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Tumour control, eye retention and visual acuity after radiotherapy for choroidal melanoma

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ABSTRACT

Objective Radiotherapy modalities such as iodine-125 (I^{125}) and ruthenium-106 (Ru^{106}) brachytherapy and proton beam radiotherapy (PBR) are well established for the treatment of choroidal melanoma. This study aimed to evaluate the rates of local tumour control, globe retention and visual acuity (VA) outcomes in patients with choroidal melanoma treated with I^{125} or Ru^{106} brachytherapy or PBR.

Methods and analysis A review was conducted of all cases of choroidal melanoma treated with Ru^{106} or I^{125} brachytherapy or PBR over a 10-year period. Patient demographics, comorbidities, tumour characteristics, treatment parameters and VA outcomes were analysed. A predictive nomogram was developed to estimate final VA based on baseline clinical, tumour and radiation parameters.

Results A total of 310 eyes from 310 patients were included, comprising 175 patients (56.5%) treated with Ru^{106}, 72 (23.2%) treated with I^{125} brachytherapy and 63 (20.3%) treated with PBR. Local tumour control was achieved in 95.8% of cases. The recurrence rates were 4.0%, 4.2% and 4.8% for Ru^{106}, I^{125} and PBR, respectively. Retention rates were 96.0% for Ru^{106}, 94.4% for I^{125} and 95.2% for PBR. LogMAR VA of 1.0 or better was maintained in 50.9% of Ru^{106}patients, 27.8% of I^{125}patients and 39.7% of those treated with PBR. Baseline LogMAR VA, tumour volume, radiation dose to the fovea, radiotherapy modality and follow-up duration were significant predictors of final VA and were incorporated into the nomogram.

Conclusions Each radiotherapy modality demonstrated high rates of local tumour control and globe retention. The predictive nomogram may serve as a practical tool to support individualised visual prognostication and patient counselling in the management of choroidal melanoma.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Brachytherapy (Ru-106, I-125) and proton beam radiotherapy are well-established modalities to achieve local tumour control in uveal melanoma as an alternative to enucleation. The Collaborative Ocular Melanoma Study demonstrated no survival benefit with primary enucleation compared with radiotherapy.

WHAT THIS STUDY ADDS

⇒ This study reports single-centre follow-up of clinical outcomes (tumour control, eye retention and visual acuity) with brachytherapy (Ru-106 and I-125) and proton beam radiotherapy. It also introduces a predictive nomogram for post-treatment visual acuity, integrating tumour volume, baseline visual acuity and radiation treatment parameters.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings can guide patient counselling regarding likely treatment outcomes and support shared decision-making for eye-conserving treatment options. The nomogram devised here could aid clinicians in advising patients in regard to likely medium and long-term visual outcomes following radiation treatment for choroidal melanoma.

INTRODUCTION

Uveal melanoma (UM) originates from melanocytes in the uveal tract and accounts for 85% of all ocular melanomas.[1] Tumours occur in the iris (4%), ciliary body (6%) or the choroid (90%).[2] As many as 40% of affected patients develop metastases over a 10-year period.[3]

Subsequent to a diagnosis of UM, treatment options include brachytherapy (with either β-emitting ruthenium-106 or γ-emitting iodine-125 plaques or palladium-103), proton beam radiation, stereotactic radiotherapy, gamma-knife radiosurgery, endoresection, trans-scleral exoresection, transpupillary thermotherapy (TTT) laser, photodynamic therapy (PDT) or enucleation.[4] The decision on the modality used depends on a number of factors, namely tumour dimensions and location, visual potential and patients' preferences. There has been a shift over the last 40 years towards eye-conserving treatment options, but enucleation is still undertaken for larger tumours. Brachytherapy with radioactive plaques (I^{125} or Ru^{106}) and proton beam is classified as radiation treatments for UM.

