Silicone Oil during I-125 Plaque Brachytherapy in the Treatment of Choroidal Melanoma

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Introduction

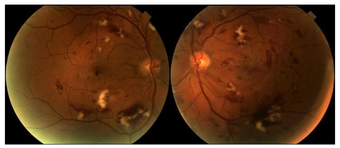
Purpose

- Plaque brachytherapy is an effective treatment for choroidal melanomas but damages healthy ocular structures.
- In vitro studies have shown the radiation attenuating effects of silicone oil on ocular structures; subsequent case series have showed potentially beneficial outcomes on post-operative macular thickness, architecture, and visual acuity.
- **Does this radiation sparing procedure's benefits outweigh its surgical risks in the community setting?**

(A) Iodine-125 radioactive plaque used in the treatment of uveal melanomas has replaced enucleation as primary therapy. (B) Radioactive plaque, placed surgically on sclera.

Background

- Previously, the treatment for choroidal melanoma was enucleation, to prevent metastasis.
- Since the Collaborative Ocular Melanoma Study (COMS), we know that plaque brachytherapy is as effective as enucleation, saves the eye, and can preserve vision.



Gupta, Abha; Dhawahir-Scala, Felipe; Smith, Amy; Young, Lorna; Charles, Steve (1 January 2007). "Radiation Retinopathy: Case report and review". *BMC Ophthalmology*. **7** (1): 6.

- However, radiation retinopathy (RR) occurs due to radiation damage to retinal endothelial cells and manifests similarly to other vascular retinal pathology, with microaneurysms, neovascularization, cotton wool spots, and macular edema.
- This complication has a delayed onset (months to years) and is slowly progressive.
- Demographic risk factors for developing RR include diabetes, hypertension, and male gender.
- Radiation dose to the macula, tumor size, and tumor distance from the fovea are also closely correlated to development of RR.

Previous Studies

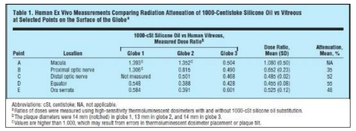


Table 1. Human Ex Vivo Measurements Comparing Radiation Attenuation of 1000-Centistoke Silicone Oil vs Vitreous at Selected Points on the Surface of the Globe*

Point	Location	1000-cSt Silicone Oil vs Human Vitreous, Measured Dose Ratio†			
		Globe 1	Globe 2	Globe 3	Dose Ratio, Mean (SD)	Attenuation, Mean, %
A	Macula	1.393‡	1.252‡	0.504	1.060 (0.50)	NA
B	Proximal optic nerve	1.395‡	0.815	0.400	0.643 (0.73)	36
C	Distal optic nerve	Not measured	0.601	0.468	0.480 (0.02)	52
D	Equator	0.548	0.398	0.428	0.490 (0.08)	50
E	Ora serrata	0.564	0.391	0.601	0.525 (0.12)	48

Abbreviations: cSt, centistoke; NA, not applicable.
*Ratios of doses were measured using high-sensitivity thermoluminescent dosimeters with and without 1000-cSt silicone oil substitution.
†The plaque diameters were 14 mm (notched) in globe 1, 13 mm in globe 2, and 14 mm in globe 3.
‡Values are higher than 1.000, which may result from errors in thermoluminescent dosimeter placement or plaque tilt.

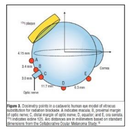


Figure 3. Dosimetry points in a cadaveric human eye model of silicone substitution for radiation brachyte. A indicates macula, B, proximal margin of optic nerve; C, distal margin of optic nerve; D, equator; and E, ora serrata. Reprinted from the Collaborative Ocular Melanoma Study.[1]

Oliver SC, Leu MY, DeMarco JJ, Chow PE, Lee SP, McCannel TA. Attenuation of Iodine 125 Radiation With Vitreous Substitutes in the Treatment of Uveal Melanoma. Arch Ophthalmol 2010;128(7): 888-893.

