


 Uveal Melanoma


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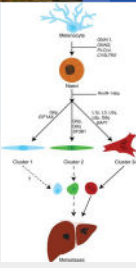


 Disclosure

- Castle Biosciences (Advisory Board)
- Astra Zeneca (Advisory Board)
- Ideaya Biosciences (Consultant)

 Uveal Melanoma


- Most common primary intraocular malignancy in adults (3%-5% of all melanomas)
- 5-7 new cases per million per year
- Median age at diagnosis: 55-60 years
- Caucasian
- Metastases to liver and lungs



• Future perspectives of uveal melanoma blood based biomarkers. *British Journal of Cancer* (2022)
• Incidence of noncutaneous melanomas in the U.S. 2005 American Cancer Society.
• Trends in incidence, survival, and management of uveal melanoma: a population-based study of 7,516 patients from the Surveillance, Epidemiology, and End Results database (1973-2012). *Can Ophthalmol*. 2016 Oct 25;10:2113-2119

Uveal Melanoma: Risk Factors

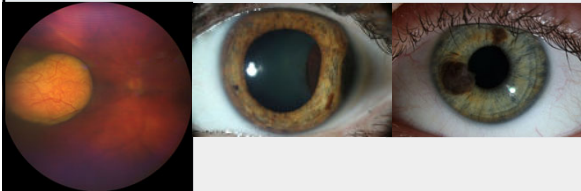
- Light eyes
- Fair skin
- Ocular melanocytosis
- BAP1 mutations
- Role of sun exposure: controversial



Shields CL, Kalki S, Livsey M, et al. Association of ocular and oculodermal melanocytosis with the rate of uveal melanoma metastasis: analysis of 7872 consecutive eyes. *JAMA Ophthalmol*. 2013;131(9):993-1000.
Gallagher RP, Thibod JD, Roitman J, et al. Risk factors for ocular melanoma: Western Canada Melanoma Study. *J Natl Cancer Inst*. 1985;74(4):775-778.

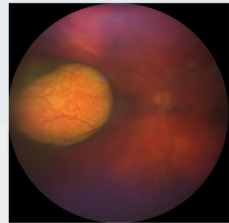
Uveal Melanoma

Choroid > Ciliary body > Iris

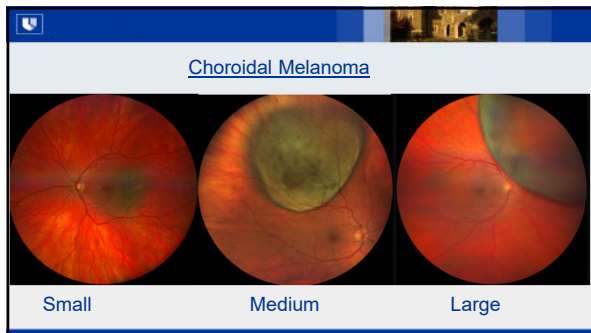


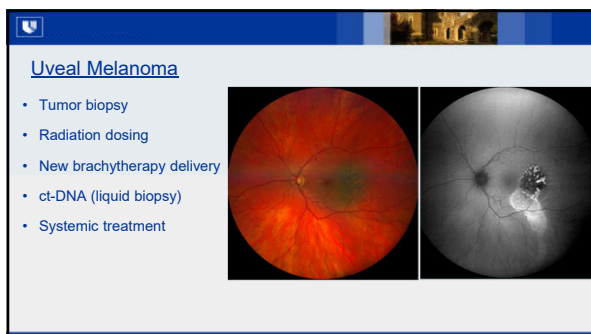
Uveal Melanoma

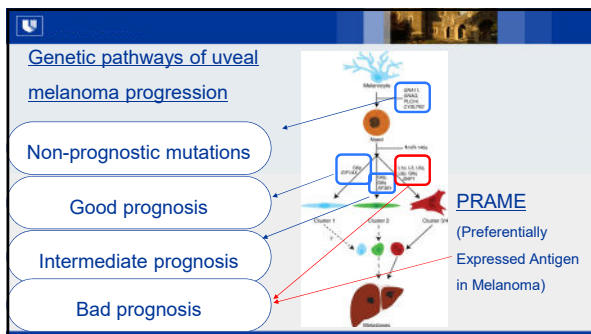
- Diagnosis:
 - Indirect ophthalmoscopy
 - Ultrasound
 - Fluorescein angiography
 - Fundus photography
 - Autofluorescence
 - Optical Coherence Tomography
 - Biopsy
 - Others

