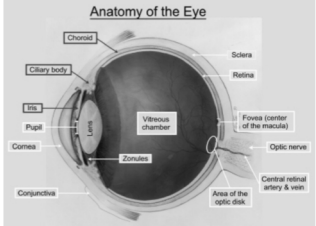
11/2010



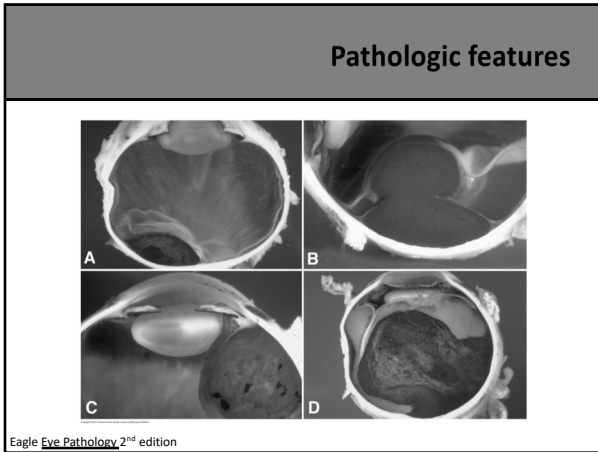
8/2012

## Ocular Melanoma Basics

- Ocular Melanoma
  - Uveal Melanoma
    - Arise from melanocytes in uveal tract
  - Anterior Uveal Melanoma
    - Iris Melanoma 5%
  - Posterior Uveal Melanoma
    - Ciliary body melanoma 5%
    - Choroidal melanoma 90%

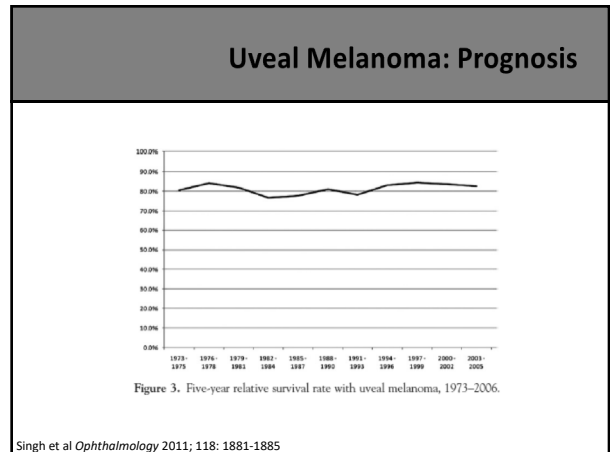
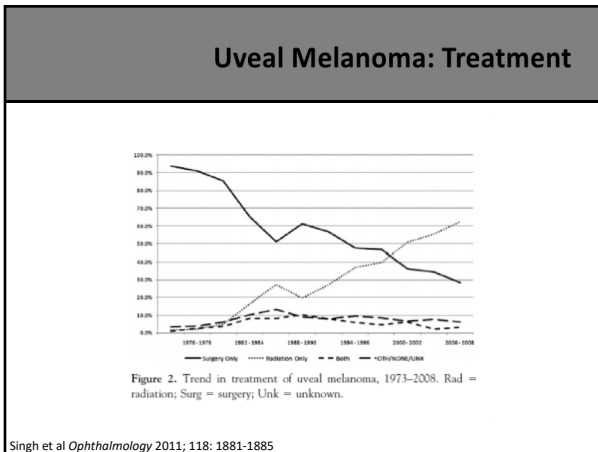
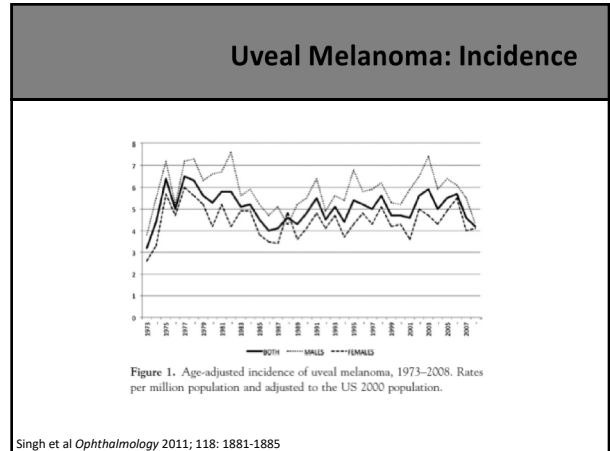


Uveitis.org



- ### Uveal Melanoma
- Most common primary intraocular malignancy in adults
  - 5-10% of all melanoma
  - A distinct disease
  - Poorer prognosis than cutaneous melanoma
  - Most patients have no known family history
  - Metastasis
    - Liver 93%
    - Lung 24%
    - Bone 16%
- National Cancer Institute Surveillance, Epidemiology, and End Results Database

- ### Current State of Affairs
- Review of Surveillance, Epidemiology, and End Results (SEER) program database in the US from 1973-2008
  - Evaluate trends in incidence, treatment and 5-year relative survival rates.
- Singh et al *Ophthalmology* 2011; 118: 1881-1885



