NEW YORK
PROTON CENTER

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Eyeing Precision: Gantry-Based Proton Treatment Planning for Uveal Melanoma

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Disclosures

- None

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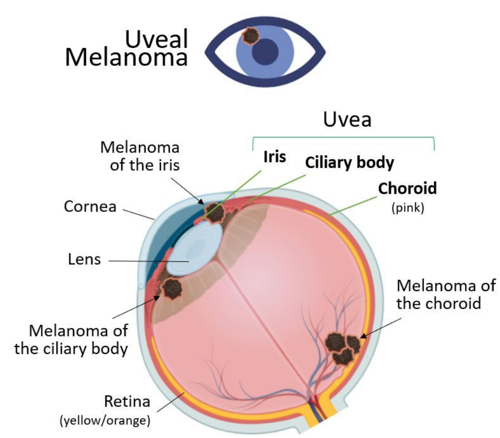
Introduction and Background

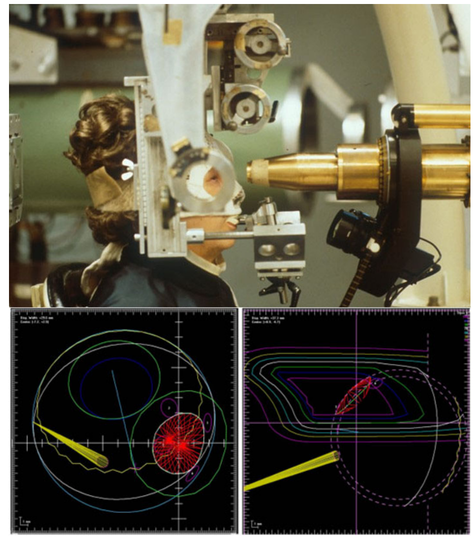
What is Uveal Melanoma (UM)?

- UM is the most common primary intraocular malignancy in adults arising from melanocytes of the uvea
- Incidence: 5-7 cases per million/year
- Local treatment is highly effective; however, this disease still poses a significant metastatic risk
- Treatment options include brachytherapy, proton therapy, and enucleation



The Traditional Approach

- Proton ocular therapy is traditionally delivered using a horizontal beamline
  - Small field sizes
  - Custom collimation
- Patient positioned in a treatment chair with a headframe or thermoplastic mask
- Dedicated TPS
  - Eyeplan or equivalent
- Sharp dose fall-off between radiation field and adjacent tissues



Images courtesy of Dr. Evangelos S. Gragoudas, Ocular Melanoma Center, Mass Eye and Ear.

The Access Gap / Our Solution

- ~3 major proton ocular centers in the United States in operation
- Many ocular patients do not have access to proton treatment, presenting an unmet need
- Pencil beam scanning (PBS) gantries are standard at virtually every modern proton center
- Gantry-based PBS can be a practical alternative to treat UM, but has unique considerations
- Gantry-based ocular protocol can open the doors to more patients, in more places.

Why Precision Matters for Ocular Treatments

- While “Eyeing Precision” is a play on words, it’s also meant literally
- Ocular tumors are located near critical structures (optic nerve, lens, cornea, brain) and require special care and precision
- Sub-millimeter accuracy is required to avoid damaging healthy tissue
- Even slight eye movements can dramatically shift dose off-target
- High-precision radiation techniques (e.g., IMPT, SBRT) require a stable gaze for the duration of treatment
- Gaze fixation is necessary to ensure reproducible eye positioning for both treatment planning and delivery

Simulation and Immobilization

CT Simulation

- Custom thermoplastic mask with openings created for the eyes
  - Allows a line of sight to the gaze BB
  - Enables active monitoring of the gaze position
- Custom gaze fixation device
- 1mm CT slice thickness
  - To ensure accurate delineation of small CTV and intricate OARs
- Verify gaze direction using mini-scans
- If the patient is struggling to focus on the BB with the treated eye, it may help to tape the contralateral eye shut