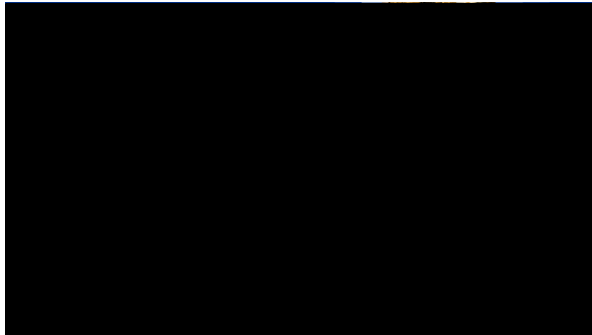


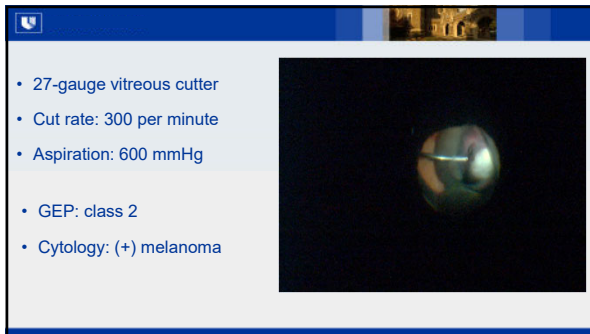
Class 1B, PRAME negative
GNA11, EIF1AX



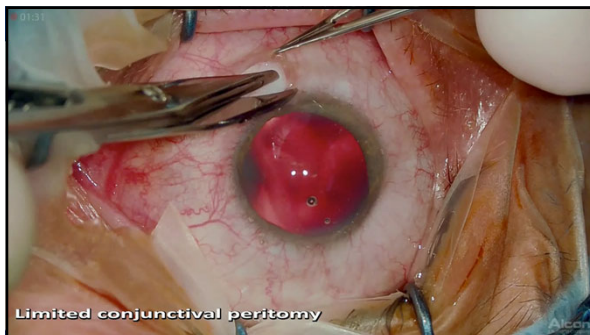








- 27-gauge vitreous cutter
- Cut rate: 300 per minute
- Aspiration: 600 mmHg
- GEP: class 2
- Cytology: (+) melanoma



Collaborative Ocular Melanoma Study (COMS)

- Minimum of 85 Gy to apex or minimum of 5mm for smaller tumors
- Tumor control at 5 years: 90% **Good**
- Globe preservation at 5 years: 87% **Good**
- Decreased visual acuity: 43-49% at 3 years **Need to do better**

Preliminary Results of Uveal Melanoma Treated With Iodine-125 Plaques: Analysis of Disease Control and Visual Outcomes With 63 Gy to the Target Volume

Wajiha J. Kheir, MD,^a Sandra S. Stinnett, DrPH,^a Sheridan Meltsner, PhD,^b Ekaterina Semenova, MD, PhD,^a Yvonne M. Mowery, MD, PhD,^b Oana Craciunescu, PhD,^b David G. Kirsch, MD, PhD,^{b,c,d,e,f,1} and Miguel A. Materin, MD^{a,1}

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Fundus Diagram

1. Choroidal melanocytosis lesion, with documented μm/mv for 10x10x1

(+) SRF on OCT
(+) Orange pigment
(-) Lack of drusen
9 mm to fovea
9 mm to CNV
(+) ultrasound hollowness

