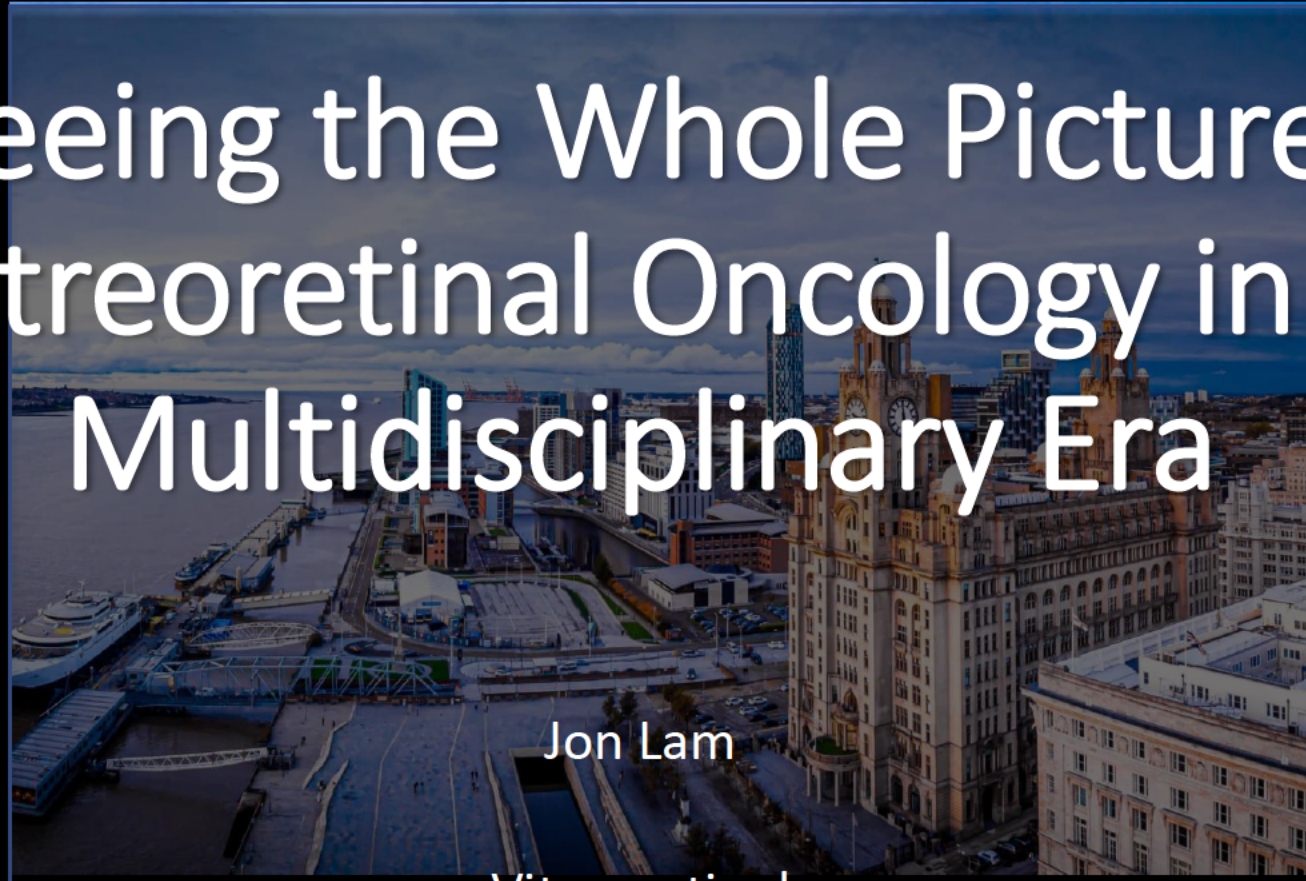


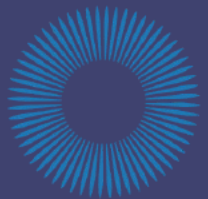
Seeing the Whole Picture: Vitreoretinal Oncology in a Multidisciplinary Era



