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Case report

# Frameless radiosurgery for intraocular metastatic tumor: Case report

*Jose Ramón Villarreal Cárdenas*[a], *Agustín del Valle Penella*[b], *Erick Cardona Ibarra*[c,*]

[a] *Department of Radiosurgery, Hospital Alta Especialidad Christus Muguerza, Monterrey, Nuevo León, México*
[b] *Ophtalmological Institute, Montemorelos, Nuevo León, México*
[c] *Derpartment of Physics, Hospital Alta Especialidad Christus Muguerza, Monterrey, Nuevo León, México*

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ABSTRACT

*Aim:* The aim of this case report is to describe the technique and response using frameless radiosurgery technique in intraocular metastases.
*Background:* Intraocular metastases are the most common malignant lesion within the eye and its prevalence is probably underestimated. This is of great interest for oncologist as there are new treatment options with high rates of tumor control maintaining patient's quality of life.
*Case Report:* We report a case of a 54-year-old female with intraocular metastases from breast cancer using a frameless radiosurgery technique allowing organ preservation.
*Conclusion:* The frameless robotic radiosurgery system is feasible and comfortable option for patients with intraocular metastases. Treatment planning and delivery requires an experienced interdisciplinary team.


## 1. Introduction

Sophisticated radiation techniques have allowed better targeting ablative radiation doses to tumors as an alternative to surgical treatments and conventional radiotherapy. The CyberKnife (Accuray Inc., Sunnyvale, CA) system allows paramount conformal precision, thus limiting damage to surrounding healthy tissue using a non-invasive fixation technique.[1] This highly sophisticated technology has the ability to fractionate treatment dose, allowing healthy cells to recover while damaging tumor cells, becomes a valuable alternative for intraocular tumors.

Intraocular metastases are rare, yet they are estimated to occur in approximately 2–7% of patients with solid tumors.[2] Due to an improvement in survival among cancer patients and improvements in radiological imaging, the diagnosis of intraocular metastases appears to be increasing.[3] Patients' symptoms vary according to size and location of the tumor, most presented with visual loss, floaters, photopsia or diplopia, affecting significantly their quality of life.

* *Corresponding author at:* Derpartment of Physics, Hospital Alta Especialidad Christus Muguerza, Hidalgo No. 2525, Col. Obispado, Centro Médico Christus Muguerza Consultorio 500A, Monterrey, Nuevo Léon CP 64060, Mexico.
E-mail address: ecar307@gmail.com (E.C. Ibarra).
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In this report, we describe a case using Cyberknife frameless robotic radiosurgery for intraocular metastatic tumor.

## 2. Materials and Methods

### 2.1. Clinical history

The patient was a 54-year-old female diagnosed with invasive stage IIIA (T2N2M0) triple negative right breast cancer since June 2014. Initially, she was treated with neoadjuvant chemotherapy based on AC (doxorubicin/cyclophosphamide) and docetaxel followed by total mastectomy and axillary dissection. Post neoadjuvant staging was ypT1$_{mic}$N1M0. Adjuvant local therapy with radiation to the chest wall, infra and supraclavicular region and axillary bed was administrated. Then, she was continued under surveillance until October 2017, diagnosed with bone and lung metastases. Chemotherapy regimen for stage IV Her2-negative disease was initiated based on anti-metabolites (capecitabine) cycled every 21 days.

In March 2018, she presented abrupt onset of blurred vision and floaters in her right eye (OD) with no prior ocular disease. Upon examination, best-corrected visual acuity was 20/400 OD and 20/20 in the left eye (OS), considered legally blind OD. Fundoscopic examination OD revealed diffuse cream colored lesions affecting the four quadrants with intrinsic vessels in the papillomacular bundle (Fig. 1A). Ocular ultrasonography mode AB reported a high reflective irregular thickness associated with metastatic tumor (Fig. 1B). Fluorescein angiography showed slow hyperfluorescence during the arterial phase with persistent pinpoint leakage. OS reported without abnormalities.

The case was evaluated in a multidisciplinary tumor board recommending robotic radiosurgery to preserve the eye globe and quality of life.