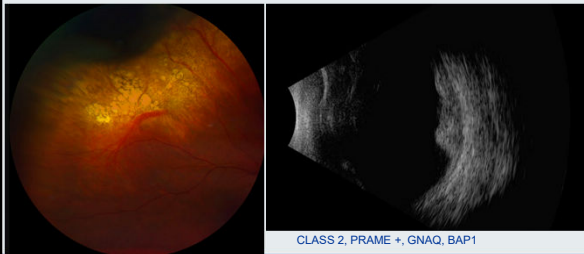
Results

- Initial 69 patients
- Local failure: 6%
- Distant metastases: 6% (LBD >11mm and Class 2 GEP)
- Visual acuity: 50% with 20/40 or better and 22% with 20/200 or worse
- 07/2024 we have now more than 400 patients treated

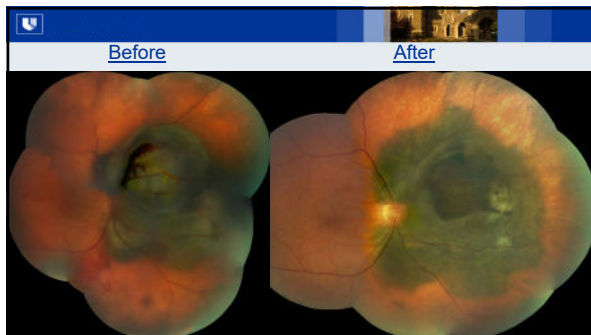
Large uveal melanoma



Large choroidal melanoma after I125 plaque



CLASS 2, PRAME +, GNAQ, BAP1



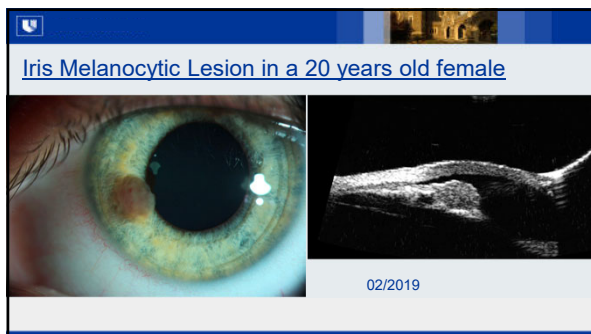
ELSEVIER   BRACHYTHERAPY

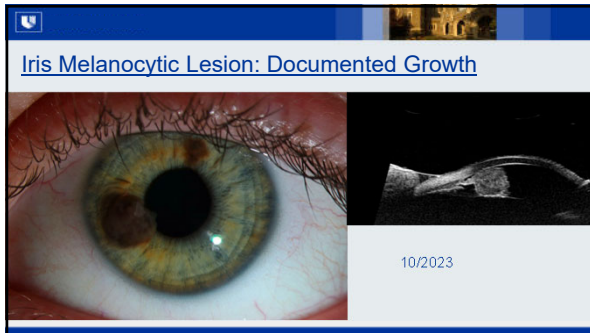
Brachytherapy 22 (2023) 416–427

First clinical implementation of Yttrium-90 Disc Brachytherapy after FDA clearance

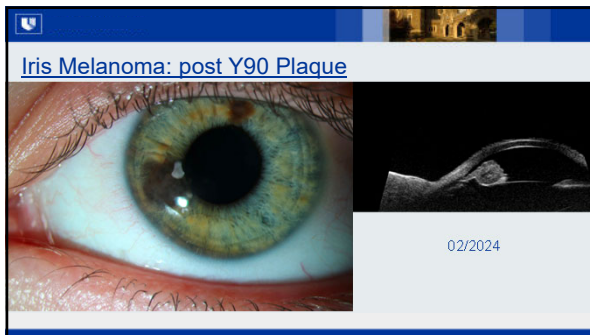
Paul T. Finger^{1,2,3,*}, Robert Stewart², Mark J. Rivard³, Raymond J. Beers², Jacob Kamen², Shyam Lama², Kimberly J. Chin^{1,2}, Kyle Mohney², Toby S. Welles³, Wolfgang A.G. Sauerwein³, Kenneth Rosenzweig²