Jon Lam

Vitreoretinal
surgeon

Ocular oncologist



PERTH
RETINA

DR TIM ISAACS
DR JON LAM



Royal Perth
Hospital



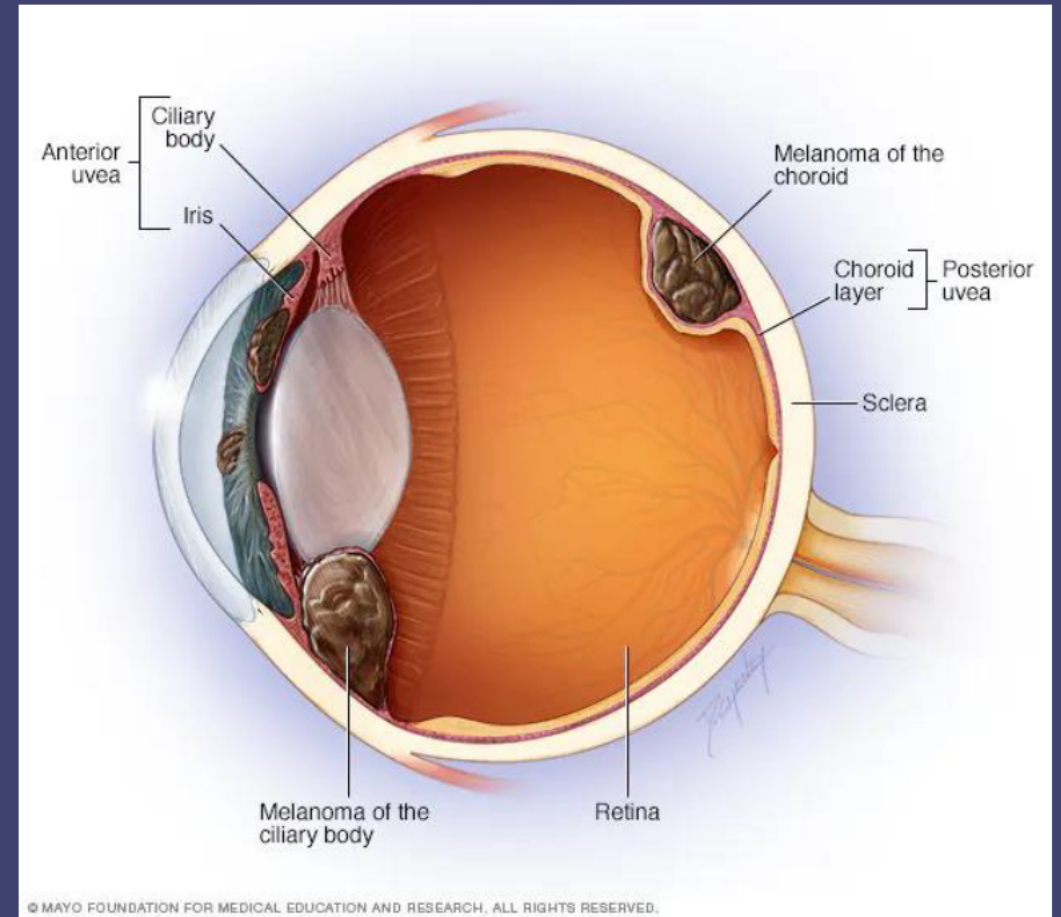
South Metropolitan
Health Service

Ocular oncology multidisciplinary era

- Conditions we treat in vitreoretinal oncology
 - **Choroidal melanoma**
 - Choroidal metastases
 - Intraocular and uveal lymphoma
 - Vascular tumors of the retina

Uveal melanoma

- Most common primary intraocular malignancy in adults.
- Incidence: ~6–7/million/year in Western populations.
- **5-year all-cause mortality:** ~30% (driven mainly by metastatic disease rather than local recurrence).
- **10-year all-cause mortality:** ~45%.
- **15-year all-cause mortality:** ~50%.
- Median survival after diagnosis: **~15 years** overall, but highly variable based on tumour genetics and stage.



Small melan

RG OptomapPlus
May 21, 2025 1:42 PM
Image: 1
4000
4000

Eye Cubed - [ID: 24615, Name: Milin, Noel]

Patient Scan Utilities Help

eyecubed etilex

Capture Reports

Scan Details
Right (OD) **OD** Left (OS)

Scan Modes
Posterior B

Posterior B-Scan Options
Probe Position

Mode
B-Scan
B+Cross Vector
Cross Vector A

1550m/s LOG [Tx: -10.0dB] [Rx: 68dB] + TGC Probe: Posterior B 10MHz ENH: OFF
Examiner: EyeCubedDemo Physician: None

Image Adjustments
68 dB
OFF
Log S1 S2 S3
Time Gain Compensation
Media Velocity 1550 (Average) m/s

Zoom and Navigate
1.5 x

Editing Tools
Clear All

Editing Options
Undo All

Press F11 to start Acquisition

Current Session Standard Report IOL Report Export Recycle Bin 5/21/2025

Session Reports OD (Right) OS (Left)

Scan image loaded. Version: 2.5.0.1 Admin: I3Administrator Database Storage: 0.7% 6/3/2025 10:55:54 AM

Perth Retina
OS, P200DTx
Laterality: R

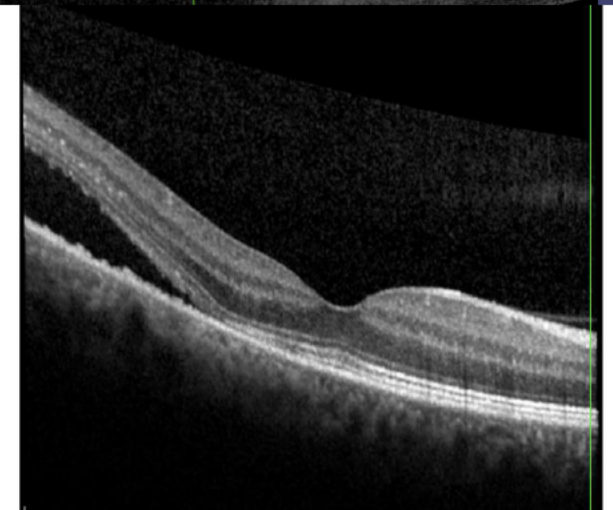
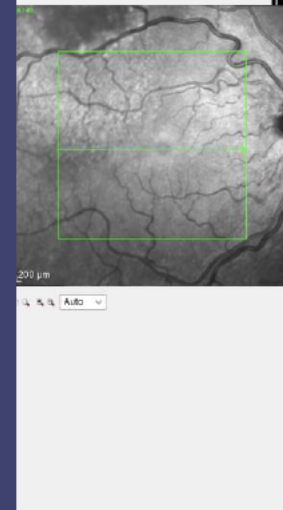
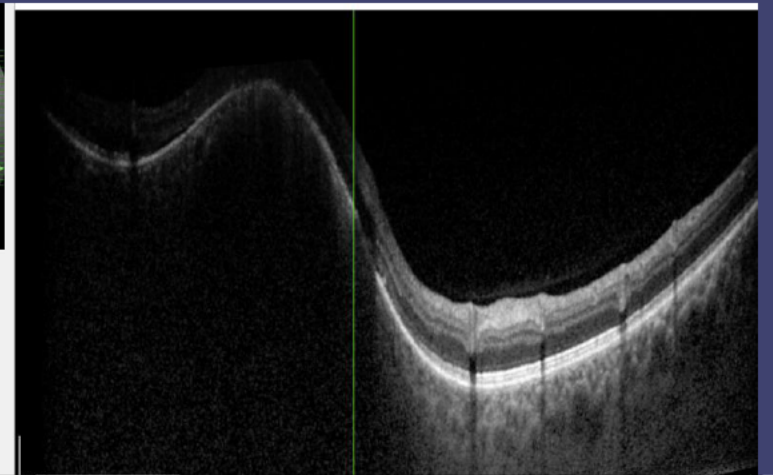
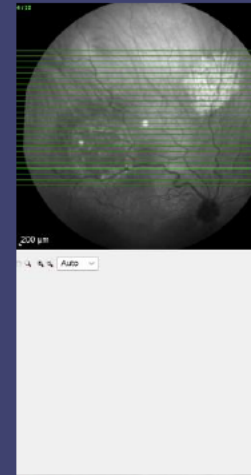
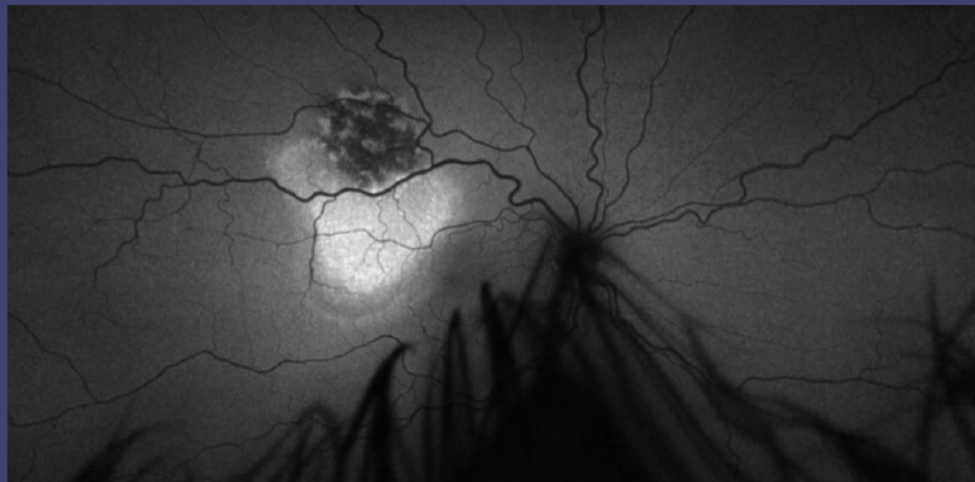
Zoom: 1.50
Tint: 100%
Presentation: Multiple

