Technology in Cancer Research & Treatment
2017, Vol. 16(3) 352–356

DOI: 10.1177/1533034617690979
journals.sagepub.com/home/tct
SAGE

Reproducibility of a Noninvasive System for Eye Positioning and Monitoring in Stereotactic Radiotherapy of Ocular Melanoma

Omar Iskanderani, MD[1,2], Dominique Béliveau-Nadeau, MSc[1], Robert Doucet, MSc[1], Geneviève Coulombe, MD, FRCPC[1], Deborah Pascale, RTT[1], and David Roberge, MD, FRCPC[1]

Abstract

Purpose: Our preferred treatment for juxtapapillary choroidal melanoma is stereotactic radiotherapy. We aim to describe our immobilization system and quantify its reproducibility. **Materials and Methods:** Patients were identified in our radiosurgery database. Patients were imaged at computed tomography simulator with an in-house system which allows visual monitoring of the eye as the patient fixates a small target. All patients were reimaged at least once prior to and/or during radiotherapy. The patients were treated on the CyberKnife system, 60 Gy in 10 daily fractions, using skull tracking in conjunction with our visual monitoring system. In order to quantify the reproducibility of the eye immobilization system, computed tomography scans were coregistered using rigid 6-dimensional skull registration. Using the coregistered scans, x, y, and z displacements of the lens/optic nerve insertion were measured. From these displacements, 3-dimensional vectors were calculated. **Results:** Thirty-four patients were treated from October 2010 to September 2015. Thirty-nine coregistrations were performed using 73 scans (2-3 scans per patient). The mean displacements of lens and optic nerve insertion were 0.1 and 0.0 mm. The median 3-dimensional displacements (absolute value) of lens and nerve insertion were 0.8 and 0.7 mm (standard deviation: 0.5 and 0.6 mm). Ninety-eight percent of 3-dimensional displacements were below 2 mm (maximum 2.4 mm). The calculated planning target volume (PTV) margins were 0.8, 1.4, and 1.5 mm in the anterior–posterior, craniocaudal, and right–left axes, respectively. Following this analysis, no further changes have been applied to our planning margin of 2 to 2.5 mm as it is also meant to account for uncertainties in magnetic resonance imaging to computed tomography registration, skull tracking, and also contouring variability. **Conclusion:** We have found our stereotactic eye immobilization system to be highly reproducible (<1 mm) and free of systematic error.

Keywords

choroidal melanoma, stereotactic radiotherapy, radiosurgery

Abbreviations

CT, computed tomography; ETS, eye tracking systems; IGRT, image-guided radiation; LED, light-emitting diode; MRI, magnetic resonance imaging; 2-D, 2-dimensional; 3-D, 3-dimensional; 6-D, 6-dimensional

Received: August 28, 2016; Revised: December 13, 2016; Accepted: January 03, 2017.

Introduction

Ocular melanoma is a rare disease. The incidence in Canada is approximately 0.7 per 100 000 population per year. This represents approximately 385 cases per year in Canada and 80 cases in the province of Quebec—most of which will be referred to our institution.[1] The reported incidence in the United States is similar, approximately 0.5 new cases per

[1] Department of Radiation Oncology, Centre Hospitalier de l'Université de Montréal (CHUM), Montréal, Québec, Canada
[2] Department of Radiation Oncology, King Abdulaziz University Hospital, Jeddah, Saudi Arabia

Corresponding Author:
David Roberge, MD, FRCPC, Department of Radiation Oncology, Centre Hospitalier de l'Université de Montréal (CHUM), Montréal, Québec, Canada H2W 1T7.
Email: david.roberge.chum@ssss.gouv.qc.ca

100 000 population.[2,3] When treatment is required, small- and medium-sized tumors can be addressed using a wide range of local treatment modalities. Although enucleation remains an appropriate option for selected patients, the Collaborative Ocular Melanoma Study confirmed that organ preservation with radiotherapy can be attempted without impacting overall survival.[4] Based on tumor size, tumor location, patient preference, treatment availability, and the physician's opinion, patients can be offered treatment with laser (including transpupillary thermotherapy), plaque radiotherapy,[5] proton therapy,[6] radiosurgery, stereotactic radiotherapy,[7] or endoresection. In our practice, we choose to offer plaque brachytherapy to most patients but prefer stereotactic radiation for juxtapapillary tumors. The CyberKnife robotic radiosurgery platform is selected to deliver a high dose of radiation in few fractions to a small well-defined target volume within the eye.[8,9] Similar to other radiosurgery platforms, the CyberKnife can accurately target structures having a rigid relationship to the skull; however, it does not provide a means to track eye movement. We achieve eye immobilization using an in-house system of which we sought to characterize the reproducibility. The more accurate and stable the eye fixation system, the tighter the planning margins and therefore the smaller the volume of normal retina to be irradiated.