### 2.2. Treatment description

A computerized tomography (CT) scan (1.25 mm slice thickness) and brain gadolinium-enhanced Magnetic Resonance Imaging (MRI) (0.5 mm slice thickness) was performed after administering retrobulbar anesthesia for complete akinesia of the globe within the orbit. The patientś head was immobilized using a thermoplastic mask fixed to the treatment table.

Gross tumor volume (GTV) defined as a macroscopic tumor visible on the T1-weighted MRI axial sequences rigidly registered to the planning CT with simultaneous reconstructions of the outlines on sagittal and coronal views. No margins were given to GTV to create clinical target volume (CTV) and planning target volume (PTV), due to the location of the lesion. PTV volume was 4.39 cc. Organs at risk (OARs) outlined included the left and right eye, optic nerves, chiasm and lenses. A highly conformal plan was created using the CyberKnife treatment planning workstation and Multiplan® inverse planning software, version 3.5.1. with a non-isocentric and non-coplanar technique. (Fig. 2)

Treatment was delivered using the 6D Skull Tracking System (Accurray, Inc., Sunnyvale, CA) which allows tracking in real time to correct for translational and rotational motion of the target within a range of 0.5–10.0 mm and 1°–3°, respectively. A total dose of 18 Gy was administered in a single fraction prescribed to the 77% isodose line.

### 2.3. Follow up

Follow up visits were scheduled at 2 weeks after treatment and every three months. The valuation included clinical and imaging assessment. Acute and late toxicity was registered according to Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer (RTOG/EORTC) Scale.[4] Tumor response was evaluated using the RECIST 1.1 scale.[5]

### 2.4. Results

The patient reported total blindness two months after treatment. No corneal ulceration, keratitis, cataract or glaucoma was registered. Fundoscopic evaluation at 6 months reported extensive splinter and blot hemorrhages surrounding the disc and extended into all quadrants of the retina highly suggestive of central retinal vein occlusion. (Fig. 3A) Tumor response by ultrasonography image reported 60% decrease of the lesion thickness at follow-up 6 months later, defined by the RECIST 1.1 criteria as a partial response. (Fig. 3B)

## 3. Discussion

It has been over a century since Perls described the first case of choroidal metastasis, currently ocular metastases are recognized as the most common intraocular malignancy.[6–8] Primary breast cancer accounts for the majority of cases, fol-

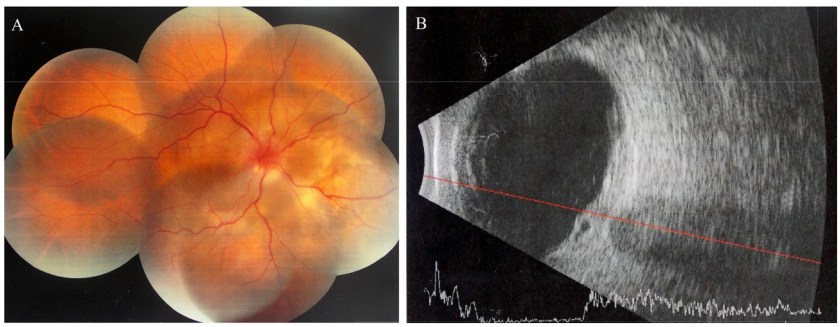


**Fig. 1 – Fundoscopy evaluation of the right eye showing cream colored lesions involving nasal, superior and temporal periphery. (A) Ultrasonography image with choroidal tumor with irregular borders (B).**