1/1

Zoom: 1.50
Presentation: Multiple

1/1

'I still see a smudge when I read'



Medium melanoma

EyeCubed - [ID: 2425], Name: Glatz, Peter

eyecubed. ellex

Patient Scan Utilities Help

Capture Reports

Scan Details

• Right (OD) **OS** • Left (OS)

Scan Modes

Posterior B

Posterior B-Scan Options

Probe Position

Mode

• B-Scan

• B+Cross Vector

• Cross Vector A

11.38mm

3.35mm

1550m/s LOG [Tx: -7.0dB] [Rx: 90dB] + TGC Probe: Posterior B 10MHz ENH: OFF

Examiner: EyeCubedDemo Physician: None

Image Adjustments

90 dB

OFF

Log S1 S2 S3

Time Gain Compensation

Media Velocity 1550 (Average) m/s

Zoom and Navigate

1.5 x

Editing Tools

Clear All

Editing Options

Undo All

Press F11 to start Acquisition

Current Session Standard Report IOL Report Export Recycle Bin 5/7/2025 1/7/2025

Session Reports OD (Right) OS (Left)

Add to Export

Add to Report

Max

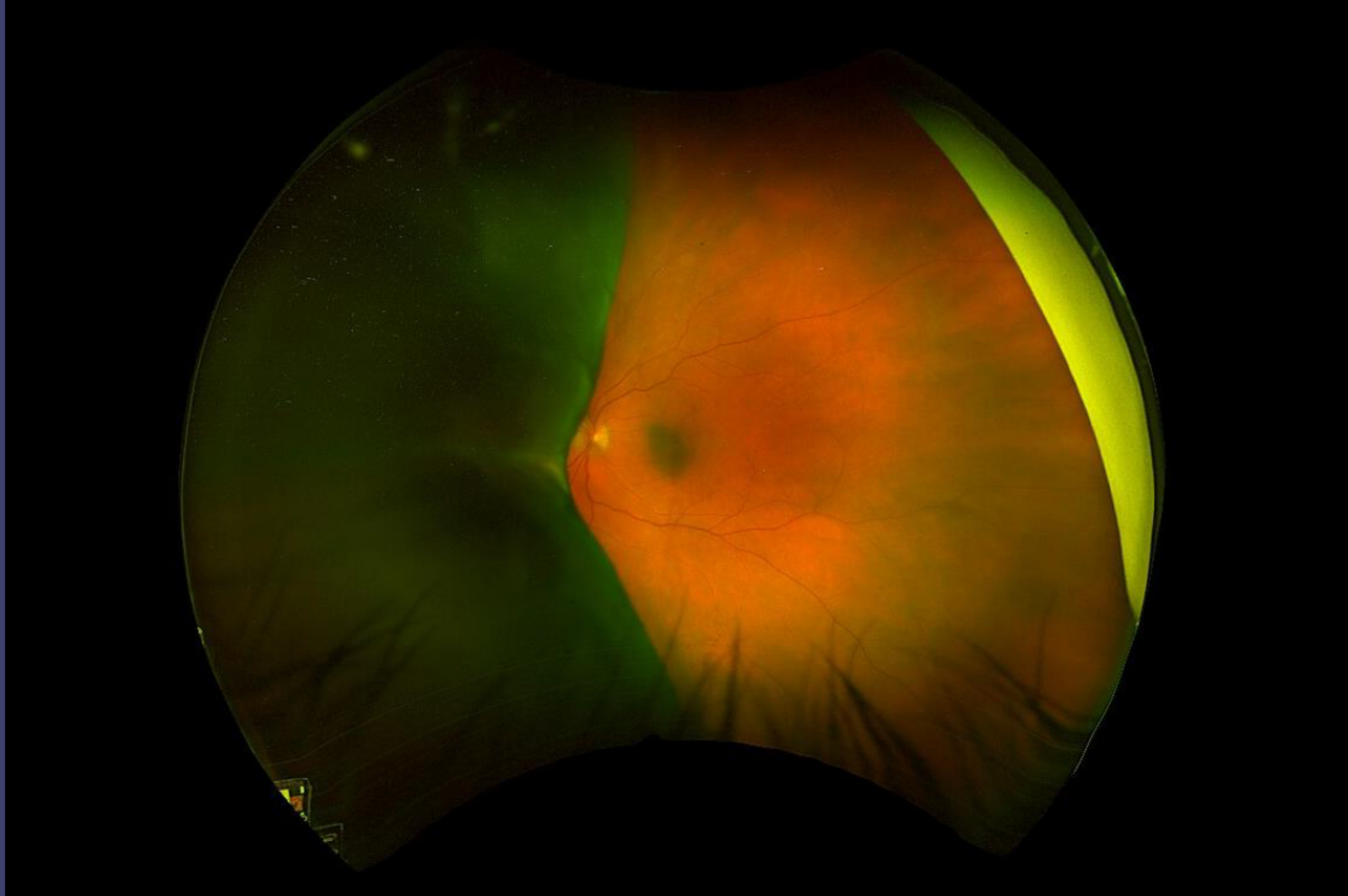
Min

End Session

Scan image loaded. Version: 2.5.0.1 Admin: I3Administrator Database Storage: 0.7% 6/3/2025 10:54:46 AM