Methods

This study was approved by our local ethics review board, and specific consent was obtained for photographing an actual patient setup. We retrospectively identified patients treated from October 2010 through September 2015 with fractionated stereotactic radiotherapy for a choroidal melanoma. As previously described, patients underwent a planning magnetic resonance imaging (MRI) during which motion was attenuated by having the patient focus on a dot within a multichannel head coil. Two sequences are obtained, a thin-slice volumetric Dixon sequence and a fast 3-dimensional (3-D) gradient-echo gadolinium-enhanced sequence. It is at computed tomography (CT) simulation that our custom immobilization device was used. All patients are immobilized supine in a standard thermoplastic mask with a cutout for the affected eye (for patients unable to see with the diseased eye, immobilization is based on the seeing eye). Our device provides a light-emitting diode (LED) for the patient to focus on—the position of which can be recorded and reproduced (Figure 1). A camera system allows monitoring of patient compliance. At simulation, the position of the iris is marked on a transparency overlaid on the video monitor linked to the device's camera. The simulation CT is acquired with 1-mm slice spacing and a field of view sufficient to visualize the entire immobilization device. In the planning system (Multiplan; Accuray, Sunnyvale, California), CT and both MRI sequences are manually coregistered using the insertion and the optic nerve and lens as principle landmarks (the dot used in the MRI only insures gross similarity in preregistration ocular orientation and aids in reducing motion artifacts). The gross tumor volume (GTV) is segmented using both MRI sequences and fundus schema. A 2- to 2.5-mm planning target volume (PTV) margin is added, which is trimmed where it obviously extends beyond the sclera. Organs at risk (oral cavity, contralateral eye, ipsilateral lens, optic nerve, and lachrymal gland) are contoured, the collimator is selected, and beam paths passing through the immobilization device are blocked. The plan is optimized using our previously described methodology.[9] Prior to treatment, the mask and device are brought to the linear accelerator to confirm that no collisions are possible. The patients were all treated in 10 daily fractions of 6 Gy. Each day, eye position was confirmed to coincide with the patient-specific transparency from simulation. The therapists thus continuously monitored patient compliance during treatment with the ability to interrupt treatment in case of noncompliance. As a typical fraction would last half an hour, the patients were given multiple breaks to rest their eye. As a quality assurance measure of our system, all patients were reimaged at least once prior to and/or during radiotherapy. In order to quantify the reproducibility of the eye immobilization system, CT scans were coregistered using rigid 6-D registration (Eclipse; Varian Medical Systems, Palo Alto, California). With the scans coregistered, x, y, and z displacements of the lens/optic nerve insertion were measured manually in 3-D (Figure 2). From these displacements, 3-D vectors were calculated. We calculated the PTV margin, which would account for 98% of this uncertainty, using a published 2-parameter model ($2.27 \times \Sigma_p$).[10,11]

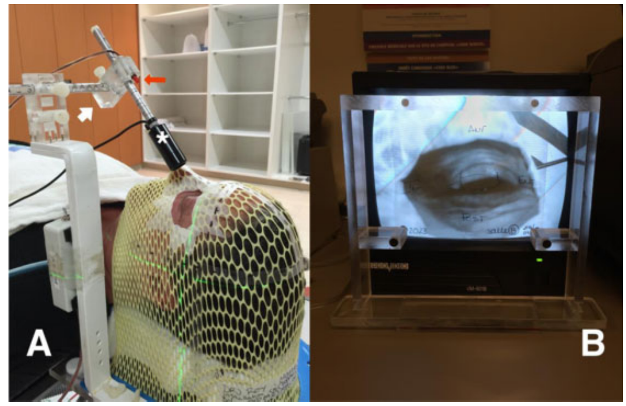

Figure 1. Patient in the immobilization system (A) and outside monitor (B) with marked overlay. The light-emitting diode (LED) is indicated by a red arrow, the camera with a star, and the indexed arm with a white arrow.

