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BRACHYTHERAPY

Long-term visual acuity outcomes in patients with uveal melanoma treated with ^{125}I episcleral OSU-Nag plaque brachytherapy

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ABSTRACT

PURPOSE: To report our experience in long-term follow-up of ocular melanoma patients treated with custom OSU-Nag eye plaques using ^{125}I sources.

METHODS: A retrospective chart review was conducted for 113 consecutive ocular melanoma patients with follow-up visual acuity data who were treated with OSU-Nag plaque episcleral brachytherapy at The Ohio State University Medical Center from 1994 to 2009. Visual acuity, complication data, and recurrence rates were recorded up to 120 months after brachytherapy.

RESULTS: Median age at presentation was 63.0 years (range, 22−93). Median follow-up was 65.5 months (range, 2−180). Median radiation dose at the prescription point was 85.8 Gy (range, 51.8−103.7). Preservation of useful visual acuity, defined as better than 20/200, was noted in 43 of 74 (58%) of patients in the present study at 36 months compared with 50.1% of Collaborative Ocular Melanoma Study participants. By 120 months, 17 of 30 (57%; 95% confidence interval, 45−69%) progressed to visual acuity worse than 20/200, whereas 9 of 30 (30%) retained visual acuity of 20/40 or better, and 4 of 30 (13%) were 20/50−20/200. The rate of retinopathy after radiation was approximately 40% of all those observed by 60 months. Baseline visual acuity, apical tumor height, American Joint Committee on Cancer tumor category, and distance between the tumor and the fovea were all significantly associated with loss of visual acuity. The local tumor control rate by 60 months of follow-up was 93% (95% confidence interval, 85−97%).

CONCLUSIONS: The OSU-Nag custom ^{125}I plaque is an effective treatment for uveal melanoma, with preservation of useful visual acuity in 58% of eyes 3 years after treatment and 43% of eyes 10 years after treatment.

Keywords: Brachytherapy; Uveal melanoma; Visual acuity; OSU-Nag plaque; Collaborative ocular melanoma study

Introduction

Uveal melanoma is the most common primary intraocular cancer in adults (1). Over the last several decades, brachytherapy has become the standard treatment for primary uveal melanoma at most centers (2−4). The effectiveness of ^{125}I brachytherapy for primary treatment was supported by the multicenter, NIH-funded Collaborative Ocular Melanoma Study (COMS), which showed equivalent survival for patients treated with globe-sparing brachytherapy compared with enucleation (5−7).

The COMS group provided initial evidence suggesting the preservation of visual acuity in patients treated with episcleral brachytherapy (8). Three years after treatment, 49% of eyes treated demonstrated significant loss of visual

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acuity, defined as loss of six lines or more from baseline, with 43% demonstrating vision of 20/200 or worse (2). Other series using ^{125}I episcleral brachytherapy have shown similar or superior preservation of visual acuity over a longer follow-up period (3,9−11). Additionally, studies using alternative radioactive isotopes for brachytherapy (e.g., palladium-103 and ruthenium-106) have demonstrated superior preservation of visual acuity with long-term follow-up (3, 12, 13). Radiation-related complications, including radiation retinopathy, neovascular glaucoma, and cataracts, have also been described by post-COMS studies (12, 14).

The COMS protocol used five standard circular plaques of varying diameters and required that the tumor be covered with a minimum 2-mm margin (2). These plaques are widely used today. At our institution, for patients who did not meet the inclusion criteria for COMS, or who did not want to participate in the study, custom gold ^{125}I OSU-Nag eye plaques were made to encompass the tumor according to its shape, plus a 1−2 mm margin. All patients treated with plaque brachytherapy subsequent to completion of the COMS were treated with these customized plaques. The shape of each plaque was determined by the size and location of the lesion and included circular, oval, notched, and kidney-shaped plaques. The customized plaques allowed for more conformal tumor coverage for irregular (i.e., noncircular) lesions, improved the dose conformity and distribution for peripapillary tumors, and irradiated a smaller area of normal retina (15).

