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CLINICAL INVESTIGATION **Eye**

STEREOTACTIC FRACTIONATED RADIOTHERAPY IN THE TREATMENT OF JUXTAPAPILLARY CHOROIDAL MELANOMA: THE MCGILL UNIVERSITY EXPERIENCE

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Purpose: **To report our experience with linear accelerator-based stereotactic fractionated radiotherapy in the treatment of juxtapapillary choroidal melanoma.**

Methods and Materials: **We performed a retrospective review of 50 consecutive patients diagnosed with juxtapapillary choroidal melanoma and treated with linear accelerator-based stereotactic fractionated radiotherapy between April 2003 and December 2009. Patients with small to medium sized lesions (Collaborative Ocular Melanoma Study classification) located within 2 mm of the optic disc were included. The prescribed radiation dose was 60 Gy in 10 fractions. The primary endpoints included local control, enucleation-free survival, and complication rates.**

Results: **The median follow-up was 29 months (range, 1–77 months). There were 31 males and 29 females, with a median age of 69 years (range, 30–92 years). Eighty-four percent of the patients had medium sized lesions, and 16% of patients had small sized lesions. There were four cases of local progression (8%) and three enucleations (6%). Actuarial local control rates at 2 and 5 years were 93% and 86%, respectively. Actuarial enucleation-free survival rates at 2 and 5 years were 94% and 84%, respectively. Actuarial complication rates at 2 and 5 years were 33% and 88%, respectively, for radiation-induced retinopathy; 9.3% and 46.9%, respectively, for dry eye; 12% and 53%, respectively, for cataract; 30% and 90%, respectively, for visual loss [Snellen acuity (decimal equivalent), <0.1]; 11% and 54%, respectively, for optic neuropathy; and 18% and 38%, respectively, for neovascular glaucoma.**

Conclusions: **Linear accelerator-based stereotactic fractionated radiotherapy using 60 Gy in 10 fractions is safe and has an acceptable toxicity profile. It has been shown to be an effective noninvasive treatment for juxtapapillary choroidal melanomas.** **© 2011 Elsevier Inc.**

Choroidal melanoma, Juxtapapillary, Local tumor control, Stereotactic radiotherapy, Toxicity.

INTRODUCTION

Choroidal melanomas arise from melanocytes in the choroid and account for 85% to 90% of all uveal melanomas. Although rare, with an annual incidence of 6 to 7 cases per 1 million people, the disease is nevertheless the most common primary intraocular malignancy in the adult population (1, 2).

Standard treatment previously consisted of complete removal of the tumor by enucleation. However, studies have failed to demonstrate any advantage of enucleation over eye-conserving therapy in reducing metastasis or in improving overall survival (3, 4). The management of choroidal melanomas is aimed at tumor control with organ

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preservation, prevention of metastasis, and, ultimately, increased overall survival. The choice of the treatment modality depends on tumor size and intraocular location, and various alternatives exist, including photocoagulation, transpupillary thermotherapy, photodynamic therapy, endoresection, and radiotherapy (RT) (5). Basically, enucleation has been reserved for larger tumors, cases in which there is no possibility of vision preservation, and symptomatic lesions or as a salvage approach.

RT in the form of brachytherapy or external beam RT (EBRT) is the standard eye-conserving treatment for choroidal melanomas. Although this disease is historically regarded as radioresistant, studies have shown that RT is effective in achieving local tumor control and improving overall survival (3, 6). Brachytherapy with iodine-125, ruthenium-106, or other isotopes is usually not recommended for juxtapapillary tumors; however, it is used effectively for lesions located away from the optic disc (7, 8). For medium to large sized lesions and tumors located near the optic disc and fovea, EBRT is the recommended treatment modality, allowing more adequate dose coverage of the tumor. Although results with EBRT using charged particles (protons and helium ions) have been reported since the 1970s (9, 10), the use of photon-based stereotactic RT (SRT) is more recent and less frequently reported in the literature. Nevertheless, SRT with Gamma Knife and linear accelerators (LINAC) has presented results that are attractive and comparable to those of proton therapy (11–13).

Since 2003, the Division of Radiation Oncology at the McGill University Health Centre has adopted the use of LINAC-based fractionated SRT as a treatment option for patients with choroidal melanomas, and results of this experience are presented in this article.