Perth Reti
OPTOS, P200D
Laterality
Red: 50
Green: 50

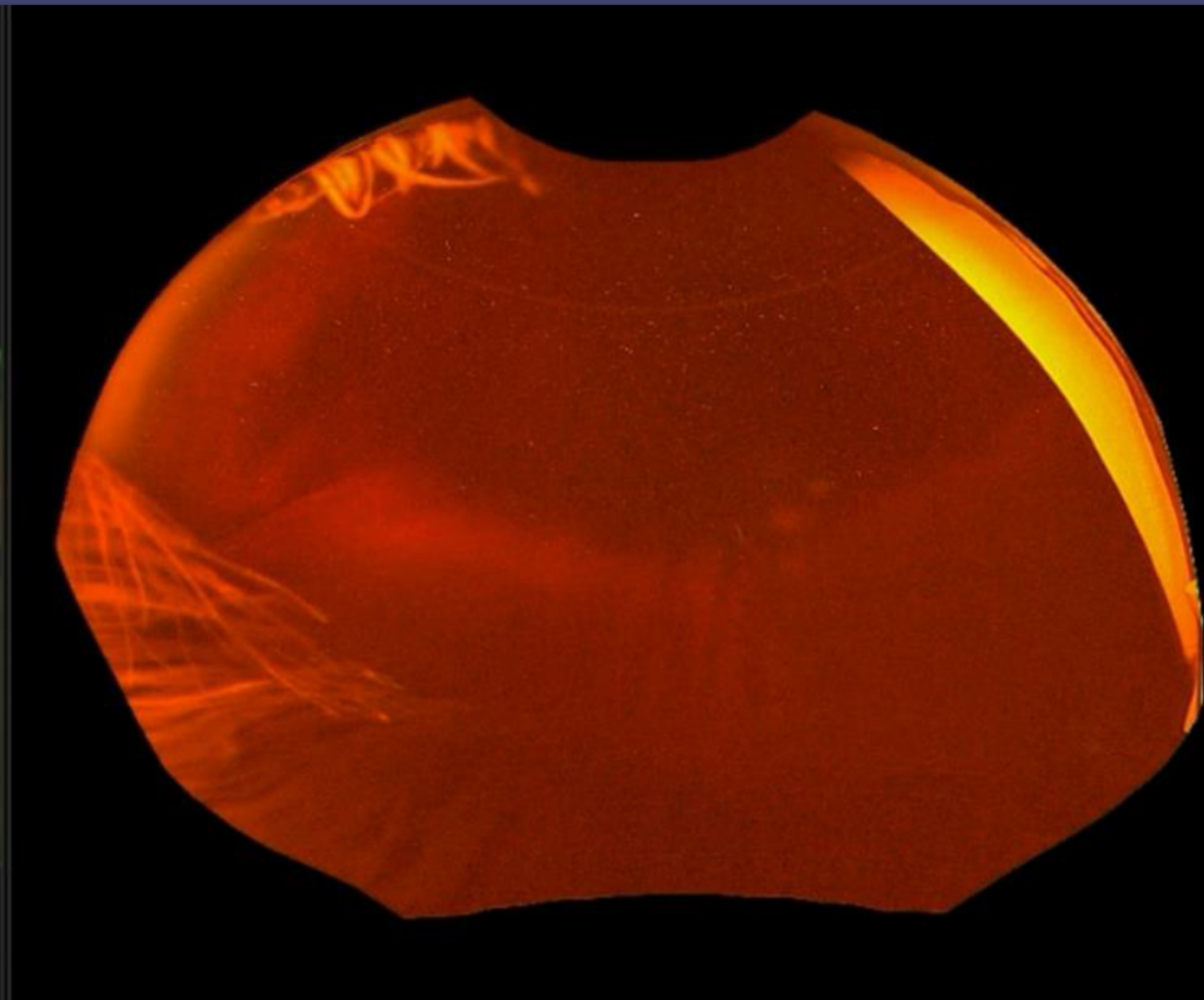
Large melanoma



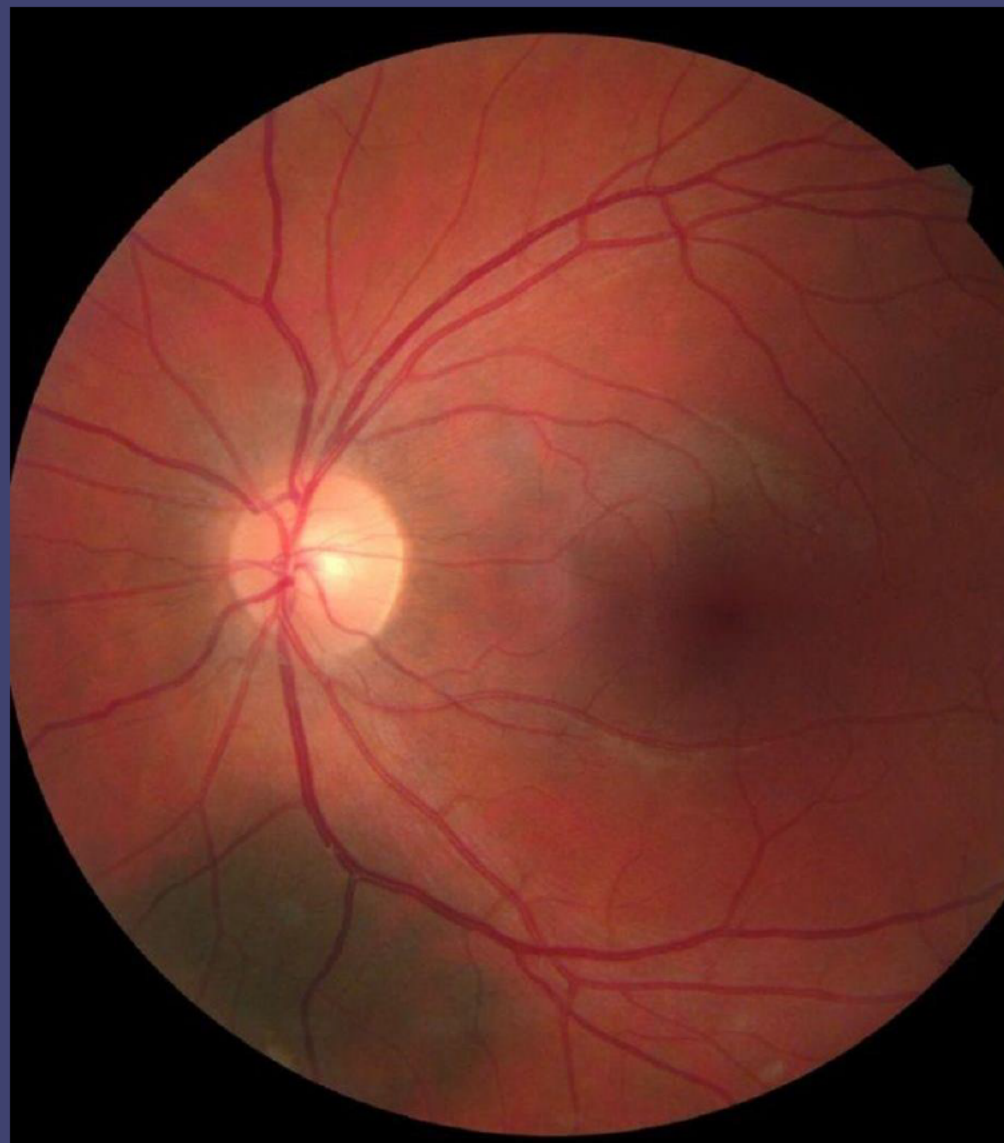
Iris/Ciliary Body melanoma

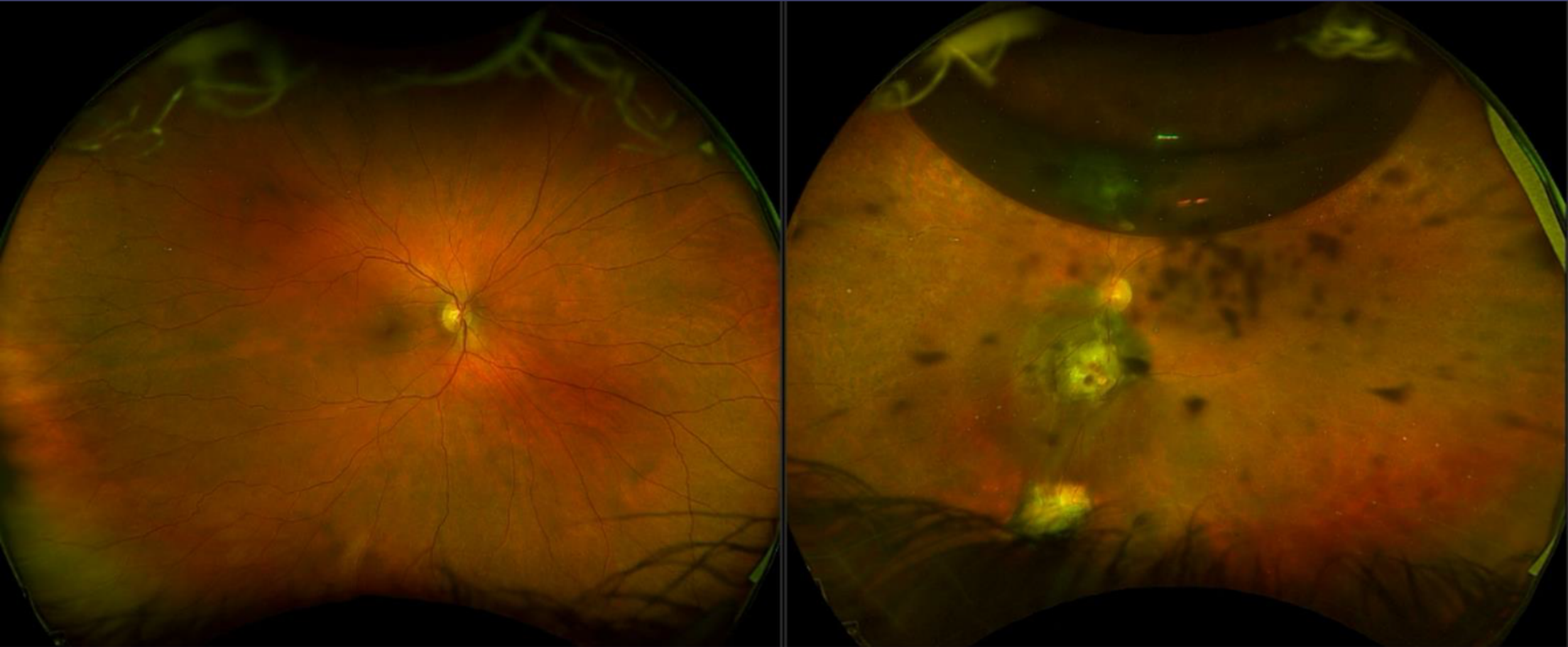


Unusual presentations – no view to posterior segment



Call to optometrist for last fundus photos 2022





Vitrectomy, subretinal haemorrhage drain, transretinal choroidal biopsy
Tantalum marker insertion for presumed choroidal melanoma

Treatment - Do they all die from metastasis ?

- For years the COMS study suggested that there was no difference in mortality depending on treatment, and we could observe small melanoma
- Not true

Article

Small High-Risk Uveal Melanomas Have a Lower Mortality Rate

Rumana N. Hussain ^{1,*}, Sarah E. Coupland ², Helen Kalirai ², Azzam F. G. Taktak ^{2,3}, Antonio Eleuteri ^{2,3}, Bertil E. Damato ⁴, Carl Groenewald ¹ and Heinrich Heimann ¹

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³ Department of Medical Physics and Clinical Engineering, Royal Liverpool University Hospital, Liverpool L69 8ZX, UK

⁴ Ocular Oncology Service, Moorfields Eye Hospital, London EC1V 2PD, UK; bertil.damato@mcln.ox.ac.uk

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Simple Summary: The current paradigm concerning metastatic spread in uveal melanoma is that the critical point for dissemination occurs prior to presentation and that treatment of the primary tumor does not change outcome. However, we show that patients with small uveal melanomas with genetic characteristics typical for high risk for metastatic disease have a lower mortality rate from metastatic disease, if treated earlier. Our data demonstrate that such small melanomas are potentially lethal (like larger tumors), but that there is a window of opportunity to prevent life-threatening metastatic spread if actively treated, rather than being monitored, as is often done currently.