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Gaze Fixation

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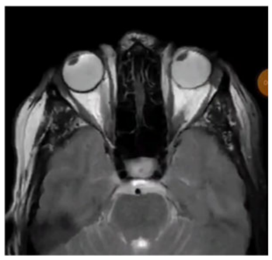
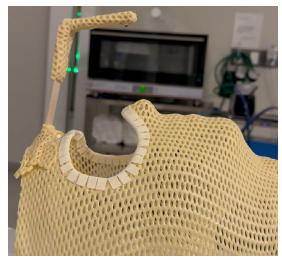
Gaze Fixation Device

- Construction:
  - Strips of thermoplastic mask & tongue depressor stick
  - BB to mark specified gaze position (with goal of positioning the tumor superficially to be better accessed without passing OARs)
- Purpose:
  - To create a focal point that allows the patient to maintain a reproducible gaze position





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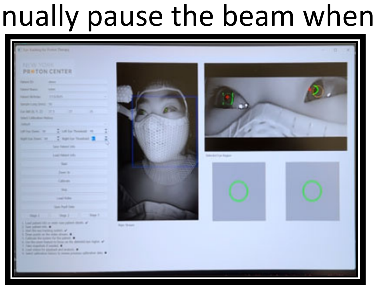
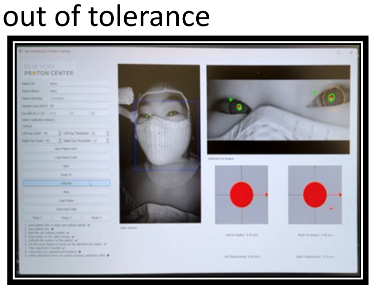
Eye Monitoring During Simulation & Treatment

- In-house camera-based eye tracking system
- Used for SBRT ocular treatments, which have longer delivery times
- Role in setup reproducibility and intrafraction motion management
- System is calibrated using gaze position captured at simulation
  - Color coded: in tolerance & out of tolerance
  - Therapist manually pause the beam when out of tolerance





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Treatment Planning

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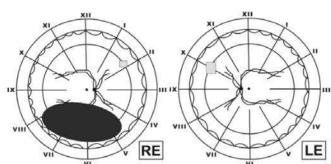
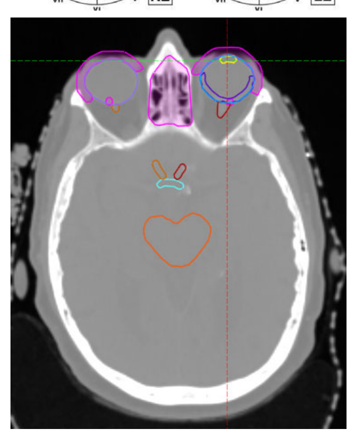
Contouring – Target & OARs

- Target delineation relies on a fundus map and position relative to tantalum markers
- OARs (contoured in hi-res)
  - Cornea – anterior aspect of the eye relative to the lens
  - Conjunctiva – 4mm outer ring of eye; keep anterior to globe equator
  - Retina – 2mm inner ring of eye; keep posterior to globe equator
  - Optic nerves - track continuously from the eye to chiasm





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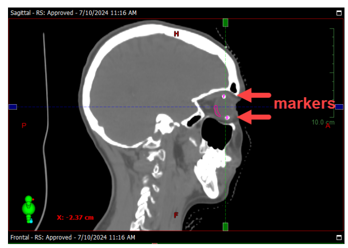
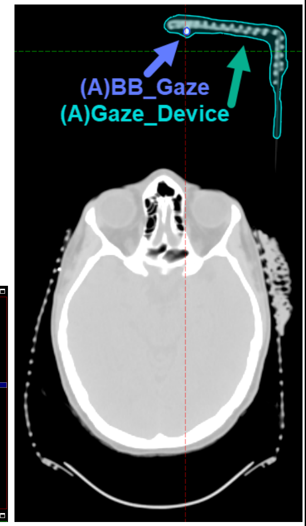
Contouring – Overrides & (A) Structures to Aid Setup