Results

Thirty-four patients were identified (Table 1); 39 coregistrations were performed using 73 scans (2-3 scans per patient). Thirty-one patients fixed the LED with the diseased eyed and 3 patients with the contralateral eye. All patients were treated with CyberKnife stereotactic radiotherapy with a median number of fields of 79 (148-50) delivered during a median of 36 minutes (59-26 minutes). The median number of days between image sets was 15 (6-42 days). Based on measurements in the

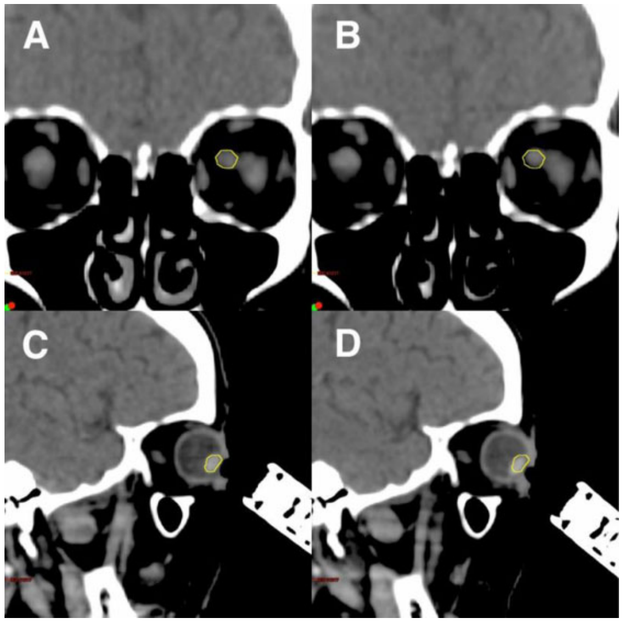

Figure 2. Skull-based coregistration between planning (A/C) and midtreatment (C/D) scans showing superolateral displacement of the optic nerve and inferior displacement of the lens.

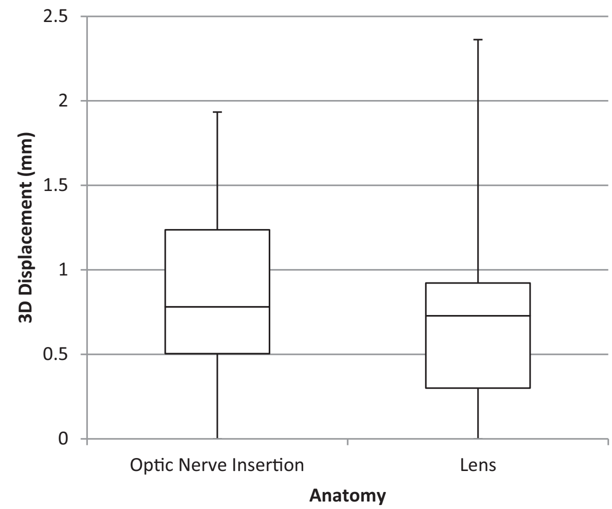

Figure 3. Distribution of 3-dimensional (3-D) displacements of lens and nerve insertion.

Table 1. Patient Characteristics.

Median age (range)	(59) 26-88
Sex	17 male; 17 female
Eye	14 right; 20 left
Median visual acuity (range)	6/15 (6/6-finger counting)
Median tumor diameter (range)	12 mm (5-20 mm)
Total dose	60 Gy in 6 Gy fractions

coregistered scans, the mean displacements of lens and optic nerve insertion were 0.1 and 0.0 mm. There was thus no systemic shift in eye position from planning to treatment. The median 3-D vectors (absolute value) of the lens and optic nerve insertion were 0.8 and 0.7 mm (standard deviation: 0.5 and 0.6 mm). Ninety-eight percent of 3-D displacements was below 2 mm (maximum 2.4 mm; Figure 3).

Using the 2-parameter model, the calculated PTV margins were 0.8, 1.4, and 1.5 mm in the anterior–posterior, craniocaudal, and right–left axes, respectively.

Discussion

High-precision cranial radiosurgery and stereotactic radiotherapy have long been possible through more or less invasive immobilization of the skull. The role of immobilization systems has changed with the advent of image-guided radiation (IGRT). In the era of IGRT, cranial immobilization needs only reproducing a head position close enough to that at simulation in order to allow correction at the treatment device. The system should not interfere with imaging and should limit movement during treatment.

The treatment of intraocular tumors is complicated by potential movement of the eye relative to the skull.[12,13] Intraocular tumors are often difficult to visualize even on diagnostic imaging, and thus surrogates for the tumor are used in IGRT. Position of the tumor is inferred from the position of the eye as a whole, the iris, or implanted markers. Ocular motion is mostly rotational, although there may be minor translations. Translation is mostly in the horizontal axis as Whitnall's ligament above and Lockwood's ligament below limit vertical translation.[14-16]