Abstract: Our aim was to determine whether size impacts on the difference in metastatic mortality of genetically high-risk (monosomy 3) uveal melanomas (UM). We undertook a retrospective analysis of data from a patient cohort with genetically characterized UM. All patients treated for UM in the Liverpool Ocular Oncology Centre between 2007 and 2014, who had a prognostic genetic tumor analysis. Patients were subdivided into those with small (≤ 2.5 mm thickness) and large (>2.5 mm thickness) tumors. Survival analyses were performed using Gray rank statistics to calculate absolute probabilities of dying as a result of metastatic UM. The 5-year absolute risk of metastatic mortality of those with small monosomy 3 UM was significantly lower (23%) compared to the larger tumor group (50%) ($p = 0.003$). Small disomy 3 UM also had a lower absolute risk of metastatic mortality (0.8%) than large disomy 3 UM (6.4%) ($p = 0.007$). Hazard rates showed similar differences even with lead time bias correction estimates. We therefore conclude that earlier treatment of all small UM, particularly monosomy 3 UM, reduces the risk of metastatic disease and death. Our results would support molecular studies of even small UM, rather than 'watch-and-wait strategies'.

Keywords: uveal melanoma; monosomy 3; metastatic risk

 check for updates

Citation: Hussain, R.N.; Coupland, S.E.; Kalirai, H.; Taktak, A.F.G.; Eleuteri, A.; Damato, B.E.; Groenewald, C.; Heimann, H. Small High-Risk Uveal Melanomas Have a Lower Mortality Rate. *Cancers* **2021**, *13*, 2267. <https://doi.org/10.3390/cancers13092267>

Academic Editor: Elin S. Gray

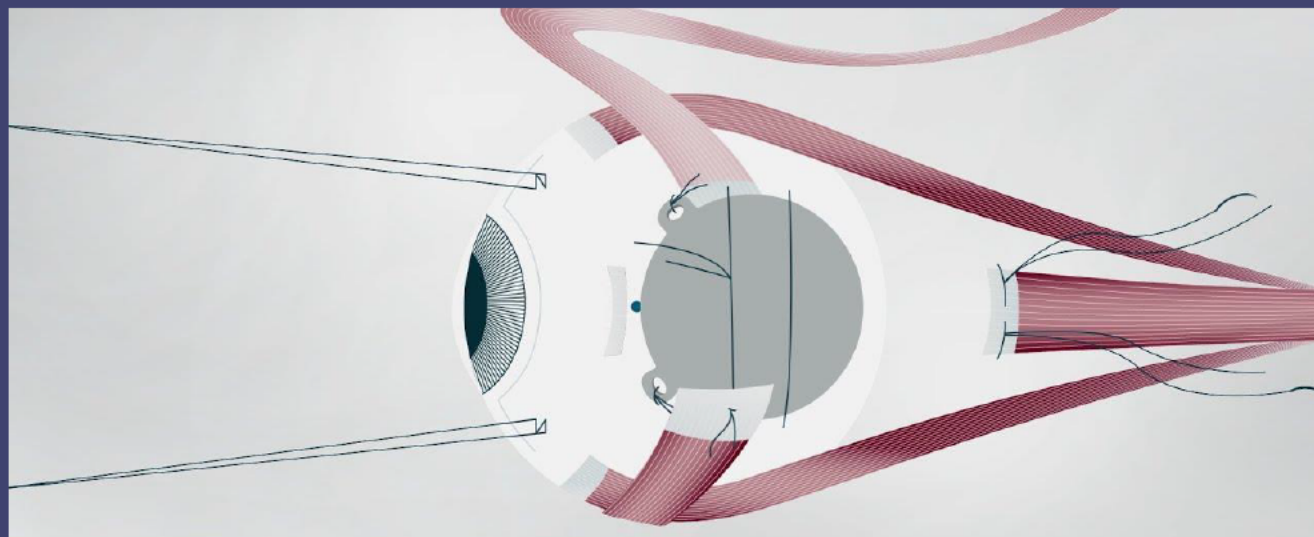
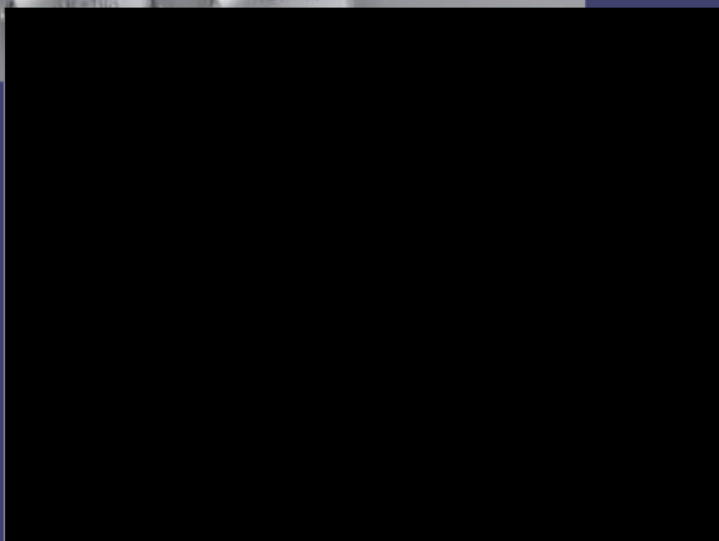
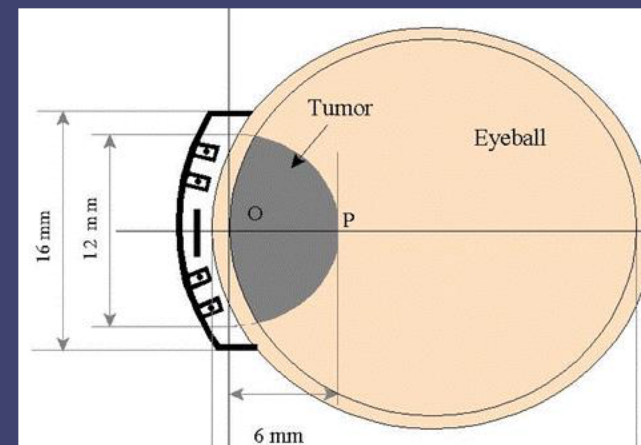
Received: 13 April 2021
Accepted: 5 May 2021
Published: 8 May 2021