Radiotherapy treatment options for UM vary across countries and individual radiation oncology units, with proton beam radiotherapy (PBR) available at only a limited number of specialised centres worldwide.[5 6] Therefore, treatment choice may be limited by local availability. The Ocular Oncology Unit at the Royal Victoria Eye and Ear Hospital in Dublin, Ireland, serves as a national referral centre and is uniquely positioned to offer three major radiotherapy modalities to patients: I^{125} or Ru^{106} brachytherapy and PBR through collaboration with the Liverpool Ocular Oncology Centre/Clatterbridge Cancer Centre, United Kingdom. This enables the direct comparison of radiotherapy modalities in patients diagnosed and followed at a single centre. This study was conducted to ascertain rates of local tumour control, globe retention and visual acuity (VA) outcomes following brachytherapy (iodine or ruthenium plaque) and teletherapy (PBR) in UM patients diagnosed in our institution.

MATERIALS AND METHODS

This study was designed as a retrospective analysis of a prospectively maintained clinical database comprising patients diagnosed with UM. All patients diagnosed with UM at the ocular oncology service of the Royal Victoria Eye and Ear Hospital, Dublin, between June 2010 and December 2020 were included. All cases were diagnosed based on clinical findings, supported by ancillary investigations including ultrasonography; anterior segment and colour fundus photography; fundus autofluorescence; and optical coherence tomography (OCT). Posterior pole imaging was performed using the Topcon TRC-50DX (Topcon Corporation, Tokyo, Japan), while widefield images were acquired using the CLARUS 500 (Carl Zeiss Meditec, Dublin, California) or Optos California (Optos PLC, Dunfermline, UK). OCT was performed using the CIRRUS 6000 (Carl Zeiss Meditec).

Clinical data were routinely and prospectively entered at the time of diagnosis, treatment and follow-up into a dedicated departmental UM database, maintained for research and audit purposes. For the purposes of this study, relevant data were retrospectively extracted from the database to assess the association between final VA and baseline tumour characteristics, demographics and radiation treatment parameters. Where necessary, missing information was supplemented through review of electronic and paper medical records. The collected data were subsequently used to develop a nomogram predicting final VA based on initial patient, tumour and treatment characteristics.

This study was conducted in accordance with the Declaration of Helsinki, European Union General Data Protection Regulation rules and the Data Protection Act (Ireland). The study protocol was reviewed and approved by the Research and Audit Committee of the Royal Victoria Eye and Ear Hospital, reference number RVEEH-2024–14. Informed consent was waived as this is a retrospective study.

Treatment and radiation doses

I^{125} and Ru^{106} brachytherapy procedures were undertaken at St Luke's Hospital Dublin. In general, Ru^{106} was used for tumours up to 5.5 mm in thickness and I^{125} was used for tumours 5.5–10 mm thickness. There is no proton-beam facility in Ireland, therefore patients who were recommended for PBR (circumpapillary and the majority of juxtapapillary tumours (<3 mm from the optic nerve margin)) were referred to the Liverpool Ocular Oncology Centre at St Paul's Eye Unit in the Royal Liverpool University Hospital and treated at Clatterbridge Cancer Centre in the United Kingdom. Some juxtapapillary tumours (within 3 mm of the optic nerve) were treated with notched Ru^{106} plaques. All treated patients attended the Royal Victoria Eye and Ear Hospital, Dublin for follow-up, usually at 2, 4, 8 and 12 months following treatment, then 6-monthly up to year 3 post-treatment and annually thereafter.

Patients treated with Ru^{106} plaque received a minimum dose of 80 Gy to the tumour apex and/or 350 Gy to the external sclera. Patients treated with I^{125} plaque received an apex dose of 80–90 Gy to the tumour apex. Binocular indirect ophthalmoscopy and/or transillumination was used to identify the tumour meridian and anterior tumour margin intraoperatively. A dummy plaque was then used to appropriately preplace two 5–0 nylon sutures at the position of the plaque eyelets. The live plaque was then attached to the globe and remained in situ until the required radiation dose was delivered. Bebig (Berlin, Germany) Ru^{106} plaques (round: CCA (15.3 mm), CCD (17.9 mm), CCB (20.2 mm); notched: COB (19.8 mm), COC (25.4 mm)) and COMS I^{125} (16 mm, 18 mm and 20 mm) plaques were used according to the tumour basal diameter and/or proximity to the optic nerve.