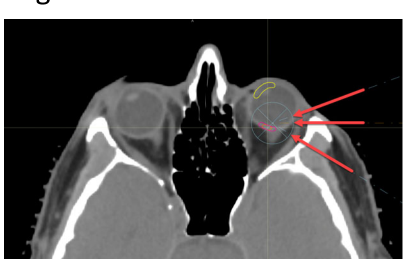
- Overrides
  - BBs & wires (outline hairline/eyebrow) – air
  - Saturated eye markers (hi-res: 2.5mm) – tantalum
  - Artifacts (from hi-density materials) – muscle/adipose
- Setup Contours
  - (A)BB_Gaze & (A)Gaze_Device – verify position
  - (A)Marker_1 & 2 – clips to help localize orientation of eye
  - (A)OBI_10% - represents beam paths
  - (A)CTV_5000
  - (A)Patient

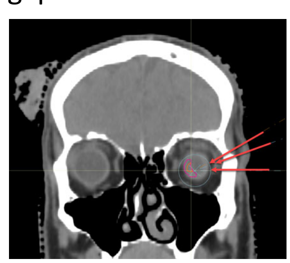




Plan Setup

- Beam Arrangement
  - Standardized 3-field non-coplanar arrangement
    - Anterior oblique (often most parallel to the target shape; avoid lateral canthus of the eye)
    - Lateral superior oblique (couch kick <30°; improves air gap by 5-10cm)
    - Posterior superior oblique (couch kick <30°; improves air gap by 5-10cm)
  - Energy layer 0.6 (1.5-2MeV); Spot Spacing 0.3 (2-2.5mm)
  - Lateral margin 0.6 (0.1 for beam with most parallel incidence to the target)
  - 2-3cm range shifter RS – but minimize the air gap!

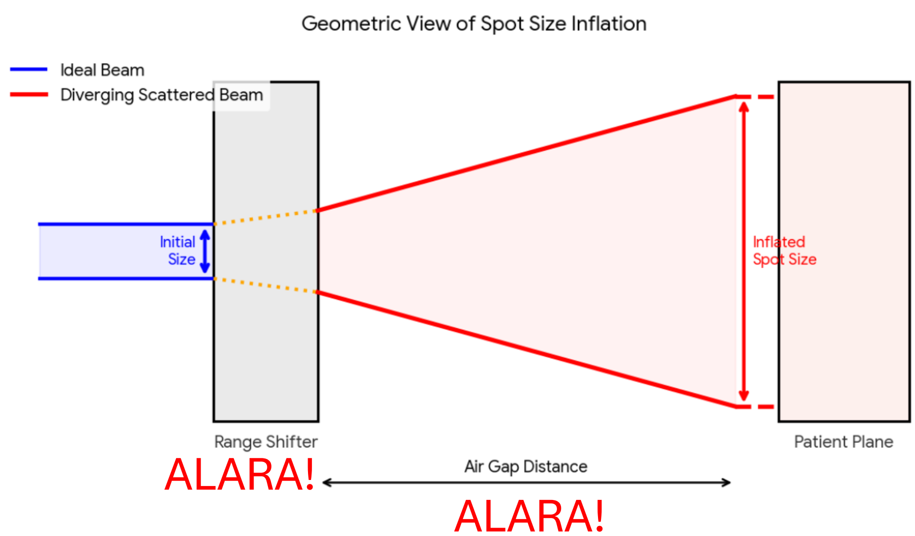




The Range Shifter Dilemma

- Our cyclotron generates a proton with a minimum energy of 70MeV = 4cm of water equivalent thickness (WET)
  - Most of the tumors we are targeting are more superficial than 4cm
- Range shifters are the solution! But…
  - RS broadens the beam by Coulomb scattering, which continues to diverge until it reaches the patient
- So best practice is to…
  - Use the thinnest possible range shifter (2 or 3cm)
  - Bring the snout as close as possible without risk of collision

Range Shifter – Minimize the air gap & RS thickness!