### Uveal Melanoma: Prognosis

- Metastasis evident in <3% at initial Dx
  - Can occur more than 20 years after local treatment
- Currently no curative therapy for metastatic disease
  - Median survival after mets: 9 months
- Benefit of early detection debated
  - Variable surveillance recommendations

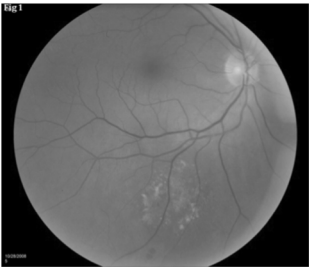
Kath et al 1993

### Uveal Melanoma: DDX

- Choroidal nevus
- Metastasis
- Hemangioma
- Choroidal hemorrhage

### Uveal Melanoma: DDX

- Choroidal nevus
  - Common benign pigmented lesion of uveal tract
  - Present in 10%



Aao.org

### Uveal Melanoma: Epidemiology

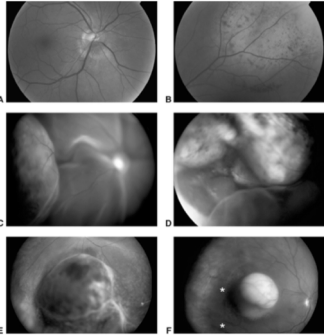
- Age
  - Increases with age, peaks at 60
- Race
  - Rare in non white races
- Genetics
  - Most cases are sporadic
- Risk Factors
  - Fair skin, blue iris color
  - Congenital ocular melanocytosis, neurofibromatosis

### Uveal Melanoma: Diagnosis

- Clinical diagnosis
  - Fundoscopic exam
    - Thickness, fluid, symptoms, orange pigment, margin
    - To Find Small Ocular Melanoma
- Ultrasound
  - Shape, acoustic hollowness, vascularity
- Fluorescein angiography
  - Vascularity

Kath et al 1993

### Uveal Melanoma Clinical Exam



BCSC 2018-19

### Uveal Melanoma: Iris

BCSC 2018-19

### Uveal Melanoma: Management

- Observation
- Enucleation
- Brachytherapy
- Proton Beam irradiation
- Surgical resection
- Thermal laser treatment

Kath et al 1993

### Enucleation

### Radiation

©ECN

### PBRT

- MRI orbits
- Tantalum marker clip placement in the OR
- CT scan with clips in place
- PRBT given in Seattle
  - Seattle Cancer Care Alliance

### Uveal Melanoma: Metastasis Risk Factors

- Tumor size
- Tumor location
- Cell type (spindle vs. epithelioid)
- Vascular patterns
- Patient age
- Tumor genetics

## Fine Needle Aspirate Biopsy

### Why do we perform biopsies?

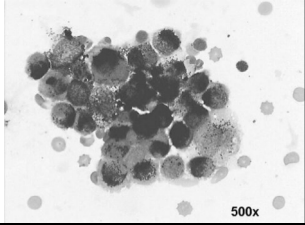
- Diagnosis
- Prognosis

### Diagnostic Biopsy

- Cases in which diagnosis is unclear
- Can assist in determining appropriate therapy
- Not performed very frequently
- Sample is used for cytology
  - often referred to as the "wet" specimen

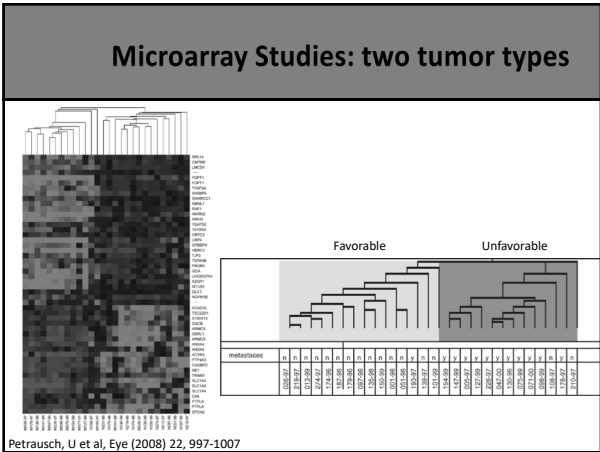
### Cytology

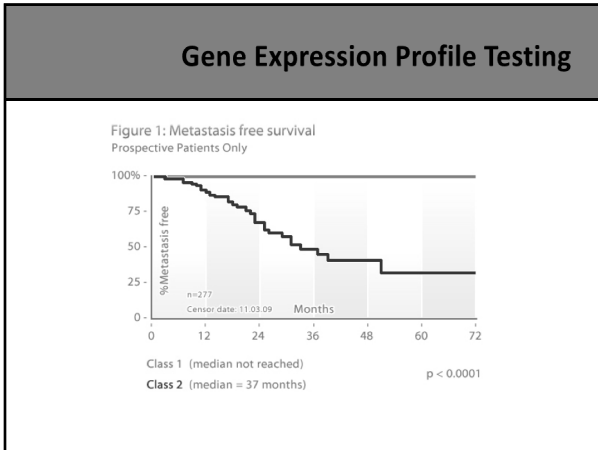
- Purpose is to evaluate cells under microscope
- Specimens should go directly to the cytology lab in anatomic pathology



### Prognostic Biopsy: Gene Expression Profile (GEP) Testing

- Commercially available
- Predicts with great accuracy which patients will develop metastatic disease
- Currently no curative therapy available
- Sample is used for RNA testing
  - often referred to as the "dry" specimen in the OR





Clinical Scenario:  
Prognosis

**RESULTS**

DecisionDX-UM Class = 2

Discriminant Value = 1.14

Patients with a Class 2 molecular signature have a high risk of experiencing near term (within 5 years) clinical metastasis. A discriminant value  $\geq 0.100$  is reported with normal confidence.