For patients undergoing PBR, tantalum markers were attached to the eye with 5–0 mersilene to delineate tumour margins and a 62 MeV proton beam was used to deliver the radiation. These markers were placed by our surgical colleagues in the Liverpool Ocular Oncology Centre (HH and RH). Over 4 consecutive days, four daily fractions were administered with a total dose of 53.1 proton Gy with a relative biological effect of 1.1, equating to a total dose of 58.5 Gy.

Data were available for all patients who underwent brachytherapy or PBR. However, ciliary body and iris melanomas were excluded from the analysis because proton beam radiation was not utilised in our cohort for these lesions and inclusion of these cases would have skewed the comparison of brachytherapy and PBR patient outcomes. Therefore, only choroidal tumours were included for the purpose of this report.

Data collection

The following clinical data were recorded: age, sex, gender, affected eye, treatment type, tumour height (mm), maximum basal diameter (mm), tumour location (distance to fovea and distance to nerve, mm), VA and duration of follow-up. Radiation characteristics were

also collected and these included apex dose, dose to sclera, dose to optic nerve, dose to fovea and external scleral dose (scleral dose is not applicable for PBR and was collected for iodine and ruthenium plaques only). Tumour recurrence was defined as an increase in basal diameter and/or thickness compared with measurements from the previous visit. Best-corrected VA (BCVA) was recorded for all patients at initial presentation and at their most recent follow-up, which was used as the final VA. Initial BCVA was compared with final BCVA and length of follow-up was recorded in months.

Statistical analysis

BCVA was recorded in Snellen format in metres and was subsequently converted to the logarithm of the minimum angle of resolution (logMAR) for the purpose of statistical analysis. A VA of count fingers, hand motion, perception of light (PL) and no PL (NPL) were denoted 2.1, 2.4, 2.7 and 3.0 on the logMAR scale, respectively.[7] Fisher's exact test was used to compare the proportions of local tumour recurrence across treatment groups.

We aimed to test the association of logMAR at last follow-up with all the variables as outlined in table 1. Due to the large number of predictors compared with the sample size, the strength of marginal relationships between the logMAR at last follow-up and the predictors has been estimated using the non-monotonic generalised Spearman ρ^2 statistic[8] (see online supplemental appendix 1). To increase the power of the analysis and reduce the potential impact of collinearities among the baseline characteristics (ie, all predictors excluding the follow-up years), a hierarchical clustering analysis using Hoeffding's D similarity statistic[8] was performed, with the aim of aggregating some of the predictors. The Alternating Conditional Expectations non-parametric additive regression method was then used to non-linearly transform the measurements of logMAR at baseline. Principal component analysis was used to aggregate distance to macula, distance to nerve and tumour volume, and radiation to fovea and radiation to nerve. Tumour volume was estimated as: $\pi/6 \times$ thickness $\times$ largest basal diameter $\times$ (largest basal diameter $\times$ 0.85).[9] One principal component was kept for each set of aggregated factors. For both sets of aggregated factors, the first principal component explains more than 90% of the variance, which suggests that there is not much information loss in the aggregation process.

A regression model was then fitted to the outcome logMAR VA at follow-up, with the following individual predictors: age, sex, length of follow-up, logMAR VA at baseline (nonlinearly transformed), first principal component of tumour characteristic (volume), distance to fovea, distance to nerve, first principal component of radiation (radiation to fovea, radiation to nerve), apex dose, treatment type. After fitting the model, the Breusch-Pagan test for heteroskedasticity (non-uniformity of variance) was performed,[10] which resulted in strong rejection of the homoskedasticity hypothesis ($\chi^2(10)=30$, p=0.0008). Since heteroskedasticity may negatively affect the test statistics, the covariance matrix of the model's parameters was corrected by using the HC5 estimator.[11] Wald statistics were used to assess the significance of these individual predictors in the regression model. Based on the final model, a simplified nomogram was developed to estimate expected final logMAR VA from the significant predictors.

Statistical analysis was performed using R statistical software (V.3.3.2, R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was deemed to be a p value <0.05.