Plan Study

- Evaluated the dosimetric impacts of different parameters
  - Energy layer spacing – minimal impact
  - Spot spacing – 0.6 improves coverage and OAR sparing
  - Min MU – no impact
  - Mixed RS – substantially improves gradient, especially with 0.6 spot spacing
  - Anterior beams – improve gradient but reduce conformity & coverage

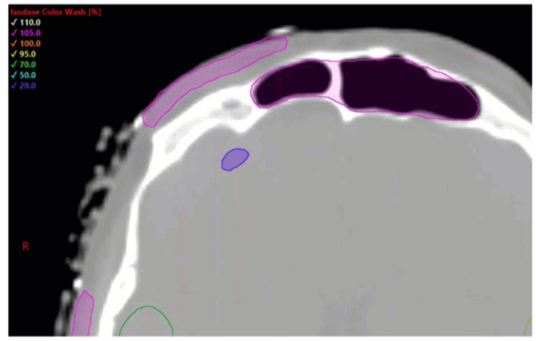
	Clinical	Reference	Energy layer spacing		Spot spacing		Spot+Energy	Min MU	Mixed RS		Beam arrangement		
			0.8	0.6	0.8	0.6	0.6	1.5	Only	& 0.6 spacing	Only	& mixed RS & 0.6	& Push
CTV D95% [cGy]	4938	4921	4902	4917	4964	4986	4975	4930	4979	5052	4974	5085	4998
CTV D95% [%]	99%	98%	98%	98%	99%	100%	100%	99%	100%	101%	99%	102%	100%
CTV D99% [cGy]	4782	4794	4776	4773	4829	4884	4855	4797	4913	4917	4863	4998	4923
CTV V100% [cc]	0.34	0.31	0.31	0.32	0.33	0.34	0.31	0.34	0.34	0.35	0.33	0.36	0.35
CTV V100% [%]	94%	86%	87%	89%	92%	94%	86%	94%	94%	98%	93%	99%	96%
Cornea Dmean [cGy]	1813	1845	1834	1861	1818	1847	1853	1858	1813	1763	1801	1593	1306
Cornea Dmax [cGy]	2491	2466	2460	2496	2454	2483	2497	2478	2496	2432	2462	2298	1951
Eyebrow Dmax [cGy]	2941	2972	2943	2755	2839	2750	2713	2940	2739	2620	2669	2420	2346
V50% [cc]	20.84	24.7	24.1	23.8	25.51	21.23	19.96	24.7	21.02	18.43	22.79	16.26	13.87
V100% [cc]	1.22	0.97	0.97	1.14	1.16	1.16	1.14	0.97	1.27	1.29	1.09	1.31	1.00
Gradient	17.1	25.5	24.8	20.9	22.0	18.3	17.5	25.5	16.6	14.3	20.9	12.4	13.9
Conformity	3.6	3.1	3.1	3.6	3.5	3.4	3.7	2.9	3.8	3.6	3.3	3.7	2.9

Treatment Planning

- 50Gy (RBE) in 5 fractions
- CTV based planning
- SFO
- Robust optimization
  - 3mm setup
  - 3.5% RU
- MC optimization/final dose calculation/1mm dose grid

Treatment Plan Evaluation

- Target CTV Goal: D95% ≥ 100%
- Cornea Dmean< 5 Gy (limit < 10 Gy)
  Cornea Dmax< 15 Gy (limit < 20 Gy)
- Other ipsilateral optic structures
  Dmax< 105%
- Contralateral optic structures
  Dmax< 10Gy
- Robust evaluation – ideally, D95% ≥ 95% for the second worst case



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Clinical Case Reviews

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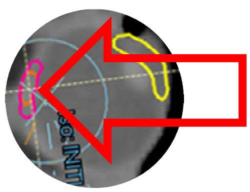
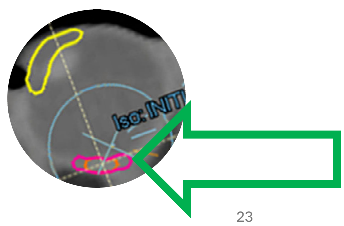
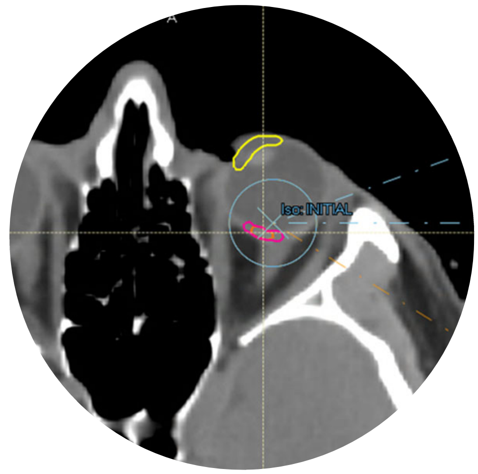
Case #1

