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Evidence for Dose De-escalation in Brachytherapy for Choroidal Melanoma

Bao han A. Le, BS[a,b], Rima Patel, MD[a], Richard Jennelle, MD[c], Jesse L. Berry, MD[a,d,*]

[a]Roski Eye Institute, Department of Ophthalmology, University of Southern California Keck School of Medicine, 1450 San Pablo Street, Los Angeles, CA 90033 USA; [b]John A. Burns School of Medicine, University of Hawaii, 651 Ilalo Street, Honolulu, HI 96813 USA; [c]Department of Radiation Oncology, University of Southern California Keck School of Medicine, 1441 East Lake Avenue, Los Angeles, CA 90033 USA; [d]The Vision Center, Department of Ophthalmology, Children's Hospital Los Angeles, 4650 Sunset Boulevard, Los Angeles, CA 90027 USA

Keywords

• Uveal melanoma • Choroidal melanoma • Brachytherapy • Dose reduction • Brachytherapy complications

Key points

- Brachytherapy has been shown to be a safe and effective globe-conserving therapy for uveal melanoma. At the current standard dose of 85 Gy, modeled after the Collaborative Ocular Melanoma Study (COMS) trials, brachytherapy is associated with high rates of radiation-related complications.
- There is evidence that a prescription dose of less than 85 Gy for brachytherapy of uveal melanomas would maintain equivalent rates of local tumor control.
- Reduction of radiation doses to critical ocular structures may result in a clinically significant improvement in rates of complications and rates of visual decline.
- Prospective dose de-escalation trials using ^{106}Ru brachytherapy, proton beam, and gamma knife radiosurgery have demonstrated favorable results.
- A randomized prospective trial is necessary to determine a reduced prescription dose for ^{125}I brachytherapy that would maintain acceptable local tumor control while minimizing dose-dependent radiation complications.

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*Corresponding author. 1450 San Pablo Street, Los Angeles, CA 90033. *E-mail address:* jesse.berry@med.usc.edu

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INTRODUCTION

Choroidal melanoma is the most common primary intraocular malignancy in adults with an incidence of 6 per million in the United States [1]. Of all melanomas, ocular and adnexal melanomas comprise about 5%, with uveal melanomas making up the majority (85%) of ocular melanomas [2,3]. Similar to cutaneous melanoma, ocular melanoma is significantly (8–10 times) more common in white than in black populations, and most cases occur in non-Hispanic whites [2,4]. Of uveal melanomas, most occur in the choroid, with a much smaller proportion occurring in the iris and ciliary body [4]. The iris is the least common site of origin but carries the best overall prognosis, whereas melanomas of the ciliary body have the worst prognosis, but this may be because they often present later and with larger tumors [5].

When uveal melanoma was first described in the early nineteenth century, it was considered to have an extremely poor prognosis, often presenting late with large tumors, extraocular extension, and advanced metastatic disease [6]. As such, enucleation was the mainstay of treatment for many decades. ^{60}Co plaque brachytherapy for treatment of melanoma was first reported in the 1960s in England [7]. Subsequently, lower-energy ^{106}Ru and ^{125}I plaques were developed in the 1970s to minimize radiation dose and side effects to the orbital adnexa [6]. Many radioisotopes can be used in ocular brachytherapy, with ^{125}I being the most commonly used in the United States [8].

In the 1980s, the Collaborative Ocular Melanoma Study (COMS) was a landmark multicenter randomized trial of ^{125}I brachytherapy versus enucleation for treatment of choroidal melanoma [9,10]. COMS set a standard for brachytherapy treatment, and as a result, their guidelines were widely adopted. Before the COMS trials, brachytherapy had been tested in smaller studies, but was not widely accepted because of concern that eye-conserving treatment would compromise survival; this fear was disproven in the COMS trials.

Today, plaque brachytherapy is widely used for globe-conserving treatment of uveal melanoma. Since the COMS trials, there have been many advances in the treatment of choroidal melanoma. The use of intraoperative ultrasonography for plaque placement was recommended, based on evidence that it improves the accuracy of plaque placement and local tumor control [11,12]. Plaque planning software using 3-dimensional (3D) modeling has enabled customized plaques for each tumor as well as offering improved ease of intraoperative plaque localization for surgeons [13,14]. Fine needle aspiration biopsy has been used for diagnosis as well as prognosis with gene expression profiling [15–17]. Since the original COMS trials, which evaluated medium-sized tumors (base $<$20 mm and height 2.5–10 mm), the indications for brachytherapy have expanded to include small, medium, and some large melanomas, as well as certain ciliary body, iris, and peripapillary melanomas [9,18]. In addition, notched plaques now allow treatment of juxtapapillary tumors that were previously not amenable to brachytherapy [19].

Plaque brachytherapy is a commonly accepted modality for globe salvage with very high rates of tumor control. Across multiple studies, tumor control