A previously published series from our institution suggested that episcleral brachytherapy using ^{125}I OSU-Nag plaques produced survival rates similar to those of the COMS patients after a median follow-up of 49 months. The series also reported local control rates similar to the COMS (15).

The present updated series expands on local recurrence statistics from the previous ^{125}I OSU-Nag plaque study, with long-term follow-up of a larger number of patients. The study also details the long-term effects on visual acuity, with comparison to the COMS group results, and evaluates the impact of American Joint Committee on Cancer (AJCC) T-category and other anatomic factors such as distance to fovea and optic nerve on visual acuity outcome and development of radiation retinopathy, the most common cause of visual acuity loss in this population (15).

Methods

A retrospective chart review of 113 consecutive primary choroidal or ciliary body melanoma patients treated with OSU-Nag episcleral plaque brachytherapy for whom follow-up visual acuity data were available at The Ohio State University Medical Center from 1994 to 2009 was performed. The diagnosis of choroidal melanoma was made using funduscopy, fundus photographs, B-scan ultrasonography, and fluorescein angiography. Patients were treated with episcleral brachytherapy (15) and were followed at approximately 6-month intervals. At each follow-up visit, corrected visual acuity and pinhole visual acuity were measured using a Snellen eye chart. The better measurement was used in the study analysis. Those patients treated with the OSU-Nag plaque brachytherapy during the time the COMS was concurrently being conducted either did not meet the inclusion criteria for or declined participation in the COMS. Baseline characteristics of each patient, including gender, age at diagnosis, concurrent diabetes at enrollment, presence/absence of macular edema at baseline, visual acuity, and tumor characteristics, were obtained from the patient’s initial referral visit and from initial tumor workup notes. The distances of the tumor to the fovea and optic nerve were determined using the COMS measurement data sheet, with data from ophthalmoscopy and imaging studies. Radiation dose at the prescription point was recorded. In addition, visual acuity and the presence of any complications or retinopathy were recorded at 6, 12, 18, 24, 36, 60, 84, and 120 months after brachytherapy.

Radiation retinopathy was evaluated with ophthalmoscopy and fluorescein angiography. Radiation retinopathy was diagnosed if any of the following features were present in the macula: retinal edema, retinal exudation, intraretinal hemorrhages, microaneurysms, cotton wool spots, vascular sheathing, or capillary nonperfusion. In addition, a diagnosis of radiation retinopathy was made if any of the listed features were present in combination with retinal neovascularization, vitreous hemorrhage, or extensive retinal ischemia on fluorescein angiography. Radiation optic neuropathy was diagnosed if there was peripapillary exudation and hemorrhage, optic disc swelling, or neovascularization of the disc. Neovascular glaucoma was defined as elevated intraocular pressure with accompanying neovascularization of the iris and/or angle on slit lamp examination and gonioscopy. Local recurrence was evaluated with color fundus photography, fluorescein angiography, A-scan, or B-scan ultrasound and defined using the COMS definition (7).

Brachytherapy

The OSU-Nag eye plaques (Fig. 1) were specially fabricated from 0.6-mm-thick 18K gold, with each one having a counterpart ‘‘dummy’’ plaque with a central cutout (Fig. 2), allowing the surgeon to ensure adequate coverage of the base of the tumor before placing the active plaque. Although most plaques are circular or oval, we have made kidney-shaped plaques for tumors close to the optic disc. By turning the concave surface anteriorly, these can also be used to treat tumors adjacent to the cornea. To assist the surgeon in placing and securing plaques that are posterior, ‘‘rabbit-ear’’ plaques having 2−3 elongated anterior wings (Fig. 2) are specifically designed to reach posterior-located tumors. The inner surface of the plaque is raised 2 mm from the surface of the sclera to reduce the dose to the sclera and increase the depth dose.