- 62 yo M with cT1aN0M0 uveal melanoma of left choroid in juxtapapillary position, not amenable to plaque brachytherapy and declining enucleation
- Gaze direction considerations
  - CTV located posteriorly
  - Allows access to target without passing through the cornea

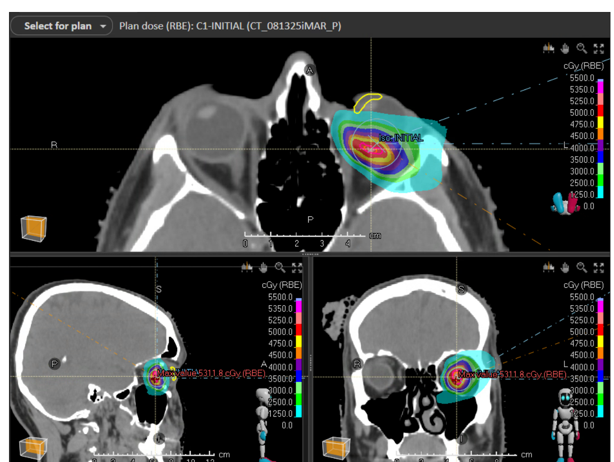






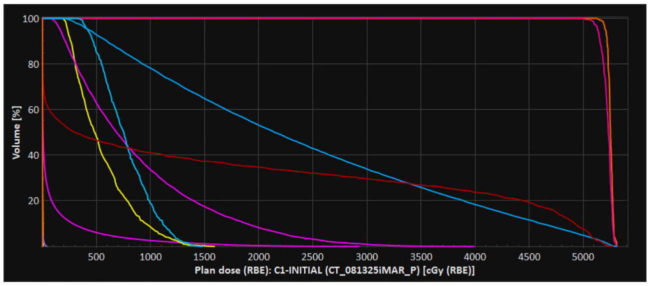
Case #1

- This planning approach effectively minimizes dose to the ipsilateral cornea
- This is the #1 priority for these plans!
- Overdosing the cornea may result in the need to enucleate the eye



Spot placement				Target margins		
Spot pattern	Energy layer spacing	Spot spacing	Angle [deg]	Proximal [Layers]	Distal [Layers]	Lateral
Hexagonal	Automatic with scale 0.6	Automatic with scale 0.3	0.00	1	1	Automatic with scale 0.6