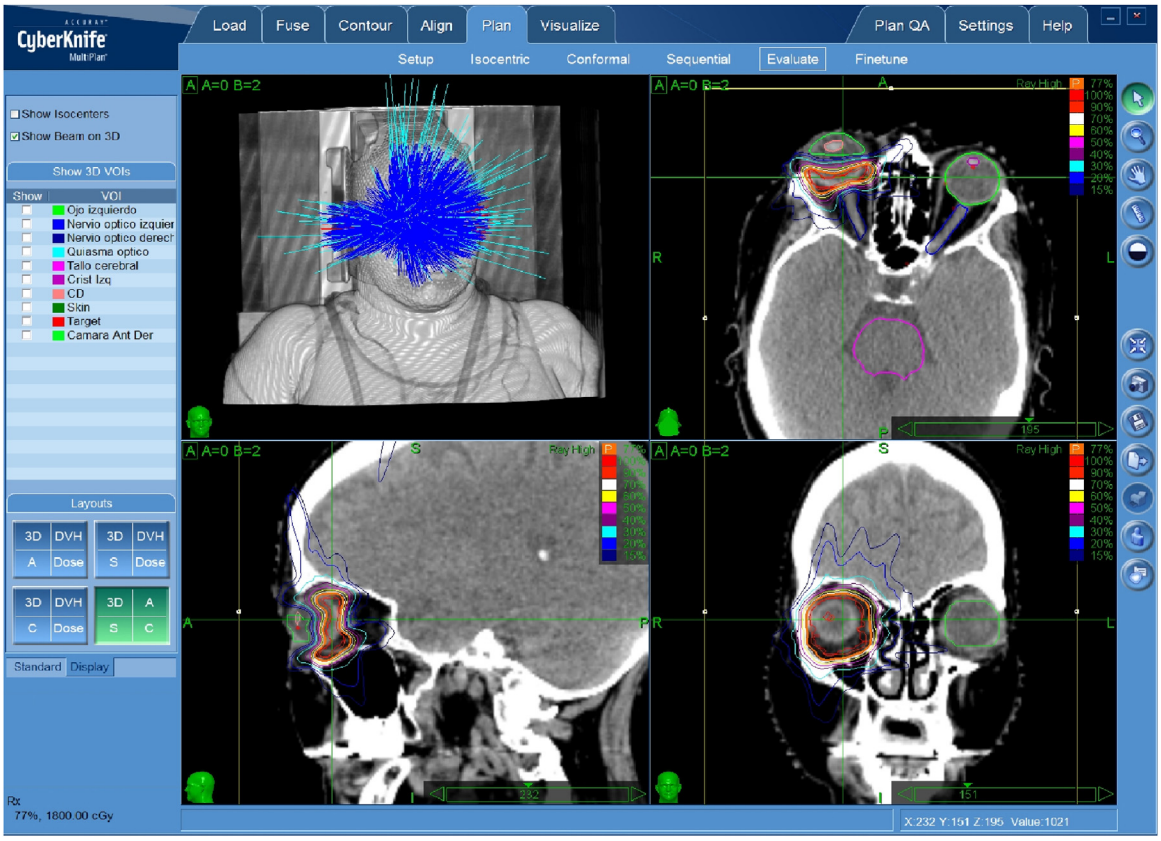


**Fig. 2 – Treatment planning with a non-isocentric technique to deliver high dose radiation to the target while sparing organs at risk using a frameless radiosurgery CyberKnife system.**

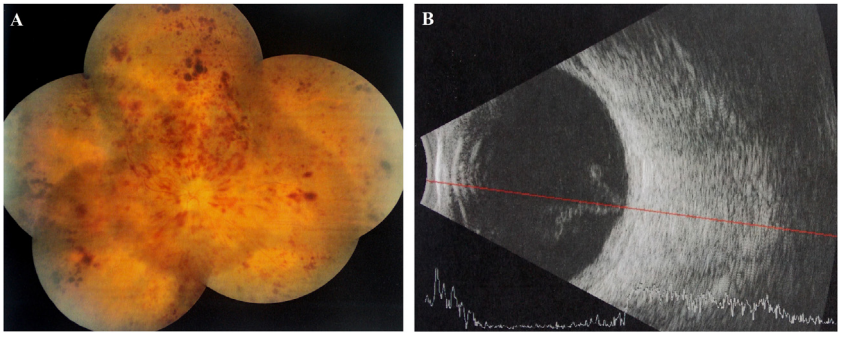


**Fig. 3 – Fundoscopy evaluation after radiosurgery of the right eye showing diffuse splinter and blot hemorrhage extended into all quadrants of the retina. (A) Ultrasonography image revealed decrease in thickness due to partial response of the tumor (B).**

lowed by the lung, skin or gastrointestinal tract.[9,10] The most common location within the intraocular space is the choroid metastases, due to the nature of choroidal circulation. Patients usually report abrupt blurred vision, diplopia, floaters and pain.