RESULTS

Case numbers and patient demographics

A total of 511 cases of UM were diagnosed between June 2010 and December 2020. With regard to treatment, 294 underwent plaque brachytherapy (206 were ruthenium plaques and 88 were iodine plaques) and 63 had treatment with proton beam radiation. The remaining 154 patients were treated with either enucleation (138), endoresection (4), PDT (4), TTT (3), cyberknife radiosurgery in a different hospital (1) or observation and/or palliative care (4). Patients with ciliary body and/or iris lesions were excluded from the radiation cohort leaving 175 eyes in the ruthenium group, 72 eyes in the iodine group and an unchanged 63 eyes in the proton beam group, a total of 310 eyes available for statistical analysis.

Patient demographics and clinical features of the patients who underwent radiation treatment for their UM (n=310, 100%) are summarised in table 1 and subdivided by treatment modality. Ru^{106} plaques were used in the majority of cases (175/310, 56.5%), including 55 cases treated with notched COB plaques and 17 with COC plaques. I^{125} plaques were used in 72 cases (23.2%) and PBR was used in 63 cases (20.3%). The mean age at the time of treatment was 68.2 years (range 24–98 years; SD 14.0 years). There were 175 males and 135 females. The mean tumour thickness was 4.7 mm (range 1.1–11.4 mm, SD 2.3 mm) and the average maximum basal diameter was 11.7 mm (range 3–19.1 mm, SD 3.4 mm). The mean length of follow-up was 76.9 months (range 12.1 to 125 months, SD 45 months), with a mean follow-up of 85.6 months in the iodine group, 77.5 months in the ruthenium group and 65 months in the PBR group. Radiation dose to the apex, fovea, disc and external sclera was recorded. The average apex dose was 108.3 Gy, 89.3 Gy and 58.4 Gy for the ruthenium, iodine and PBR group, respectively. Average and median radiation doses to the fovea and to the nerve are recorded in table 1 alongside average external scleral dose for plaque treatments.

Local tumour control/local recurrence

In total, there were 13 cases (4.2%) of local tumour recurrence in this cohort. The choice of management for these cases was guided by the overall health of the eye, the likelihood of retaining useful vision and patient preference. Ultimately, all cases of recurrence were managed

Table 1 Patient demographics subdivided by radiation type

	All N=310	Iodine-125 N=72	Ruthenium-105 N=175	Proton beam N=63
Patient age				
Mean±SD (years)	68.2±14	70.4±15	69.5±13	60.8±12
Range (years)	24–98	39–97	28–98	24–82
Patient sex				
Male	175	43	97	35
Female	135	29	78	28
Affected eye				
Right	172	40	98	34
Left	138	32	77	29
Basal diameter				
Mean±SD (mm)	11.7±3	14.1±3	11.1±3	10.4±4
Range (mm)	3.5–19.1	5–19.1	3.5–18.2	4–17.9
Thickness				
Mean±SD (mm)	4.7±2.3	7.7±2.2	3.8±1.2	3.5±1.7
Range (mm)	1.1–11.4	5.1–11.4	1.2–6.3	1.1–8.3
Follow-up				
Mean±SD (months)	76.9±45	85.6±47	77.5±46	65±34
Range (months)	12.1–125	12.1–122.6	14.1–120	18.9–125
Apex dose				
Mean±SD (Gy)	93.8±36	89.3±11	108.3±40	58.4
Range (Gy)	58.4–177.7	75.16–137.3	73.2–177.7	58.4–58.4
Scleral Dose				
Mean±SD (Gy)	357.1±143	346.8±111	361.4±154	NA
Range (Gy)	159.8–1021	159.8–604.8	188.9–1021	NA
Radiation dose to fovea				
Mean±SD (Gy)	81.1±93	71.6±55	96.4±116	49.4±18
Range (Gy)	0–756.5	7.6–256.4	0–756.5	0–58.4
Radiation dose to nerve				
Mean±SD (Gy)	39.1±32	51.9±40	28.7±29	53.1±14
Range (Gy)	0–334.7	9.3–334.7	0–150.4	0–58.4
Distance to macula				
Mean±SD (mm)	4.57±4	6.3±4	4.9±4	1.5±2
Range (mm)	0–15.5	0.3–15.2	0–15.5	0–5.5
Distance to nerve				
Mean±SD (mm)	4.8±4	6.6±3	5.6±3	0.6±1
Range (mm)	0–18.5	0–13.5	0–18.5	0–5.7