In general, systems for eye immobilization can be dichotomized as invasive or noninvasive. An exception would be the tantalum buttons which are sutured around the tumor in proton therapy. Although cumbersome to implant, these are easily discerned on 2-D image guidance X-ray images.[17] The systems which require contact with the patient include those using retrobulbar or peribulbar anesthesia, installation of custom contact lenses,[18] suction fixation devices,[14] or suturing of the anterior sclera to a conventional radiosurgery frame.[19] Noninvasive systems typically combine a standard means of immobilizing the head, a target for the patient to fixate, and a means of monitoring compliance through visualization of the iris. Daftari et al have described such a system using a standard thermoplastic mask and 2 articulated plastic arms. An LED is attached to 1 arm and a mirror mounted to the second. A closed-circuit television (CCTV) is used to monitor the pupil from the treatment console.[20] The general principle of this device is similar to ours; however, our device is indexed and compact. Our device is attached to the mask system, with indexing providing a means to verify that diode and camera do not move (as well as allowing the treatment of multiple concurrent patients). Other such devices have been described with variations in the immobilization system, fixation target, and monitoring system.[12,21,22] With current IGRT technology (including the stereoscopic system used in the CyberKnife), aggressive immobilization of the head with dental plates would now appear superfluous.[23] In the published descriptions of ocular immobilization systems, the accuracy is typically not evaluated in patients or may be based on theoretical correlations between pupillary stability and treatment accuracy. One exception is the report of Buchgeister et al.[15] In this report, an invasive Brown-Roberts-Wells (BRW) headring is coupled with a set of goggles that support a light for the patient to fix. Twenty patients were scanned twice, and the 2-D (right-left and up-down) position of the insertion of the optic nerve was compared on the paired scans. The average displacement was 0.7 mm with a maximum of 2.4 mm. Although this immobilization system is no longer relevant today, the findings are in keeping with our own.

More sophisticated methods have been proposed for eye tracking and eye tracking systems (ETS). There is ample work done in tracking eyes during interaction with computer screens, and the relevant principles have been translated to radiotherapy. An example ETS used 3-D video-oculography to detect ocular features on a video stream coming from a pair of calibrated cameras. The glints and the pupil center are recognized on the calibrated camera images and their 3-D position calculated through triangulation. Eye torsion is thus also assessed and taken into account. The coordinates of the tumor with respect to the eye local reference system are estimated during treatment planning.[24] Although such systems may improve accuracy by a fraction of a millimeter, the rarity of ocular tumors makes it highly unlikely that sophisticated systems will be commercialized or acquired by radiotherapy departments. We present an extensive quantitative clinical evaluation of a noninvasive ocular immobilization system. We have found our simple system to be satisfactorily accurate—this is in part due to the fact that we record and verify the position of the eye fixation target. Although we have implemented our system with a specific fractionation scheme and delivery device, our findings translate to a wider range of stereotactic ocular treatments. Our patients had tumors near the optic nerve, but the magnitude of the potential 3-D displacement should be the same everywhere along the outer surface of the eyeball as it is essentially a rigid structure. Our technique can certainly be further refined. For example, we now allow the mask to dry at least 24 hours prior to simulation to allow for maximal shrinkage presimulation. After having treated more than 50 patients, our confidence in the system has improved to a point where the midtreatment resimulation may be unnecessary in order to reassure us that the setup is stable. The position of our device was similar for all patients and was chosen to minimize interference with imaging and treatment. However, for selected patients with lateral tumors, there may be a benefit to optimizing gaze in order to better spare the lachrymal gland. Our quantitative data using 3-D vectors indicated that our system was highly reproducible. The PTV margins we use would be excessive if they aimed only to account for immobilization of the eye and targeting accuracy. Following this work, we have not changed our GTV to PTV margin of 2 to 3 mm as it is also meant to account for uncertainties in planning MRI to CT registration, skull tracking, and also contouring variability.

Conclusion

A simple in-house indexed monitoring system is used for ocular stereotactic radiotherapy. When patients were reimaged with the device, there was no systematic shift and the median 3-D vectors (absolute value) of the displacements of the lens and optic nerve insertion (relative to the skull) were 0.8 and 0.7 mm. Ninety-eight percent of the 3-D displacements were below 2 mm. We continue to use this device in daily practice.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: David Roberge has received honoraria and research support unrelated to this work from Accuray Inc.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Dr Roberge has received honoraria and research support from Accuray Inc.