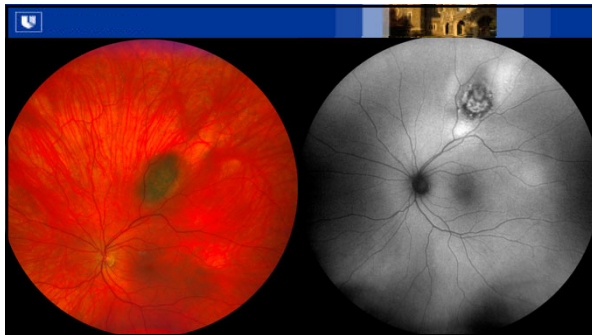
¹The Department of Ocular Tumors, Orbital Disease, and Ophthalmic Radiation Therapy, The New York Eye Cancer Center, New York, NY
²The Departments of Ophthalmology, Radiation Oncology, and Radiation Safety, New York Eye and Ear Infirmary of Mount Sinai and Icahn School of Medicine at Mount Sinai, New York, NY
³Scientific Advisory Board and Employers of Liberty Vision Corporation, Portsmouth, NH

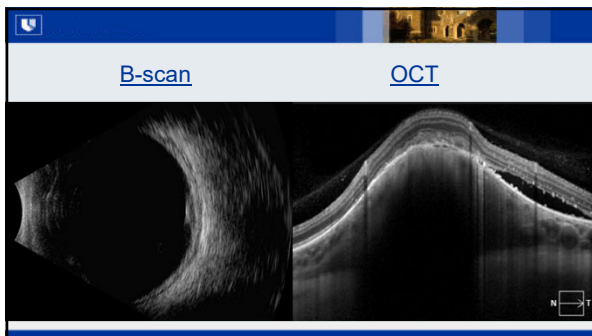










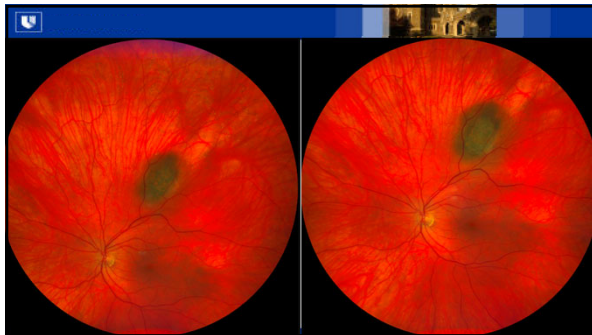


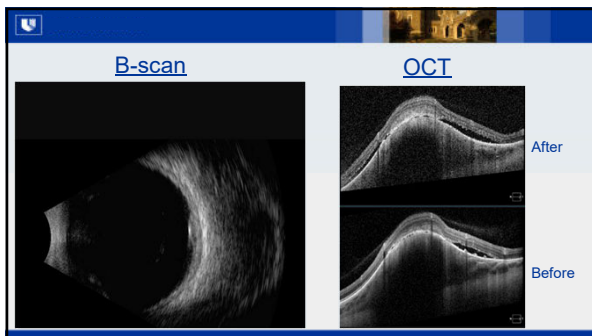
Case Reports > J Vitreoretin Dis. 2024 Feb 18;8(2):210-214.
doi: 10.1177/24741264241227684. eCollection 2024 Mar-Apr.

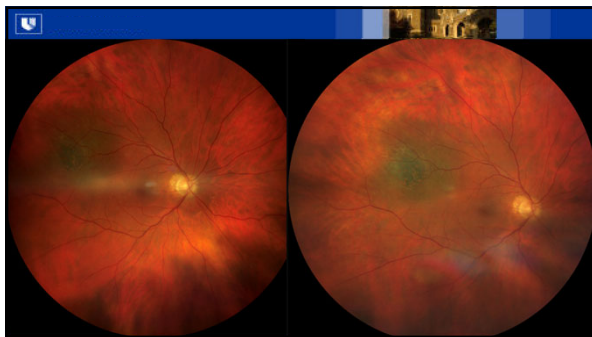
Yttrium-90 Episcleral Plaque Brachytherapy for Choroidal Melanoma

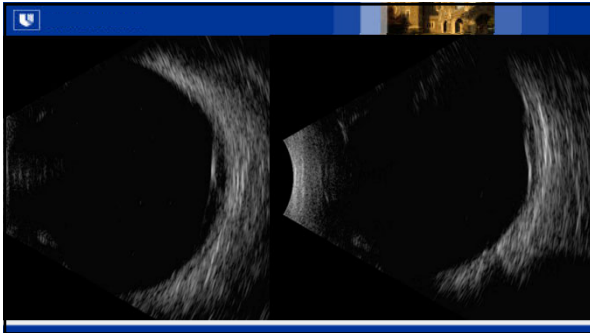
Paul T Finger¹

Affiliations + expand
PMID: 38465362 PMCID: PMC10924596 DOI: 10.1177/24741264241227684