with secondary enucleation. In the iodine group (n=72), three eyes (4.2%) underwent a secondary enucleation for evidence of tumour recurrence. In the ruthenium group (n=175), seven eyes (4.0%) underwent subsequent enucleation secondary to documented regrowth of the tumour. In the proton beam group (n=63), three eyes (4.8%) had a secondary enucleation, all for local progression of disease. There was no statistically significant difference in local recurrence rates among the treatment groups (p=0.9).

All cases of local recurrence were confirmed histologically. The presence of viable-appearing (non-necrotic) tumour cells and positive Ki67 proliferation-marker staining was considered as evidence of viable recurrent tumour. Mean time to recurrence was 31.3±15 months for patients treated with I^{125}, 24.9±41 months for those

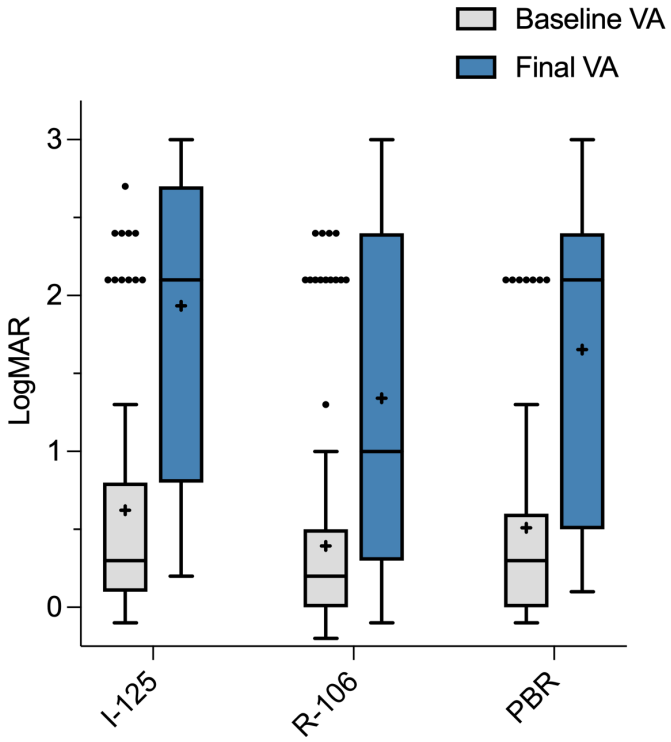

Figure 1 Box and whisker plot demonstrating the baseline and final logMAR VA across treatment groups: Iodine-125 (I-125), Ruthenium-106 (R-106) and PBR. + represents the mean VA. PBR, proton beam radiotherapy; VA, visual acuity.

treated with Ru^{106} and 72±68 months for patients treated with PBR.

Eye retention

At a mean follow-up of 76.9 months (range 12.1–125 months), the treated eye was preserved in 94.4% (68 of 72 eyes) of the I^{125} group, 96% (168 of 175 eyes) of the Ru^{106} group and 95.2% (60 of 63 eyes) of the PBR group. No patient in the Ru^{106} group (0/175) or the PBR group (0/63) required secondary enucleation for a painful eye/neovascular glaucoma (NVG). One patient in the iodine group (1/72, 1.4%) underwent secondary enucleation for a blind painful eye due to NVG secondary to radiation retinopathy, 32 months after initial treatment. This occurred in a female in her early 40s with a choroidal melanoma measuring 18 mm in maximal basal diameter and 11.4 mm in thickness at presentation.

VA analysis

At baseline

The average logMAR VA pre-treatment was 0.6, 0.4 and 0.5 in the I^{125}, Ru^{106} and PBR group, respectively. 116 (66.3%) ruthenium patients, 39 (54.2%) of the iodine patients and 38 (60.3%) of the PBR patients had a pre-treatment logMAR VA of 0.3 (6/12) or better.