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

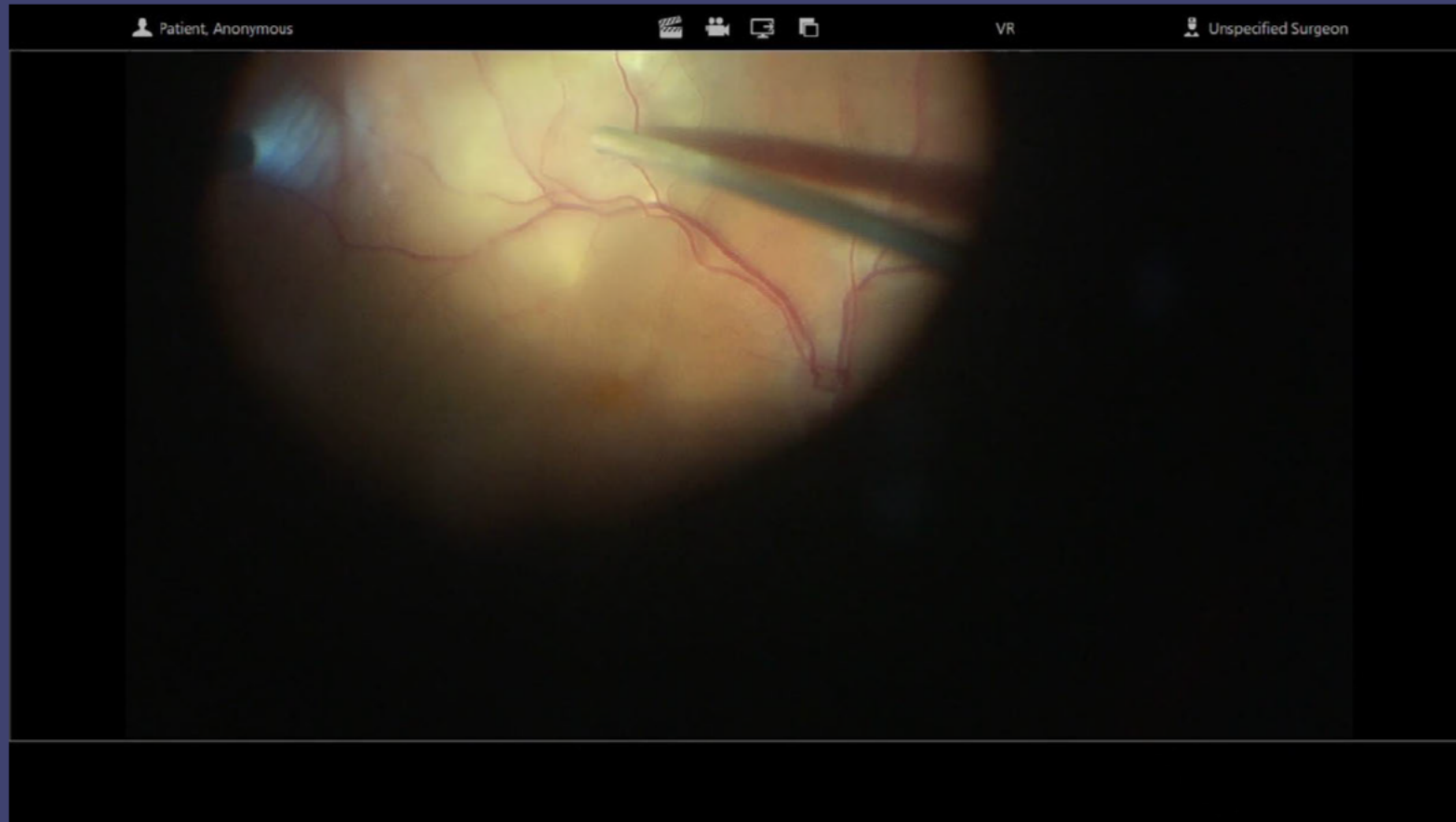
Plaque brachytherapy – Ru-106 coated



- CCA and CCB
15mm and 20mm
plaque sizes
respectively



Prognostication of tumor – transretinal biopsy



Prognostication of tissue – DNA / RNA analysis

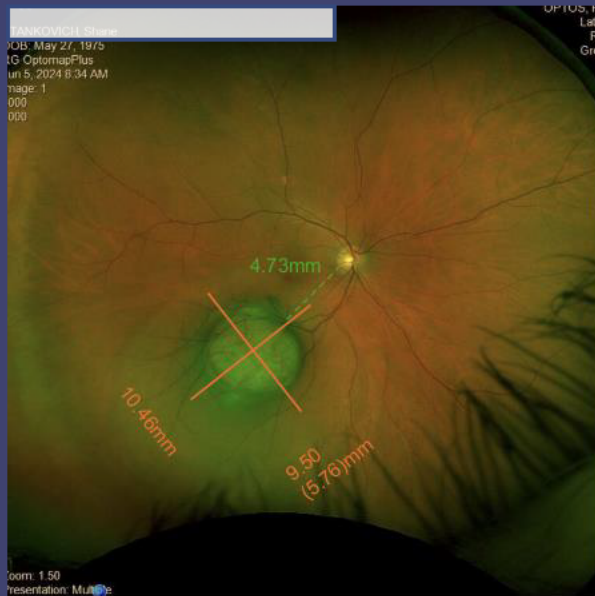
Prognostic Feature	Good	Poor
Tumour size	Small	Large
Location	Posterior pole	Ciliary body/extraocular
Cell type	Spindle	Epithelioid
Chromosome 3	Disomy 3	Monosomy 3
Gene class	GEP 1A	GEP 2
Age	Younger	Older
Treatment	Early, globe-sparing	Delayed or recurrent