References

1. Statistics Canada. Health indicator profile, annual estimates, by age group and sex, Canada, provinces, territories, health regions (2013 boundaries) and peer groups. 2016. http://www5.statcan.gc.ca/cansim/a26?lang=eng&retrLang=eng&id=1030553&pattern=cancer. Accessed March 15, 2015.
2. Singh AD, Topham A. Incidence of uveal melanoma in the United States: 1973-1997. *Ophthalmology*. 2003;110(5):956-961.
3. Singh AD, Turell ME, Topham AK. Uveal melanoma: trends in incidence, treatment, and survival. *Ophthalmology*. 2011;118(9): 1881-1885.
4. Singh AD, Kivela T. The collaborative ocular melanoma study. *Ophthalmol Clin North Am*. 2005;18(1):129-142, ix.
5. Lommatzsch PK, Lommatzsch R. Treatment of juxtapapillary melanomas. *Br J Ophthalmol*. 1991;75(12):715-717.
6. Seddon JM, Gragoudas ES, Egan KM, et al. Uveal melanomas near the optic disc or fovea. Visual results after proton beam irradiation. *Ophthalmology*. 1987;94(4):354-361.
7. Emara K, Weisbrod DJ, Sahgal A, et al. Stereotactic radiotherapy in the treatment of juxtapapillary choroidal melanoma: preliminary results. *Int J Radiat Oncol Biol Phys*. 2004;59(1): 94-100.
8. Phillips MH, Stelzer KJ, Griffin TW, Mayberg MR, Winn HR. Stereotactic radiosurgery: a review and comparison of methods. *J Clin Oncol*. 1994;12(5):1085-1099.
9. Béliveau-Nadeau D, Callejo S, Roberge D. Technique for robotic stereotactic irradiation of choroidal melanoma. *Cureus*. 2016; 8(4):e582.
10. Yan D, Lockman D, Martinez A, et al. Computed tomography guided management of interfractional patient variation. *Semin Radiat Oncol*. 2005;15(3):168-179.
11. Shah C, Kestin LL, Hope AJ, et al. Required target margins for image-guided lung SBRT: assessment of target position intrafraction and correction residuals. *Pract Radiat Oncol*. 2013;3(1): 67-73.

12. Dieckmann K, Bogner J, Georg D, Zehetmayer M, Kren G, Potter R. A linac-based stereotactic irradiation technique of uveal melanoma. *Radiother Oncol*. 2001;61(1):49-56.
13. Dieckmann K, Zehetmayer M, Poetter R. Fractionated stereotactic radiotherapy for choroidal melanoma. *Radiother Oncol*. 1998; 49(2):197.
14. Eter N, Schuller H, Spitznas M, Klein W, Schuttoff T. Fixation monitoring during radiation therapy for subfoveal neovascularization. *Graefes Arch Clin Exp Ophthalmol*. 1998;236(11):806-810.
15. Buchgeister M, Grisanti S, Susskind D, Bamberg M, Paulsen F. A new fixation aid for the radiotherapy of eye tumors. *Med Phys*. 2007;34(12):4649-4653.
16. Via R, Fassi A, Fattori G, et al. Optical eye tracking system for real-time noninvasive tumor localization in external beam radiotherapy. *Med Phys*. 2015;42(5):2194-2202.
17. Brockhurst RJ. Tantalum buttons for localization of malignant melanoma in proton beam therapy. *Ophthalmic Surg*. 1980;11(5):352.
18. Van de Voort MR. Fixation of the eye in radiological treatment of retinoblastomas. *Radiol Clin Biol*. 1973;42(1):30-33.
19. Furdova A, Sramka M, Chorvath M, et al. Stereotactic radiosurgery in intraocular malignant melanoma—retrospective study. *Neuro Endocrinol Lett*. 2014;35(1):28-36.
20. Daftari IK, Petti PL, Larson DA, O'Brien JM, Phillips TL. A noninvasive eye fixation monitoring system for CyberKnife radiotherapy of choroidal and orbital tumors. *Med Phys*. 2009; 36(3):719-724.
21. Bogner J, Petersch B, Georg D, Dieckmann K, Zehetmayer M, Potter R. A noninvasive eye fixation and computer-aided eye monitoring system for linear accelerator-based stereotactic radiotherapy of uveal melanoma. *Int J Radiat Oncol Biol Phys*. 2003; 56(4):1128-1136.
22. Adamczyk M, Janiga P. Staged radiosurgical ablation for choroid melanoma: a case report with emphasis on the role of patient preparation, treatment planning, and precision of delivery. *Cureus*. 2016;8(5):e611.
23. Jaywant SM, Osei EK, Ladak S. Stereotactic radiotherapy in the treatment of ocular melanoma: a noninvasive eye fixation aid and tracking system. *J Appl Clin Med Phys*. 2003;4(2): 156-161.
24. Ruegsegger MB, Geiser D, Steiner P, Pica A, Aebersold DM, Kowal JH. Noninvasive referencing of intraocular tumors for external beam radiation therapy using optical coherence tomography: a proof of concept. *Med Phys*. 2014;41(8): 081704.