At last follow-up

Figure 1 compares the baseline and final logMAR VA across treatment group. At the last follow-up, the mean VA was 1.9, 1.3 and 1.7 logMAR in the I^{125}, Ru^{106} and PBR groups, respectively. A VA of 1.0 logMAR or better was maintained in 20 eyes (27.8%) in the I^{125} group, 89 eyes (50.9%) in the Ru^{106} group, and 25 eyes (39.7%) in the PBR group. A post-treatment VA of 0.3 logMAR or better, the minimum required for driving in Ireland, was achieved in four eyes (5.6%) in the I^{125} group, 49 eyes (28%) in the Ru^{106} group, and nine eyes (14.3%) in the PBR group. Overall, 36 eyes (11.6%) had a final VA of 3.0 logMAR, indicating NPL. This included 12 eyes (16.7%) in the I^{125} group, 15 eyes (8.6%) in the Ru^{106} group, and nine eyes (14.3%) in the PBR group.

The average vision loss across all groups was 1.06±1.0 logMAR. The mean increase in logMAR (indicating reduced acuity) was 1.27±0.9 in the I^{125} group, 0.95±0.9 in the Ru^{106} group, and 1.13±1.0 in the PBR group.

Table 2 Wald statistics of logMAR VA model

Predictor	F	P value
Age	0.02	0.89
Sex	0.18	0.67
LogMAR VA at baseline	91	<0.0001
Radiation dose to fovea	16	0.0001
Apex dose	0.85	0.36
Tumour volume	6.2	0.013
Follow-up years	3.9	0.0036
Treatment modality	24	0.022

VA, visual acuity.

The association between final logMAR VA and various patient, tumour and treatment-related predictors was assessed using Wald statistics (table 2). Final logMAR VA was significantly associated with baseline logMAR VA ($p < 0.0001$), radiation dose to the fovea ($p = 0.0001$), tumour volume ($p = 0.013$), duration of follow-up ($p = 0.0036$), and treatment modality ($p = 0.022$). The baseline logMAR VA, treatment modality and radiation dose to the fovea were the strongest predictors of final VA. Age, sex and apex radiation dose were not significantly associated with final VA.

Effects of specific treatments were assessed using contrast differences,[8] which estimate the mean difference in final logMAR VA between treatment groups, adjusted for all other covariates in the regression model. The contrasts in expected logMAR are reported in online supplemental table 1. The largest difference was observed between PBR and Ru^{106}, with a mean difference of 0.46 logMAR (p=0.01).

From the Wald statistics, the variables that significantly predicted final VA were incorporated into a simplified nomogram (figure 2), which explains 98% of the variance in final logMAR VA across all included predictors. For instance, a patient with a tumour volume of 400, logMAR VA at baseline of 0, radiation dose to the fovea of 300 Gy, treated with a ruthenium plaque will have a predicted