- Previous cadaveric studies using silicone oil insertion after pars plana vitrectomy (PPV) demonstrated radiation dose attenuations of 35-55% at locations on the circumference of the globe, depending on arc length from the radioactive plaque edge.
- Two subsequent case-control studies at large academic institutions have shown potentially beneficial outcomes regarding central macular thickness, macular abnormalities, and visual outcomes (when paired with cataract extraction).

Methods

- Five patients who received a diagnosis of choroidal melanoma from 2011 to 2016 received I-125 plaque brachytherapy implanted by the same surgeon (BB), with prescribed doses of 85 Gy to tumor apices.
- Plaque placement was confirmed using indirect ophthalmoscopy and transillumination of the tumor intraoperatively.
- Fine needle aspiration biopsies of all tumors were collected via transcleral or transvitreal approach, followed by PPV with either 1000 or 5000 cSt silicone oil injection into the posterior segment.
- After seven days of therapy, the plaque and silicone oil were removed in a single procedure.
- A retrospective chart review was performed; data regarding relevant patient demographics, tumor location and size, and planned radiation doses to the macula are detailed in Table 1.
- Outcome measures including visual acuity, development of RR, and surgical complications are listed in Table 2.

Results

Table 1: Relevant Patient Demographics, Tumor Position, Macular Doses and Follow Up Time

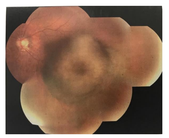
Patient	Age	PMH	Tumor Size (mm)	Tumor Location	Macular Dose (Gy)	Total Follow Up (months)
1	60	DM, HTN	H 11.02 L 9.7 W 9.41	Encroaching on macula inferotemporally	141.5	56
2	61	DM, HTN	H 6.2 L 12.0 W 12.0	Inferotemporal	21.25	45
3	84	HTN	H 3.18 L 12.92 W 8.87	Nasal	12.55	26
4	68	DM	H 7.3 L 13.6 W 14.5	Temporal	43.17	12
5	39		H 5.6 L 11.44 W 10.62	At superior macula	118.5	51

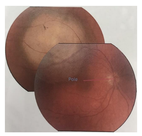
*Abbreviations: PMH- past medical history. DM: type II diabetes mellitus. HTN- hypertension.

Table 2: Outcome Measures

Patient	VA pre-op, 1 year, 2 year, 3 year	RR, Time to Development	Other Toxicity or Complication	Surgical Complications
1	20/60 +2, HM, LP, HM	Yes, 34 months, with subsequent NVG	Optic atrophy, choroidal atrophy	Vitreous hemorrhage intra-op. Post-op hyphema
2	20/20, 20/20 -1, 20/40-2, 20/30	No	None	Rhegmatogenous RD (treated with full recovery of vision)
3	20/40 +1, 20/30 -2, 20/30 -1, NA	No	None	
4	20/50 -1, 20/30 -2, NA, NA	No	None	
5	20/125, 20/60 -1, CF@6ft, LP	Yes, 15 months, with subsequent NVG	Exudative RD, eventually enucleated	

*Abbreviations: HM- hand motion. CF- counts fingers. LP- light perception. NVG- neovascular glaucoma. RD- retinal detachment.





Fundus photos showing the macula-encroaching tumors of both patients who went on to develop RR; these two patients had the largest radiation doses to the posterior pole given the location of the growths.

- No patient developed melanoma recurrence.
- Patient demographics were skewed towards a higher risk for developing RR (DM, HTN, male gender).
- Additionally, 4/5 patients had tumors >4 mm thick and 2/5 had radiation doses of >90 Gy to the macula.
- The two patients who developed RR had the greatest doses of radiation to the macula with tumors located in the posterior pole encroaching on the macula.

Conclusion

- Attenuation of RR seems to be augmented by utilization of silicone oil in certain situations.
- However, silicone oil can only attenuate radiation dose when it interposes between source and tissue.
- Tumors located more posteriorly may not benefit from this additional surgical maneuver especially when considering postoperative complications and operating time.
- Rather, we propose that it may beneficial to use location and size of tumor, along with anticipated macular radiation dosage to determine which individuals might benefit from silicone oil.

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