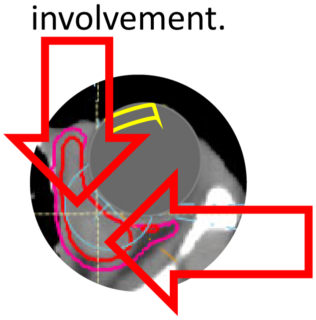
Case #1

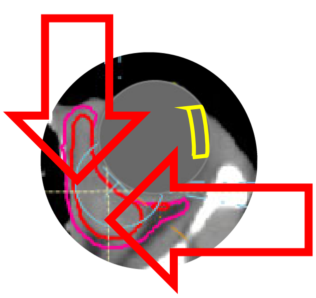


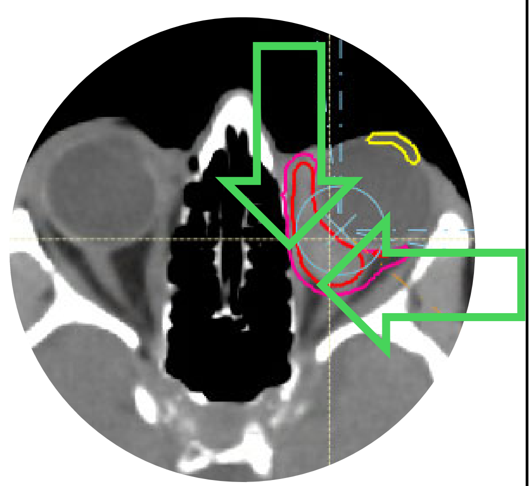
ROI/POI	Clinical goal	Value	Result
(A)CTV_5000	At least 4750.0 cGy (RBE) dose at 99.00 % volume	5080.2 cGy (RBE)	✓
(A)CTV_5000	At least 5000.0 cGy (RBE) dose at 95.00 % volume	5134.1 cGy (RBE)	✓
(A)CTV_5000	At most 20.00 % volume at 5500.0 cGy (RBE) dose	0.00 %	✓
BODY	At most 5750.0 cGy (RBE) dose at 0.00 % volume	5311.8 cGy (RBE)	✓
Brain	At most 3000.0 cGy (RBE) dose at 0.00 % volume	2116.0 cGy (RBE)	✓
BrainStem	At most 2500.0 cGy (RBE) dose at 0.00 % volume	1.1 cGy (RBE)	✓
Chiasm	At most 1000.0 cGy (RBE) dose at 0.00 % volume	0.3 cGy (RBE)	✓
Conjunctiva_L	At most 5500.0 cGy (RBE) dose at 0.00 % volume	3993.4 cGy (RBE)	✓
Cornea_L	At most 2000.0 cGy (RBE) average dose	549.9 cGy (RBE)	✓
Cornea_L	At most 3000.0 cGy (RBE) dose at 0.00 % volume	1593.8 cGy (RBE)	✓
Cornea_R	At most 1000.0 cGy (RBE) dose at 0.00 % volume	8.5 cGy (RBE)	✓
Eye_L	At most 5500.0 cGy (RBE) dose at 0.00 % volume	5311.8 cGy (RBE)	✓
Eye_R	At most 1000.0 cGy (RBE) dose at 0.00 % volume	46.2 cGy (RBE)	✓
Eyebrow_L	At most 2000.0 cGy (RBE) dose at 0.00 % volume	1573.8 cGy (RBE)	✓
LacrimalGland_L	At most 5500.0 cGy (RBE) dose at 0.00 % volume	3976.9 cGy (RBE)	✓
LacrimalGland_R	At most 1000.0 cGy (RBE) dose at 0.00 % volume	0.0 cGy (RBE)	✓
OpticNerve_L	At most 5500.0 cGy (RBE) dose at 0.00 % volume	5278.7 cGy (RBE)	✓
OpticNerve_R	At most 1000.0 cGy (RBE) dose at 0.00 % volume	0.2 cGy (RBE)	✓
Retina_L	At most 5500.0 cGy (RBE) dose at 0.00 % volume	5311.8 cGy (RBE)	✓
SinonasalCavity	At most 3000.0 cGy (RBE) dose at 0.00 % volume	2934.0 cGy (RBE)	✓

Case #2

- 82 yo with melanocytic neoplasm of left orbit, declining orbital exenteration, electing for definitive radiotherapy.
- Challenging anatomy due to larger size with proximity to the cornea and medial involvement.

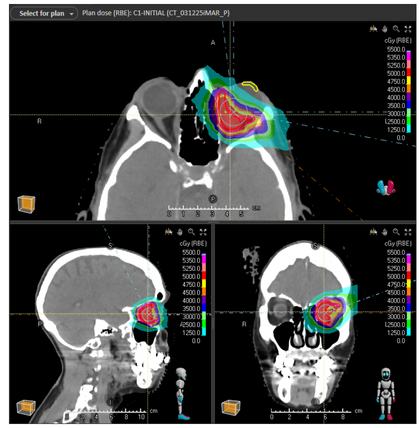






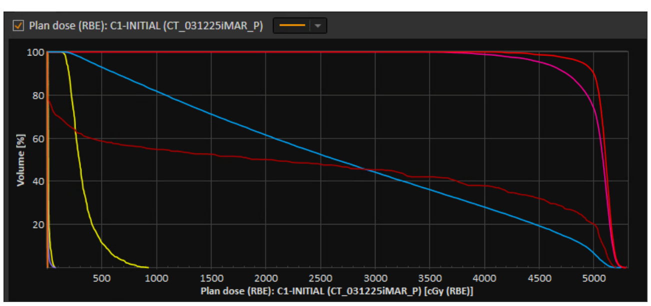
Case #2

- A 5-field MFO approach was necessary to maximize coverage while sparing cornea
- Max beam contribution was capped at 40%
- Spots were blocked from a cornea+1cm
- Given the superficial target, range shifters (RS) were necessary; however, the RS was removed for the LPO to reduce penumbra towards the cornea