Diagnosis is mainly based on clinical evaluation and imaging studies. Dilated fundoscopic examination presents with a yellowish/cream, elevated, diffuse lesion with irregular borders. Multifocal lesions are found in approximately 25% of cases.[11] Ecographically, internal reflectivity is generally medium to high, usually lie deep in the macular region and is associated with retinal detachment.[12] Fluorescein angiography pattern of metastatic choroid tumors usually presents with early and continued progressive fluorescence; however, it is difficult to distinguish from choroidal melanomas and hemangiomas.[13]

Intraocular metastases are associated with poor prognosis due to its association with diffuse metastatic disease. However, with new therapeutic options, patients may have longer survival periods with good quality of life. Therefore, these patients can be candidates for organ preservation treatments maximizing their function with quick alleviation of

symptoms. Systemic therapies rarely yield a durable response in choroidal metastases and symptoms potentially rebound or worsen after discontinuation. Local treatments can offer a cost-effective widely feasible consolidative and definitive option.

Radiotherapy is the most common local treatment, options include brachytherapy plaque, external beam irradiation (EBRT), proton beam irradiation and radiosurgery. Brachytherapy plaque technique has had good results; however, it is an invasive procedure where success rate depends on the experience of radiation oncologist and ophthalmologist.[14] Photon beam radiotherapy is well known to achieve great local control rates, but proton centers are scarce and treatment cost considerably higher.

EBRT has proven to be an effective treatment for intraocular metastases with the strongest experience among other treatments. As regard dose and fractionation, different schemes have been proposed, recommending total doses no less than 30–35 Gy in standard fractionation to achieve local control.[15,16] However, this technique carries high risk of acute and late complications, such as permanent blindness, conjunctivitis, dry eye syndrome, corneal ulceration, keratopathy, cataract and optic neuropathy, among others. Shah et al. reported a 41% rate of deteriorated visual acuity with a medium follow-up of 12 months and Rudoler et al. reports up to 20% of blindness.[14,17]

The radiosurgery technique has evolved to gain a wide acceptance and become a routine procedure, mainly in patients with less radiosensitive tumors (melanoma, kidney cancer, sarcoma). In addition, where systemic treatment is necessary to control extrachoroidal metastases, hypofractionated radiation schemes are of particular interest. But the question still remains open if high doses per fraction can efficiently spare the vision and safe the globe without damaging several potential structures within the eye. Based on the published studies, radiosurgery has proven to be effective in controlling tumor growth with low toxicity in intraocular tumors, including metastases.[18–20]

Most radiosurgery techniques require invasive immobilization of the eye to accurately deliver a high-dose treatment. The CyberKnife offers a frameless option using retrobulbar anesthesia and image-guided system without suturing the rectus muscles.[1,21] First to describe the use of CyberKnife for intraocular lesions was Hirschbein and associates in 2008. They retrospectively analyzed 16 patients with intraorbital lesions (both benign and malignant), finding that all patients had stable or improved visual field with decrease or stabilization of the tumor size after delivering a mean dose of 20 Gy (10–25 Gy) in 2–5 fractions.[22] Klingestein et al. reported 16 orbital metastases treated with a median dose of 18 (16–20 Gy) with up to 87% local control and no adverse reactions or progression symptoms.[23]

The largest series published until date is from Riva and associates, with 24 orbital metastases from different primary tumors. Local disease control and palliation of symptoms was achieved in all patients using a median dose of 18 Gy (15–24 Gy) given in a median of three fractions (2–3 fractions) performed each other day.[3] We reported a partial response in a patient with intraocular breast cancer metastases. Mexico's health care institutions agree that legal blindness is defined as visual acuity of 20/200 or worse and our case presented with OD visual acuity of 20/400. It is important to mention that our patient presented central retinal vein occlusion 6 months after radiosurgery, which did not influence the quality of life since the patient was legally blind before treatment. However, it is important to take it into consideration in patients with preserved vision.

## 4. Conclusion

In summary, Cyberknife frameless radiosurgery for intraocular metastases allowed organ preservation. Treatment planning and delivery require an experienced interdisciplinary team comprising an ophthalmologist, radiation oncologist, medical physicist and radiologist. Based on our experience, the frameless robotic radiosurgery system is a feasible and comfortable option for patients with intraocular metastases. Longer follow-up is necessary to asses long-term side effects. Further trials are required to compare with other local therapies.

## Conflict of interest

None declared.

## Financial disclosure statement

None declared.

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