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Outcomes of medium choroidal melanomas treated with ruthenium brachytherapy guided by three-dimensional pretreatment modeling

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ABSTRACT

PURPOSE: The Collaborative Ocular Melanoma Study (COMS) established iodine-125 (I-125) plaque brachytherapy for eye preserving treatment of medium-sized choroidal melanomas in the United States. Eye Physics I-125 plaque treatment modeled with Plaque Simulator (PS) software yields similar results to COMS. Herein, we report results from a series of 15 patients treated with ruthenium-106 (Ru-106) plaque brachytherapy using PS pretreatment modeling for plaque localization and dosimetry.

METHODS AND MATERIALS: Fifteen patients with medium-sized choroidal melanomas (2.84–5.5 mm in apical height and a basal diameter of 7.8–12.6 mm) treated with ruthenium brachytherapy from 2003 to 2005 were evaluated retrospectively. Baseline and followup data were evaluated for tumor height, best corrected visual acuity, radiation retinopathy, radiation optic neuropathy, postradiation cataract formation, diplopia, and ptosis. Tumor response for both Ru-106 and I-125 plaques planned using the same PS pretreatment modeling was evaluated and compared.

RESULTS: Isotope-specific radiation profiles were compared, and rates of local treatment failure (0%), optic neuropathy (6.7%), retinopathy (20%), and cataracts (33%) were evaluated. Five year–treated tumor heights were approximately 0.61 ± 0.29 (I-125, $n = 16$) and 0.53 ± 0.17 (Ru-106, $n = 6$) of their heights at diagnosis.

CONCLUSIONS: This patient subset had background characteristics very similar to those of the COMS and patients treated at our institution with I-125 plaques. Treatment response was equivalent although radiation complications occurred slightly less frequently in the Ru-106 group compared with those treated with I-125. Image-guided three-dimensional pretreatment modeling for plaque localization and dosimetry seems to work equally as well for Ru as for I-125 plaques and justifies more extensive investigation.

Keywords: Uveal; Melanoma; Plaque; Brachytherapy; Toxicity; Ruthenium

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Conflict of interest: Dr Astrahan holds an ownership position in Eye Physics LLC, which was incorporated in 2007 to continue development of the Plaque Simulator software and Eye Physics plaques after Dr Astrahan's emeritus retirement from the University of Southern California (USC) in 2010. During 1990–2010, no outside funding for development or material support for any of his contributions was received by USC. No compensation was received for any patient in this study. From 1995 to 2010, USC and Dr Astrahan shared a royalty derived from licensed distribution of the Plaque Simulator software to other institutions. No other disclosures were reported.

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Introduction

Episceral plaque brachytherapy is a well-established and effective treatment for medium-sized choroidal melanomas. The Collaborative Ocular Melanoma Study (COMS) showed that treatment with plaques loaded with iodine-125 (I-125) achieved survival rates equal to enucleation (1). I-125 brachytherapy has become the standard approach to globe preservation in the treatment of medium-sized choroidal melanomas in the United States.

Various surgical techniques have been described to localize COMS plaques on the episcleral surface, including scleral transillumination, indirect ophthalmoscopy with scleral depression, scleral diathermy, and ultrasonographic confirmation of plaque localization (2). An alternative brachytherapy system to the COMS plaques using preoperative localization has been previously described (3–7). The Eye Physics (EP) plaques are thin plaques with custom, conformal radiation profiles that are configured using Plaque Simulator (PS) software (6). The PS software constructs a three-dimensional model of the eye and tumor from a fusion of fundus photography, ultrasound, and computed tomography or magnetic resonance imaging. PS provides coordinates for plaque placement preoperatively, which obviates the need for significant intraoperative localization. The PS software also enables selection of seed positions to customize radiation profiles for a variety of tumor shapes and sizes. EP I-125 brachytherapy has been shown to have similar long-term clinical outcomes as compared with the COMS plaques and has the additional benefit of enabling most of the treatment planning to be performed preoperatively rather than intraoperatively (8).

Plaque brachytherapy for uveal melanoma can be administered using gamma radiation emitters such as I-125 or Palladium-103 or primarily beta radiation emitters such as ruthenium-106 (Ru-106/Rh-106). In the 1980s, I-125 became the *de facto* radionuclide used for uveal melanomas of medium size by the COMS because, for tumors >5 mm in apical height, I-125 delivers much better dose penetration compared with ruthenium. However, the caveat is that the radiation dose gradient surrounding I-125 plaques is not as steep as the gradient surrounding the beta-emitting Ru-106. Therefore, the benefits of a more homogeneous dose to the tumor and its immediate environs by I-125 may, at times, be offset by increased radiation to distal critical eye structures such as the macula, optic nerve, or lens.

A dosimetric comparison of I-125 vs. Ru-106 plaques has shown that Ru plaques can provide adequate radiation dose to small tumors although sparing critical nearby structures more effectively than I-125 (9). Wilkinson *et al.* showed that the use of Ru plaques could potentially reduce radiation dose to the macula, optic disc, and lens by 18%, 53%, and 89%, respectively. The primarily beta-emitting radiation properties of Ru-106/Rh-106 decay are responsible for this steep dose gradient; the surface dose rate near the peripheral edge of a Ru Plaque drops to about 70% of its central strength and about 2 mm beyond the edge the radiation dose rate drops to <5%. Because of this dosimetric advantage for small uveal melanomas (<5.5 mm in apical height), Ru plaques were recently reintroduced as a potentially safer radiation source for brachytherapy in the United States. Several groups have reviewed their experience with Ru plaques for small and medium uveal melanoma in both anterior and posterior locations (10–12). Barker *et al.* (13) have further suggested that planning for Ru-106 plaque brachytherapy should be performed carefully at centers with experience in COMS protocols with the possible need for special consideration to ensure sufficient dose delivery to tumor margins given the specific dosimetric considerations with Ru-106.

Herein, we report results from a series of 15 patients with posterior choroidal melanomas treated with Ru plaque brachytherapy using PS for preoperative planning, at the University of Southern California (USC) from 2003 to 2005. We further compare the radiation profiles with previously published results from similar tumors treated at our institution with I-125 EP plaques (8, 14).

Methods

This is a retrospective review of all patients who underwent episcleral plaque brachytherapy with Ru-106 for medium-sized choroidal melanomas at the USC between January 1, 2003 and December 31, 2005. This study was approved by the Institutional Review Board at USC.

Patient eligibility

Eligible patients were older than 18 years of age and were diagnosed by an ocular oncologist (ALM) with a primary, medium-sized choroidal melanoma with an apical height of less than 5.5 mm and maximum basal diameter of less than 16.0 mm (15). Large, diffuse, ill-defined tumors, tumors contiguous with the optic nerve for more than 3 clock-hours, tumors primarily involving the ciliary body or iris, and tumors with extrascleral extension were not treated with brachytherapy.

All patients were educated on treatment options including observation, enucleation, and proton beam therapy. Patients who chose brachytherapy were treated with Ru-106 plaques (Bebig GmbH, Berlin, Germany) with a prescribed dose of 85 Gy to the tumor apex (average dose rate range 61.7–220.9 cGy/h).

Data collection and patient followup

At diagnosis, complete history and examination with measurement of visual acuity (VA) with pinhole or manifest refraction, slit lamp examination, and fundoscopy of both eyes were completed. Tumors were characterized with