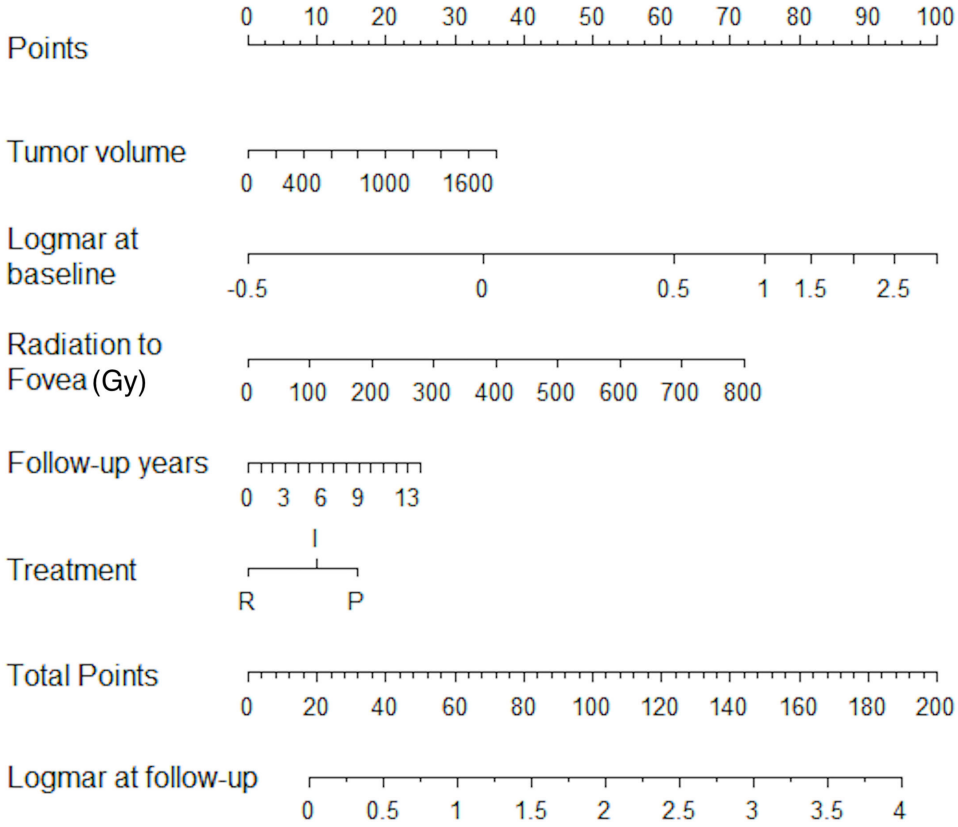

Figure 2 Nomogram comprising patient, tumour and treatment characteristics to predict final visual acuity (VA) following radiation treatment. Treatments include Iodine-125 (I), Ruthenium-106 (R) and PBR (P). Tumour volume was estimated as π/6×thickness × largest basal diameter × (largest basal diameter×0.85). PBR, proton beam radiotherapy; VA, visual acuity.

logMAR VA of approximately 1.6 (8+34+27+16+0=85 total points) at 9-year follow-up.

DISCUSSION

Tumour control

The aim of UM treatment is to achieve local control of the primary tumour in order to reduce the future risk of metastatic disease.[12] In general, where feasible, eye-preserving treatments are undertaken in preference to primary enucleation. Eye radiation treatment planning aims to achieve sufficient tumour radiation dose and to minimise collateral radiation dose to the optic nerve and fovea in so far as possible, in order to preserve some level of VA in the affected eye. In this study, local tumour control was achieved in 95.8% (297 of 310 eyes) of eyes treated with either ruthenium brachytherapy (96%), iodine brachytherapy (95.8%) or proton beam radiation (95.2%) demonstrating no significant difference in rates local tumour control rates between the three radiation treatment types. This differs from a previous report comparing plaque and proton beam treatments which demonstrated a significantly greater risk of local tumour recurrence with Ru^{106} treatment compared with PBR, and postulated that the smaller, thinner tumours were more likely to recur after Ru^{106}.[13] More recent publications have reported local tumour control in 92% of patients treated with Ru^{106},[14] 90.4% of patients treated with I^{125}[15] and 96.1% of those treated with PBR.[16]

Eye retention

In our study cohort, the rate of secondary enucleation for a blind painful eye (as opposed to tumour recurrence) was 0.3% (1/310). On review of the literature, the rate of secondary enucleation for NVG ranges from 21% to 39%.[17 18] Notably, ciliary body tumours were excluded from this report, likely contributing to the lower rate of NVG/secondary enucleation here.

Visual acuity

For the purpose of this study, logMAR of 1.0 or better was considered as useful VA.[19] This was maintained in 50.9% of the ruthenium group, 27.8% of the iodine group and 39.7% in proton beam group at a mean follow-up of over 6 years. However, direct comparisons of VA outcomes between treatment groups are not possible here due to the inherent selection bias in treatment allocation based on tumour size, thickness and proximity to the optic nerve. Any observed differences in visual outcomes or tumour control may therefore reflect the baseline tumour characteristics rather than treatment efficacy itself. Differences in follow-up duration between treatment groups (iodine: 86 months, ruthenium: 76 months, proton beam: 63 months) may also have influenced visual outcomes, as longer follow-up allows for greater manifestation of radiation-induced visual changes. Other studies have shown that, overall, approximately two-thirds of patients treated with ruthenium plaque brachytherapy