No.	Name	Range shifter selection	Spot placement				Target margins			Radiol. depth [cm]		OAR range margin	
			Spot pattern	Energy layer spacing	Spot spacing	Angle [deg]	Proximal [Layers]	Distal [Layers]	Lateral	Min	Max	ROI	Margin [cm]
1	G130-C0 LPO	Manual	Hexagonal	Automatic with scale 0.6	Automatic with scale 0.3	0.00	1	1	Automatic with scale 0.6	0.00		zCorneaBlock	0.00
2	G100-C340 LPSO	Manual	Hexagonal	Automatic with scale 0.6	Automatic with scale 0.3	0.00	1	1	Automatic with scale 0.3	0.00		zCorneaBlock	0.00
3	G90-C340 LSO	Manual	Hexagonal	Automatic with scale 0.6	Automatic with scale 0.3	0.00	1	1	Automatic with scale 0.3	0.00		zCorneaBlock	0.00
4	G0-C0 ANT	Manual	Hexagonal	Automatic with scale 0.6	Automatic with scale 0.3	0.00	1	1	Automatic with scale 0.1	0.00		(A)Gaze_Device, zCorneaBlock	0.00
5	G353-C0 RAO	Manual	Hexagonal	Automatic with scale 0.6	Automatic with scale 0.3	0.00	1	1	Automatic with scale 0.1	0.00		(A)Gaze_Device, zCorneaBlock	0.00

Case #2



ROI/POI	Clinical goal	Value	Result
(Z)CTV_5000_eval3mm	At least 4750.0 cGy (RBE) dose at 95.00 % volume	4601.5 cGy (RBE)	!
(Z)CTV_5000_eval3mm	At least 4750.0 cGy (RBE) dose at 99.00 % volume	4189.5 cGy (RBE)	!
(Z)CTV_5000_eval3mm	At least 5000.0 cGy (RBE) dose at 95.00 % volume	4601.5 cGy (RBE)	!
BODY	At most 5750.0 cGy (RBE) dose at 0.00 % volume	5293.9 cGy (RBE)	✓
Brain	At most 3000.0 cGy (RBE) dose at 5.00 cm³ volume	1406.3 cGy (RBE)	✓
Brain	At most 4000.0 cGy (RBE) dose at 0.00 % volume	3993.5 cGy (RBE)	✓
Brain	At most 4000.0 cGy (RBE) dose at 0.03 cm³ volume	3630.7 cGy (RBE)	✓
Chiasm	At most 1000.0 cGy (RBE) dose at 0.00 % volume	0.8 cGy (RBE)	✓
Conjunctiva_L	At most 5500.0 cGy (RBE) dose at 0.00 % volume	5253.3 cGy (RBE)	✓
Conjunctiva_R	At most 1000.0 cGy (RBE) dose at 0.00 % volume	366.5 cGy (RBE)	✓
Cornea_L	At most 2000.0 cGy (RBE) average dose	329.6 cGy (RBE)	✓
Cornea_L	At most 3000.0 cGy (RBE) dose at 0.00 % volume	929.0 cGy (RBE)	✓
Cornea_R	At most 1000.0 cGy (RBE) dose at 0.00 % volume	72.0 cGy (RBE)	✓
Eye_L	At most 5500.0 cGy (RBE) dose at 0.00 % volume	5246.8 cGy (RBE)	✓
Eye_R	At most 1000.0 cGy (RBE) dose at 0.00 % volume	80.2 cGy (RBE)	✓
Eyebrow_L	At most 2000.0 cGy (RBE) dose at 0.00 % volume	1145.4 cGy (RBE)	✓
LacrimalGland_L	At most 5500.0 cGy (RBE) dose at 0.00 % volume	5048.8 cGy (RBE)	✓
OpticNerve_L	At most 5500.0 cGy (RBE) dose at 0.00 % volume	5203.2 cGy (RBE)	✓
OpticNerve_R	At most 1000.0 cGy (RBE) dose at 0.00 % volume	8.3 cGy (RBE)	✓
Retina_L	At most 5500.0 cGy (RBE) dose at 0.00 % volume	5246.8 cGy (RBE)	✓
Retina_R	At most 1000.0 cGy (RBE) dose at 0.00 % volume	28.6 cGy (RBE)	✓
SinonasalCavity	At most 5000.0 cGy (RBE) dose at 0.00 % volume	4939.1 cGy (RBE)	✓
SinonasalCavity	At most 5000.0 cGy (RBE) dose at 0.03 cm³ volume	4730.1 cGy (RBE)	✓
Skin	At most 4000.0 cGy (RBE) dose at 0.00 % volume	4231.9 cGy (RBE)	!
Skin	At most 4000.0 cGy (RBE) dose at 0.03 cm³ volume	3943.9 cGy (RBE)	✓

