3D Wrap™ Ultra-Widefield Reconstruction in Stereotactic Radiosurgery for Choroidal Melanoma

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Established Facts

- Gamma knife radiosurgery (GKR) has demonstrated encouraging results in the treatment of choroidal melanoma in terms of survival and local tumor control.
- GKR might be limited by potential damage to the healthy adjacent eye structures, such as optic nerve pathway, lens, and lacrimal glands.
- Pre-radiosurgical planning of the position of the eye is important for determining stereotactic coordinates of applied radiation, increasing safety and tolerability of the treatment.

Novel Insights

- A recently released ultra-widefield imaging instrument (Optomap California; Optos, Dunfermline, Scotland, UK) allows for an interactive three-dimensional (3D) virtual reconstruction of the globe, called 3D Wrap™.
- 3D Wrap™ is able to simulate the position of the tumor and its relationship with the other ocular structures.
- This tool provides rapid, reliable, and relatively easy support in planning the final globe positioning before GKR treatment.

Keywords

Choroidal melanoma · Ultra-widefield imaging · Gamma knife radiosurgery

Abstract

Choroidal melanoma (CM) is the most commonly diagnosed primary intraocular malignancy in adults. Gamma knife radiosurgery (GKR) has demonstrated reliable results in the

treatment of CM, but it is limited by the risk of radiation-induced ocular complications. To optimize the dose of radiation focused on the tumor, and limit side effects, the eye should be properly immobilized before treatment. A recently released ultra-widefield imaging instrument (Optomap California; Optos, Dunfermline, Scotland, UK) allows for an interactive three-dimensional (3D) virtual reconstruction of the globe, called 3D Wrap™. The authors share their experience with this rapid, reliable, and relatively easy support in planning globe positioning before GKR treatment.

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Introduction

Choroidal melanoma (CM) is the most commonly diagnosed primary intraocular malignancy in adults, and its frequency is around 2–8 cases per million per year in the USA and in Europe [1, 2]. Despite advancements in diagnosis and treatment, it remains a life-threatening tumor, with an overall mortality rate of up to 40–50% in 15 years, mainly due to systemic metastasis [3].

Strategies for local control of CM have significantly evolved over the past few decades, shifting from more destructive procedures (e.g., enucleation, orbital exenteration) to more conservative globe-sparing techniques. At present, plaque brachytherapy (iodine-125 or ruthenium-106) [4], proton beam radiotherapy [5], stereotactic radiotherapy [6], and stereotactic radiosurgery [7, 8] are among the most commonly employed approaches for localized middle-sized and selected large-sized lesions, with survival rates similar to enucleation [9].

Gamma knife radiosurgery (GKR), initially developed for the treatment of intracranial lesions, has shown promising results in the treatment of intraocular CM in terms of survival and local tumor control [10, 11]. In comparison to other treatment modalities, GKR usage has been limited by the risk of potential damage to the healthy adjacent eye structures [12], leading to sight-threatening complications.

Several studies have highlighted the importance of preradiosurgical planning of GKR, especially for ocular critical structures. In this view, modern imaging techniques, along with traditional ones (namely ultrasound, optical coherence tomography, computed tomography, and magnetic resonance imaging [MRI]) may play a pivotal role in increasing the safety and the tolerability of the treatment. Integrated data from all the aforementioned imaging techniques accurately delineate

the anatomical structures, differentiate the targeted tumor mass from the surrounding tissue, and recognize the most critical structures to be spared (i.e., optic nerve and chiasma, brain stem, lacrimal gland, and lens).

Among these techniques, ultra-widefield imaging has shown fairly good diagnostic accuracy in differentiating retinal malignant pigmented tumors from nonmalignant lesions [13]. UWF Optomap California (Optos, Dunfermline, Scotland, UK) captures up to 200° of the retina in a single shot, and, along with a flat two-dimensional pseudo-color photograph, provides an interactive 3D virtual reconstruction of the globe, called 3D Wrap™ [14]. We share our experience with the 3D Wrap™ tool in planning GKR treatment for intraocular CM.

Case Report

Starting from January 2016, all the patients with a diagnosis of CM candidate to GKR, presenting at the Ocular Oncology Service of San Raffaele Scientific Institute, Milan, Italy, have been included in this imaging protocol. The diagnosis and clinical characteristics of CM were established on the basis of complete ophthalmological evaluation, A- and B-scan ultrasonography, fluorescein and indocyanine green angiography. For patients in whom extraocular invasion of CM was suspected, MRI was also performed. Optomap photography was performed 7 days (max.) before the scheduled treatment.

In our practice, on the day of GKR, after retrobulbar anesthesia with long-acting agents (5 ml of 1% ropivacaine), two extraocular recti muscles are sutured through the conjunctiva using 3.0 black silk suture and then fixed to the stereotactic frame. The globe is fixed in order to localize the lesion as closely as possible to the center of the frame. Then, high-resolution 2-mm MRI with gadolinium is performed, “dose conformation” around the stereotactic region of interest (ROI) is planned, and irradiation is delivered in one single session [7]. While the dose and ROI strategy is made exclusively by the radiation oncologist, the choice of which two muscles to anchor is reserved to the ophthalmologist. The location of the tumor inside the globe is the main parameter influencing this choice.