Test Results should be interpreted using the Clinical Experience information contained in this report which is derived from clinical studies involving patient populations with specific clinical features as noted in section titled Clinical Experience. These results have not been validated in patients with clinical features different from those described. The discriminant value relates to Class 1 vs 2. See page 2 of initial report for discussion on discriminant value confidence.

**CLINICAL EXPERIENCE FOR CLASS 1A, 1B AND 2**

The DecisionDX-UM assay has been evaluated in over 700 patients with uveal melanoma to date. The majority of these patients participated in a prospective, multi-center study to validate the predictive accuracy of this gene expression-based molecular assay. Outcomes are collected and the ability of the molecular signature to predict metastasis is being evaluated at regular intervals. The most recent center date (June 9, 2011) of the prospective study included 814 patients with follow-up data available for analysis. The center date for this subendum is June 9, 2011. The actual outcomes for metastasis of the predicted low-risk (Class 1A), intermediate-risk (Class 1B), and the high-risk (Class 2) molecular signatures are shown below.

Molecular Signature Class	Percent Metastasis Free at 3 Years	Percent Metastasis Free at 5 Years
Class 1A	99%	98%
Class 1B	93%	79%
Class 2	50%	28%

n=514, Log-rank (Mantel-Cox) test, p<0.0001

- ### FNAB methods for intraocular tumors
- Trans-corneal
  - Trans-scleral
  - Trans-vitreous

### Trans-corneal biopsy

- For iris tumors/iridociliary tumors
- Clear cornea incision
- Pupil not dilated
  - May use preop pilocarpine or Miochol intraoperatively
- AC must be maintained
  - Injection of BSS
  - Healon

Finger et al, BJO 2005

### Trans-scleral biopsy

- Scleral flap created
- Attention to good hemostasis
- Immediate plaque or cryotherapy to bx site
- Flap sutured
- Decrease risk of seeding
  - Change suture/instruments after biopsy

Singh et al, ARVO 2011

### Trans-vitreous biopsy

- 2 Sclerotomies made
  - 25 gauge trochars
- Light pipe and 27g needle
- AVI lens
- Decrease risk of seeding
  - Cryo port
  - Suture ports

Carl Groeneveld

Singh et al, ARVO 2011

## References

- Singh AD, Turell ME, Topham AK. Uveal melanoma: trends in incidence, treatment, and survival. *Ophthalmology*. 2011 Sep;118(9):1881-5.
- Shields CL, Kaliki S, Furuta M, Mashayekhi A, Shields JA. Clinical spectrum and prognosis of uveal melanoma based on age at presentation in 8,033 cases. *Retina*. 2012 Jul;32(7):1363-72.
- Kujala E, Mäkitie T, Kivela T (2003) Very Long-Term Prognosis of Patients with Malignant Uveal Melanoma. *Investigative Ophthalmology and Visual Science* 44: 4651-4659.
- Ezekiel Weis, MD, MPH, Chirag P. Shah, MD, MPH, Martin Lajous, MD, Jerry A. Shields, MD, Carol L. Shields, MD. The Association Between Host Susceptibility Factors and Uveal Melanoma: A Meta-analysis. *Arch Ophthalmol*. 2006;124(1):54-60.
- Diener-West M, Earle JD, Fine SL, Hawkins BS, Moy CS, Reynolds SM, Schachat AP, Straatsma BR; Collaborative Ocular Melanoma Study Group. The COMS randomized trial of iodine 125 brachytherapy for choroidal melanoma, III: initial mortality findings. COMS Report No. 18. *Arch Ophthalmol*. 2001 Jul;119(7):969-82.
- Singh AD, Kalyani P, Topham A. Estimating the risk of malignant transformation of a choroidal nevus. *Ophthalmology*. 2005 Oct;112(10):1784-9.
- Collaborative Ocular Melanoma Study Group. Histopathologic characteristics of uveal melanomas in eyes enucleated from the Collaborative Ocular Melanoma Study. COMS report no. 6. *Am J Ophthalmol*. 1998 Jun;125(6):745-66.
- McCannel TA. Fine-needle aspiration biopsy in the management of choroidal melanoma. *Curr Opin Ophthalmol*. 2013 May;24(3):262-6.
- J.M. Quivey, J. Augsburger, L. Snelling et al. 125I plaque therapy for uveal melanoma. Analysis of the impact of time and dose factors on local control. *Cancer*, 77 (1996), pp. 2356–2362.