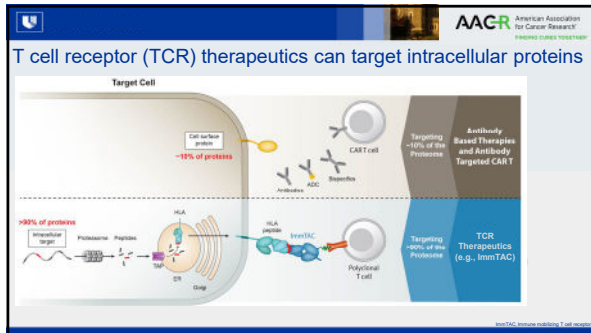
Summary: Y90 Plaque Brachytherapy

- Easy to use
- Fast delivery radiation (few minutes)
- Anterior and posterior tumors
- Longer follow up is needed (for results and adverse side effects)
- Tumors adjacent to optic nerve head might be a challenge
- Plaque size (6mm)
- Plaque size (10mm) hopefully this year

Circulating Tumor DNA Reflects Uveal Melanoma Responses to Protein Kinase C Inhibition
 John J. Park,^{1,2,3} Russell J. Dieffenbach,^{1,2} Natalie Byrns,² Georgina V. Loo,^{2,4,5} Richard A. Scully,^{2,5,6} Elin S. Gray,⁷ Matteo S. Carlini,^{2,3,5,7} and Helen Raay,^{1,2,7}

ct-DNA
 Detectability of Plasma-Derived Circulating Tumor DNA Panel in Patients Undergoing Primary Treatment for Uveal Melanoma
 Jasmine H. Francis,^{1,2} Christopher A. Berney,^{3,4} Rosa Brannon,⁴ Julia Cavestro,⁵ Melissa Robbins,¹ Christina E. Szentostotis,⁵ Sara Leitch,¹ Crystal Lee,¹ Michael F. Berens,⁴ Alexander Shoukhrat,^{4,7} and David H. Abramson,^{1,7}

Abstract
 Anatomy and Pathology/Oncology | February 2024
Evaluation of Circulating Tumor DNA as a Liquid Biomarker in Uveal Melanoma
 Christel P. de Bruijn, Natalya M. van Poppel, Tom Brands, Suzanne C. van den Boom, Ellis Ekenboom, Anja Willems, Marjolijn M. van Vliet, Florinda van Gorp, Gert-Jan van der Vliet, Corine M. van der Wal, Robert M. Verrijke, Nicole C. Naaij, Verba M. Bagger, Jeroen F. Krijgaard, Annelies de Klerk, Erwin Brons, and Helen Raay



Darovasertib – Potential to Broadly Impact Uveal Melanoma
Potential First-in-Class and Best-in-Class in (Neo)adjuvant UM and Metastatic UM

Mutations in GNAQ / GNA11 activate PKC signaling, a genetic driver of Uveal Melanoma

Darovasertib is an oral, potent and selective PKC inhibitor GNAQ or GNA11 (~95%) and other upstream mutations activate PKC signaling in UM and MUM patients

UM is typically treated with radiation and/or enucleation, with no approved systemic therapies for Neoadjuvant UM. MUM occurs in approximately 50% of UM patients and predominantly as liver metastasis in ~90% of MUM patients, with no approved therapies for HLA-A*02:01 negative MUM

Daro Mono Rationale in Primary UM

Single Agent Daro Induces Tumor Regression Uveal Melanoma (n=92) 1 mutant GNAQ

Daro + Crizo Combo Rationale for Use in Metastatic Uveal Melanoma (MUM)

Daro Phase 1 Monotherapy Efficacy Association with cMET Expression

Activation of PKC and cMET Pathways with Observed cMET Overexpression in MUM Liver Metastases

IDEA