Future direction for radiation treatment



- Un-plaqueable patients
 - Too close to nerve
 - Too large
 - Too posterior
 - Not able to survive 2x GA's

Stereotactic radiotherapy



Dose Calculation

Algorithm: Monte Carlo
 Resolution: High
 Uncertainty %: 1.0

Size to fit:
 CT Skin VOIs

Calculate Final Dose

Prescription

Prescription

Reference Point

Use max dose point
 Dose (Gy): 27.97
 Point (mm IECp): (-37.07, -488.00, 64.97)

 Set to Cross-hair Point

Save Plan

Final MC High

DVH Properties Selected DVH: GTV

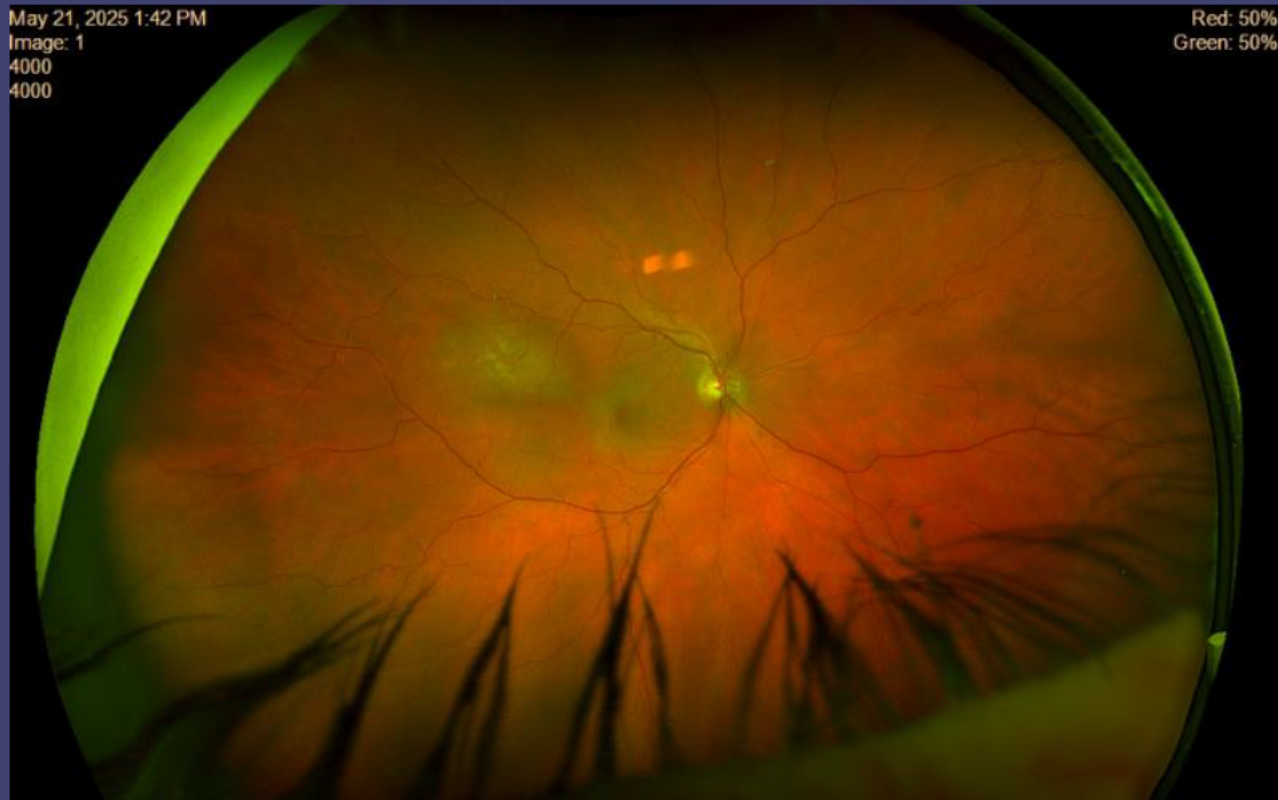
Nodes: 66 Beams: 96
 Total MU: 8544.8 Min MU/Beam: 24.8 Max MU/Beam: 101.7
 Max Dose (Gy): 27.97 Estimated Treatment Time Per Fraction (minutes): 37

Dose Statistics Table Ds Vt Values Plan Information Dose Points

Name	Min (Gy)	Mean (Gy)	Max (Gy)	CI	nCI	HI	Coverage (%)
GTV	21.23	25.25	27.97	2.09	2.09	1.40	100.00
PTV	18.78	23.52	27.97	1.02	1.09	1.40	98.00
OpticNv_R	0.74	2.30	6.62	n/a	n/a	n/a	n/a
OpticNv_L	0.06	0.11	0.46	n/a	n/a	n/a	n/a
Eye_R	0.33	4.54	27.97	n/a	n/a	n/a	n/a
Eye_L	0.02	0.06	0.10	n/a	n/a	n/a	n/a
Lens_R	0.38	0.47	0.61	n/a	n/a	n/a	n/a
Lens_L	0.03	0.05	0.07	n/a	n/a	n/a	n/a
Body	0.00	0.13	27.97	n/a	n/a	n/a	n/a
[PTV] Shell 1	18.78	19.43	21.26	n/a	n/a	n/a	n/a
[PTV] Shell 2	3.21	8.09	10.49	n/a	n/a	n/a	n/a
[PTV] Shell 3	0.64	2.92	4.93	n/a	n/a	n/a	n/a
[PTV] Shell 4	0.34	1.63	3.06	n/a	n/a	n/a	n/a

Other Treatments

- Photodynamic therapy
 - 'Sight sparing' but less efficacious ~ 60%



Systemic treatment – if metastasised

- 98% spread to liver
- Respond poorly to conventional checkpoint inhibitors
 - Unlike cutaneous melanoma (as heterogenous cell types)
 - Tebentafusp (KIMMTRAK) Bispecific T-cell engager (targets gp100 and CD3)

Parameter	Tebentafusp (IMCgp100-202)	Control Arm
Median Overall Survival (OS)	≈21.6 months	≈16.9 months
Hazard Ratio for Death	≈0.51 (initial); 0.68 (3-year follow-up)	—
3-year OS Rate	≈27%	≈18%
Objective Response Rate (ORR)	≈11%	≈5%
Median Progression-Free Survival (PFS)	≈3.4 months	≈2.9 months