METHODS AND MATERIALS

Patients and data collection

From April 2003 to December 2009, 50 consecutive patients with juxtapapillary choroidal melanoma treated with SRT were identified from medical records of Montreal General Hospital (McGill University Health Centre) and Notre Dame Hospital (Centre Hospitalier de l'Université de Montréal). Patients included in the study had lesions that were small or medium sized according to Collaborative Ocular Melanoma Study (COMS) classification (14). All lesions were localized within 2 mm of the optic disc and, thus, were not ideal candidates for plaque brachytherapy. They were excluded from the analysis if, at presentation, they had any evidence of echographic extrascleral extension or metastasis.

All information for this retrospective study was prospectively collected in a database and subsequently verified by the patients' corresponding treating physicians to ensure its accuracy. Data regarding patient demographics, ophthalmological information, RT regimen, and follow-up were assessed. Prior to treatment, staging procedures to exclude distant metastasis were performed in all patients and included physical examination, blood tests, chest X-rays, and abdominal ultrasonography. All patients underwent ocular magnetic resonance imaging (MRI) with gadolinium before treatment. The institutional ethics committee provided written consent for the review of patients' information.

Stereotactic RT

Immobilization and voluntary eye fixation. Patients were immobilized using a commercially available relocatable mask system (BrainLab Inc., Feldkirchen, Germany). Eye fixation during computed tomography (CT) scanning and treatment was provided by a voluntary fixation system (see supplementary Fig. E1). The system uses a blinking light-emitting diode that the patient gazes upon and a monitoring camera system to assess eye motion during treatment. The plastic mask was cut in the region of the eye to provide a clear line of sight. The fixation add-on attaches to the indexed metal ring of the mask system, and the position of the light source with respect to the eye can be varied to ensure a comfortable viewing angle for the patient. During treatment, the eye position is monitored on an external display using the camera system, and the treatment is interrupted when any deviations are noticed. For patients with limited or no vision in the involved eye, the eye fixation was performed using the contralateral eye.

Planning technique. All patients underwent orbit MRI with gadolinium for coregistration with the planning CT scans (with contrast). CT scanning was performed using the voluntary eye fixation system but without camera monitoring. A thin slice thickness (<2 mm) was used for both CT and MRI. The eye fixation system was not used during MRI scanning, and therefore, the globe had to be manually fused in MRI and CT scans, as the lesion was not necessarily in the same position relative to cranial anatomy in both scans. The gross tumor volume (GTV) consisted of a composite volume that included the lesion in axial, coronal, and sagittal projections, using both T_1- and T_2-weighted MRI studies. The planning tumor volume (PTV) was the GTV plus a 3-mm margin, as validated in our previous study (15). Critical structures outside the globe (lacrymal glands, optic nerve, contralateral eye, and lens) were outlined on CT alone. Treatment plans, consisting of five to eight conformal fields defined by a micromultileaf collimator (m3 model; BrainLab Inc.), were developed to treat the PTV while minimizing doses to the organs at risk. The first 3 patients received 54 Gy in 9 fractions, and subsequent patients received a total dose of 60 Gy in 10 daily fractions. The treatment was delivered as once-daily fractions for 5 fractions per week over a period of 2 consecutive weeks. With a single isocenter, the dose was prescribed to encompass the PTV with an isodose line that was in the 80% to 90% range (where 100% is the maximum dose), giving a maximum target dose-to-prescription dose ratio in the range of 1.1 to 1.25. A representative dose distribution is shown in supplementary Fig. E2.

Endpoints definition

The primary endpoints of this study were local tumor control, enucleation free-survival, and complication rates. Local progression was defined as a tumor growth of ≥30% in height on ultrasonography compared to baseline within two consecutive posttreatment visits. The complications assessed included neovascular glaucoma, dry eye, optic neuropathy, radiation cataract, retinopathy, optic neuritis, and visual loss. Distant metastasis, disease-specific survival, and overall survival were considered secondary endpoints. Tumor dimensions were analyzed at baseline and posttreatment according to ultrasonography measurements. Tumor volumes were estimated by using the ellipsoidal formula, $\pi/6 \times$ length $\times$ width $\times$ height (16).

Follow-up and complication assessment

Patients were followed every 3 months during the first year and then at 6-month intervals thereafter. If there was any suspicion of