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Brachytherapy vs. external beam radiotherapy for choroidal melanoma: Survival and patterns-of-care analyses

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ABSTRACT

PURPOSE: No modern randomized trials exist comparing external beam radiotherapy (EBRT) and plaque brachytherapy (BT) for choroidal melanoma, and the optimal treatment modality is currently unknown. This study compares the patterns of care and efficacy of EBRT vs. BT based on data in the Surveillance, Epidemiology, and End Results database.

METHODS AND MATERIALS: The Surveillance, Epidemiology, and End Results database was queried for patients aged 20−79 diagnosed with choroidal melanoma from 2004 to 2011, treated with EBRT or BT; included patients were clinically T1−T4, N0, and M0. Overall survival and cause-specific survival curves were calculated by the Kaplan−Meier method. Univariate and multivariate analyses were performed in the survival and patterns-of-care analyses.

RESULTS: A total of 1004 cases (380 EBRT and 624 BT) were included in the survival analysis. There was no difference in the 5-year overall survival (83.3% EBRT vs. 82.5% BT, $p = 0.69$) and 5-year cause-specific survival (88.3% EBRT vs. 88.3% BT, $p = 0.92$). In the survival analysis, older age and advanced tumor stage were predictors of increased risk of death. In the patterns-of-care analysis, later year of diagnosis and smaller tumor stage were predictors of BT use.

CONCLUSIONS: Advanced tumor stage and older age seem to be independent predictors for risk of death from choroidal melanoma. The use of BT favors smaller tumors and later year of diagnosis. There is no difference in survival between those treated with EBRT or BT, and the utilization of BT is increasing.

Keywords: Choroidal melanoma; Uveal melanoma; SEER database; External beam radiotherapy; Eye plaque brachytherapy

Introduction

Choroidal melanoma is the most common primary intraocular malignancy in adults. The age-adjusted incidence of choroidal melanoma is approximately 3.3 per million people in the United States (1). Certain risk factors such as Caucasian race, light eye color, fair skin, and sensitivity to sunlight are thought to be associated with its development (2). Metastases most commonly arise in the liver, followed by the lungs, bone, skin, and central nervous system (3). In general, overall survival (OS) and cause-specific survival (CSS) are favorable but vary widely based on factors such as age, location, size, and extent of disease (4).

The staging of choroidal melanoma has significantly changed over the years. Historically, the Collaborative Ocular Melanoma Study (COMS) had three classifications for choroidal melanoma: small, medium, and large (Table 1) (5−7). The American Joint Commission on Cancer (AJCC) recently changed the staging system for choroidal melanoma in 2010 from the AJCC sixth (Table 2) to the seventh edition, incorporating notable changes into the T-staging (i.e., changes to the size criteria for T1-T4, ciliary body involvement, and amount of episcleral extension) (8).

For patients with COMS small-sized choroidal melanomas, a follow-up study prospectively found that the 5-year all-cause mortality rate was 6%, supporting active surveillance for small, slow-growing tumors (5). Historically, enucleation was the standard of care for COMS medium-sized choroidal melanoma until the publication

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Table 1
COMS tumor staging criteria

Tumor classification	Basal diameter (d)	Apical height (h)	Extraocular extension
Small	5.0−16.0 mm	1.0−3.0 mm	
Medium[a]	≤16.0 mm	2.5−10.0 mm	
Large[b]	>16.0 mm	≥2.0 mm	<2 mm
	Any	>10.0 mm	<2 mm
	Any	>8.0 mm and <2.0 mm to optic disc	<2 mm

COMS = the Collaborative Ocular Melanoma Study.
[a] Until November 1990, tumors 3.1−8.0 mm in apical height were eligible.
[b] Until November 1990, tumors 8.0−10.0 mm in apical height were also eligible.

of initial mortality results from the COMS medium trial comparing ^{125}I plaque brachytherapy (BT) vs. enucleation in these patients (6). With prescribing 85 Gy to the tumor apex using plaque dosimetry based on a modification of the formalism defined in the American Association of Physicists in Medicine Task Group 43 report (9, 10), the 5- and 10-year all-cause mortality rates were 19% and 35%, respectively, and there was no difference in survival between those treated with enucleation vs. plaque BT (11−13). Maximum basal diameter >11 mm and age >60 years were predictors of both decreased time to death from all causes and melanoma metastases. Local control after ^{125}I BT was also favorable, with only 12.5% of patients treated requiring salvage enucleation (11, 13). Five-year OS was also favorable (82% at 5 years). Unfortunately, the predominant pattern of failure is distant, with 25% of patients developing distant failures at 5 years and 92% of patients with metastases succumbing to their disease within 2 years from their metastatic diagnosis (14).

Eye-sparing plaque BT then became the standard of care for medium-sized choroidal melanoma. New radionuclides have been introduced, including ^{106}Ru/^{106}Rh, ^{103}Pd, and ^{131}Cs with the present prescriptive goal to deliver 70−100 Gy to the tumor apex such that the prescription isodose line covers the entire tumor (15, 16).

More recently, there has been an increase in the use of Gamma Knife radiosurgery (GKRS; Elekta; Stockholm, Sweden) and proton beam radiotherapy (PBRT) for the treatment of choroidal melanoma (17−19). Recent reports have shown that GKRS can safely be used with a marginal prescription dose between 20 Gy and 25 Gy to the 50% isodose line (20). Nice Teaching Hospital presented their retrospective data on patients treated with PBRT for uveal melanoma and found 10-year OS results of 86% for T1, 78% for T2, 43% for T3, and 41% for T4 lesions. Overall predictors for death were higher age, greater tumor thickness, larger tumor basal diameter, increased tumor volume, and higher tumor:globe volume ratio (21).

Linear accelerator−based stereotactic radiosurgery (SRS) has also increased in popularity secondary to the publication of many series with acceptable results. Prospective data have shown excellent results in terms of local control (97−98%) and minimal toxicity (17, 22). In addition, dose conformity with linac-based SRS seems comparable with that of PBRT (23).

In 1993, Char *et al.* (24) published the only randomized trial comparing eye plaque BT using ^{125}I and helium ion charged particle therapy using 70 Gy-equivalent delivered over 2 min. Curiously, they found increased local failure with eye plaque (13% vs. 0%) and twice as many enucleations after eye plaque BT than helium ion therapy. No difference in survival was found, although there were more anterior segment complications and toxicities after helium ion therapy. Unfortunately, this older, relatively small trial (184 patients) used helium particles, whereas current charged particle therapy uses more modern treatment techniques and often incorporates the use of PBRT.

For patients who desire and are appropriate candidates for eye preservation, all the therapies discussed previously may be viable treatment options; yet, no large, modern randomized trial exists comparing these modalities. The goal of this retrospective epidemiologic review was to compare OS and CSS between external beam radiotherapy (EBRT) and BT in patients diagnosed with choroidal melanoma and explore the patterns of care over time.

Methods and materials

After filing a completed research agreement, a retrospective analysis was performed using the National Cancer

Table 2
AJCC sixth edition tumor staging criteria

Tumor classification	Basal diameter (d)		Apical height (h)	Extraocular extension
T1	d ≤10 mm		h ≤2.5 mm	
T1a				None
T1b				Microscopic
T1c				Macroscopic
T2	10 mm < d ≤16 mm		2.5 mm < h ≤10 mm	
T2a				None
T2b				Microscopic
T2c				Macroscopic
T3	d >16 mm	and/or	*h* >10 mm	None
T4	d >16 mm	and/or	*h* >10 mm	Any

AJCC = American Joint Commission on Cancer.