The 3D Wrap™ was able to realistically replicate the exact position of the tumor and its relationship with the other ocular structures (especially the optic nerve, the macula, and the lens) in the primary position. In addition, the globe could be actively twisted by the operator. By rotating the eyeball, the ophthalmologist might simulate the action of each singular extraocular muscle, deciding which one is more suitable to be pinched to the stereotactic frame. An example of a 73-year-old female with a CM in the right eye is provided in Figure 1.

The authors found significant support with the 3D Wrap™ software in achieving the final globe positioning during GKR treatment; having the printout of the previously oriented globe directly in the radiosurgery department facilitates not only the selection of the muscle, but also the exact anchoring sites for silk sutures on the

Fig. 1. Three-dimensional (3D) virtual reconstruction (3D Wrap™) coupled with ultra-widefield (UWF) imaging of an eye with choroidal melanoma. **a** UWF pseudo-color fundus photography of a right eye with a choroidal melanoma in the superonasal

quadrant. **b** Magnetic resonance imaging (MRI) of the orbits and its magnification (**c**) of the right eye. **d–f** 3D Wrap™ reconstructions of the same eye, with different orientations, showing a very good correspondence with the MRI.

Leksell stereotactic frame. In the absence of the printout, decision relying solely on the ultrasonography or traditional fundus photography might be more challenging for the eye specialist, especially if not fully confident with the technique.

A fair overlap between the virtual image and the anatomical features of the tumor on MRI was appreciated. Finally, the pseudo-color retinography acquired pre-treatment worked well as baseline documentation for comparing reference during the post-treatment follow-up (Fig. 1).

Discussion/Conclusion

The primary advantage of GKR is preservation of the globe, with complete or relative sparing of the visual function [15]. GKR also represents a precious resource in cases where brachytherapy is contraindicated, as large tumors (greater than 15 mm in diameter or 10 mm in height) or lesions within 2 mm from the optic disc [16]. Nevertheless, in the series previously published reporting the outcome of GKR in CM, several side effects have been reported, including cataract, dry eye disease, exudative retinopathy, neovascular glaucoma, vitreous hemorrhage, radiation retinopathy, radia-

tion papillopathy, and optic nerve atrophy [15]. The optic nerve pathway, as well as the lacrimal glands, have been shown to be particularly radiosensitive; their damage is linked not only to severe irreversible visual impairment, but also to significantly reduced quality of life [17, 18]. One of the first strategies that have been successfully introduced to limit GKR side effects relied either on fractionation [19] or on reduction of the global dose of irradiation; according to Schirmer et al. [20], a marginal tumor dose less than 25 Gy has been proven to provide excellent local tumor control with limited local and regional damage.

Recently, further improvement in understanding the quantitative correlation between dose-volume parameters and clinical side effects has led to the identification of major risk factors associated with severe visual loss after GKR. In detail, the fraction of the posterior segment receiving more than 20 Gy, Bruch's membrane rupture and tumor thickness have been identified as significant prognostic factors for neovascular glaucoma, while a discriminative dose received by 1% of the optic nerve greater than 14.9 Gy has been found to be significantly linked to increased risk of radiation retinopathy and radiation papillopathy [15].

At the time of the treatment, two parameters are important for determining the stereotactic coordinates of radiation that will be applied to the targeted masses: the position of the head and the relative position of the eye. To optimize the dose of radiation focused on the tumor, any movement of the eye with CM during the treatment must be prevented. Despite a sophisticated noninvasive method of eye immobilization relying on eye tracking has been proposed [21], our experience favors the use of retrobulbar anesthesia and passively positioning of the globe by means of temporary transconjunctival sutures fixed to the stereotactic head frame [7].

In 2015, a three-dimensional (3D) printing eye model (Simplify3D®, Cincinnati, OH, USA) was invented and revealed to be particularly useful in obtaining a realistic idea of the eye with CM before the stereotactic planning process, not only in optimizing dosimetry, but also in avoiding subjective errors in positioning of the eye before the treatment [22]. However, this method requires a dedicated software, 3D printer equipment, and selected folding material; not less important, the entire process may take hours or even days to print a 3D model (depending on its complexity and resolution). This leads to consistent direct and indirect costs that may severely limit the diffusion of such a method as a routine preplanning procedure.

We propose a rapid, reliable, and relatively easy to obtain method of globe visualization, based on 3D Wrap™ reconstruction, which does not need exposure of the patients to supplementary imaging examinations. We think that this device provides a consistent support to the eye specialist in the choice of the final globe orientation. Nevertheless, it does not give any clue about the area of the globe to be included in the treatment ROI and the final dosimetry plan.

Further longitudinal studies are warranted to assess the potential role of this tool in the prediction of the amount of radiation-related complications, and in the

planning of any preventive treatment. Our opinion is that innovative imaging techniques combined with modern dosing and treatment modalities would provide valuable advantages regarding the planning and execution of GKR in the setting of both primary and metastatic intraocular lesions.

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Statement of Ethics

Starting from January 2016, all the patients with a diagnosis of CM candidate to GKR, presenting at the Ocular Oncology Service of San Raffaele Scientific Institute, Milan, Italy, have been included in this imaging protocol, performed in accordance with the ethical standards laid down in the Declaration of Helsinki, and approved by the Institutional Review Board of the IRCCS San Raffaele Scientific Institute. Ethics Committee approval and written informed consent for publication were obtained by each participating patient.

Disclosure Statement

The authors have no competing interest in publishing the present work.

Author Contributions

All the authors contributed to the conception or design of the work, the acquisition, analysis and interpretation of data, drafting the work, revising it critically for important intellectual content and gave final approval of the version to be published.

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