Purpose: To determine the long-term outcomes of I-125 episcleral plaque brachytherapy for uveal melanoma and identify dosimetric factors associated with ocular complications and tumor control.

Methods: Four-hundred-fifty-two patients were treated with I-125 plaque brachytherapy for uveal melanoma from 1996 to 2011. In 218 patients tumor samples were obtained by needle biopsy and subjected to a validated 15-gene expression assay that assigned tumors to class 1 (low metastatic risk) or class 2 (high metastatic risk). Brachytherapy records were reviewed to analyze radiation doses at specific dose reference points. Ophthalmologic follow-up records were analyzed to assess the incidence of recurrence, ocular complications and visual outcomes after therapy. Survival curves were estimated using the Kaplan-Meier method. Wilcoxon rank sum and Fisher’s exact test were used to analyze the relationships of dose delivered and type of plaque to outcomes. Probit regression model was performed to predict the cumulative incidence of enucleation due to toxicity.

Results: Mean tumor thickness and long basal diameter were 4.9 mm and 12 mm, respectively. The median plaque size was 18 mm. One hundred twelve plaques (24.8%) required a notch due to proximity to the optic nerve. The median follow-up was 46.4 months (range 6-175 months). The patterns of failure were local in 4.9% of patients (n = 22) and distant in 12% of patients (n = 55), of which 2.0% (n = 9) were both. The estimated 5-year overall and cause-specific survivals were 80.3% and 89.7%, respectively (Fig 1). The estimated 3-year and 5-year metastatic rates for all patients were 8.7% and 15.5%, respectively. The estimated 3-year and 5-year metastatic rates for patients with class 1 tumors were 2.2% and 4.4% compared to class 2 tumors which were 42.6% and 52.2%. Patients with class 2 tumors had a significantly increased risk of metastatic disease compared to patients with class 1 tumors (Odds Ratio 19.6; p < 0.001).

The mean doses to the tumor apex and tumor base were 98.3 Gy and 270.1 Gy, respectively. The mean dose to the tumor base was significantly higher in those with local control compared to those with local failures (271.3 Gy versus 247.4 Gy; p = 0.05).

The corresponding radiation doses to the tumor apex were 98.5 Gy versus 94.9 Gy (p = 0.63).

The median baseline visual acuity was 20/40 and at most recent follow-up was 20/150. Thirty-five patients (7.7%) underwent enucleation due to recurrence (n = 17; 3.8%), second intraocular primary (n = 1; 0.2%) or toxicity (n = 18; 4.0%). Patients who required enucleation secondary to radiation toxicity had a significantly greater dose to the tumor base than those not requiring an enucleation due to radiation toxicity (379.2 Gy vs. 265.6 Gy, p < 0.0001). Probit model to predict the cumulative probability for enucleation due to toxicity in relation to radiation dose to the tumor base reveals a 5%, 25%, and 50% risk of enucleation when the tumor base receives 334.3 Gy, 576.7 Gy, and 745.2 Gy, respectively (Fig 2). Patients with class 2 tumors did not have a significantly increased risk of local recurrence, enucleation, or enucleation due to toxicity than class 1 patients (p values 0.22, 0.29, 0.36, respectively).

Conclusions: I-125 episcleral plaque brachytherapy leads to excellent local control and globe preservation. Patients requiring an enucleation due to radiation toxicity had a significantly higher radiation dose to the base of the tumor. Patients with class 2 tumors had a significantly increased risk of metastatic disease compared to patients with class 1 tumors.