will maintain a VA of logMAR1.0 or better at 5–9 years post-treatment.[20 21] Reports on iodine brachytherapy have demonstrated mean VA of 1.0 or better in 49% of treated eyes at 3 years[22] and in 32% at 10 years.[23] A study of patients with large choroidal melanomas treated with PBR reported VA of 1.0 logMAR or better in 15.9% of treated eyes at 5 years, falling to 8.7% at 10 years.[24] Tumour location, tumour thickness and/or volume, radiation dose to the fovea and optic nerve all significantly influence long-term VA. In our series, I^{125}-treated patients had a mean tumour thickness of 7.7 mm, compared with 3.8 mm in the Ru^{106}-treated group and 3.5 mm in the PBR group. Mean radiation dose to optic nerve was higher in the PBR (53.1 Gy) and I^{125}-treated (51.9 Gy) groups compared with the Ru^{106} group (28.7 Gy).

Vision loss after radiation treatment for UM is multifactorial. Patients with juxtapupillary and parafoveal tumours are known to have higher rates of vision loss,[25 26] as are those with thicker tumours[27] and those patient who are advanced in age.[22] Our statistical analysis revealed that the strongest predictor of final VA was presenting VA, followed by treatment modality and radiation dose to the fovea (table 2). Poor VA at presentation is usually related to subfoveal tumour location and/or exudative subretinal detachment, involving the fovea in larger tumours, conversely better acuity at presentation is usually associated with more anterior tumour location and/or smaller tumour size. Final VA had a weaker, but significant, association with tumour volume and follow-up duration. With regard to the final visual outcomes per specific treatment type, the greatest logMAR difference was seen for proton beam versus ruthenium (online supplemental table 1). This outcome may be biased because of patient selection criteria for Ru^{106} and PBR in our institution, as previously outlined.

The nomogram devised here is highly calibrated in this patient cohort but could likely be adopted by other centres and utilised as a 'quick' prognostication tool for final VA in patients considering radiation treatment for UM. It captures statistical associations between predictors across treatment modalities without imposing clinical constraints on how these variables interact. Its use should, therefore, be guided by clinician judgement and interpreted within the bounds of clinical plausibility. External validation in other centres is warranted before widespread adoption.

CONCLUSION

Uveal melanoma is a life-changing diagnosis for patients. Patients have to consider the options of primary enucleation and eye-preserving treatments, most commonly radiation. Most patients will opt for eye-conserving treatment where feasible, but some will choose enucleation over radiation if they are likely to have little residual vision in the affected eye in the medium to longer term after radiotherapy. The data from this paper may be helpful in counselling patients in regard to likely outcomes following eye-conserving radiation treatment.

This series confirms reassuringly high rates of local tumour control (95.8%) with no significant difference between ruthenium, iodine or proton beam patient groups. The rate of secondary enucleation for late-onset radiation complications (primarily uncontrolled NVG) was very low (1 of 310 eyes, 0.3%). Overall, the rate of secondary enucleation for local recurrence or NVG was 4.5% at a mean follow-up of over 6 years.

LogMAR acuity of 1.0 or better in the treated eye was maintained in an average of 39.5% across the three groups. A nomogram combining tumour volume, logMAR acuity at baseline and expected radiation dose to the fovea was found to usefully predict final VA in radiation-treated eyes.

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Contributors PM is the guarantor of this study. PM: devised study, data collection and analysis, prepared manuscript. MMO'R: data collection and analysis, prepared manuscript. VO'N: data collection. MC: devised study, data collection, reviewed paper. FD'A: devised study, reviewed paper. AE: statistical analysis, reviewed paper. AG, CB: data collection, reviewed paper. SK, RH, HH: devised study, reviewed paper. NH: devised study, reviewed data, prepared manuscript and reviewed paper.

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Patient consent for publication Not applicable.

Ethics approval This retrospective study was reviewed and approved by the Research and Audit Committee of the Royal Victoria Eye and Ear Hospital, reference number RVEEH-2024-14. Informed consent was waived as this is a retrospective study.

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Data availability statement Data are available upon reasonable request. The data that support the findings of this study are not publicly available but are available from the corresponding author upon reasonable request.

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