Key Takeaways and Summary

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Key Takeaways

- Answer the below 3 learner outcomes from the abstract
- 1. Understand the planning challenges for uveal melanoma with a PBS proton therapy system
- 2. Evaluate ocular SBRT plan quality using relevant clinical goals and robustness criteria
- 3. Gain practical knowledge to implement an ocular SBRT planning protocol

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Summary

- Gantry-based PBS can achieve high-quality ocular plans
- Precise gaze fixation and gaze tracking are essential for treatment
- An ocular PBS planning protocol can be implemented at most proton centers

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Future Directions

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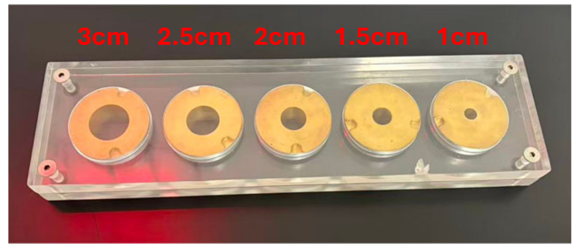
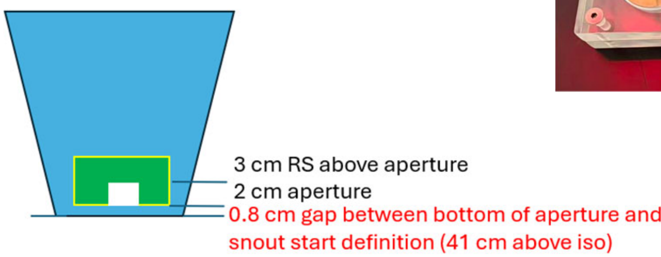
Ocular Apertures

- Improve penumbra/dosimetry
- Universal apertures of sizes ranging from 1 – 3cm
- Utilizes the existing 5cm RS slot
  - 3cm polycarbonate range shifter
  - 2cm thick brass aperture (nearest patient)





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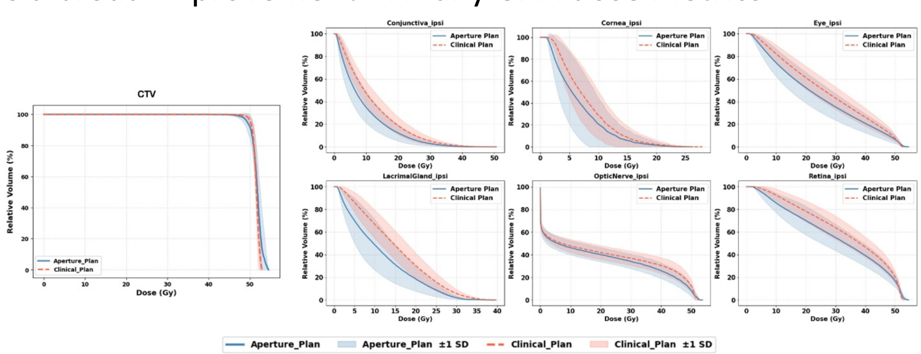
Ocular Apertures

- The 2cm brass aperture can safely block protons with energies <135 MeV, which corresponds to a water equivalent thickness (WET) of ~13cm
- Shows a broad improvement in many OAR dose metrics



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Thank you!

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Acknowledgements

Therapy

Jewel Graham, R.T.(T)

Kevin Ciraolo, R.T.(T)

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