# Gamma Knife Perfexion® radiosurgery and endo diode laser thermotherapy for choroidal melanoma with technical analysis: A case report

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**Abstract.** Radiosurgery serves an important function in the treatment of patients with intraocular tumors and preserves visual function via organ conservation. Therefore, it is important to ensure the safety and precision of GK-SRS as a primary treatment for intraocular tumors. The present case study described a 57-year-old female with uveal melanoma treated with GK-SRS. Retrobulbar anesthesia following fixation of the treated eye, via the suture of two of the extraocular muscles to the stereotactic frame, was performed to immobilize the eye during treatment. Computed tomography (CT) scans were performed following eye fixation, immediately prior to and following GK-SRS, to validate the accuracy of the tumor localization. The eye movement analysis revealed that the gravity center point deviations of the tumor and lens during treatment were <0.110 mm. At least 95% of the tumor volume was covered by the prescription dose according to three sets of CT images. The patient underwent a trans pars plana vitrectomy owing to a right eye vitreous hemorrhage. A 37-month follow-up assessment revealed tumor shrinkage, and the disappearance of the serous retinal detachments was noted on the basis of ophthalmoscopy and orbital magnetic resonance imaging. No major complications developed during the follow-up period. Using our treatment protocol, GK-SRS is a non-invasive procedure which is used as a brief single fraction treatment for intraocular tumor. The eye fixation method used in the present study has high accuracy.

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## Introduction

Uveal melanoma is a rare but life-threatening disease (1). The annual incidence of choroidal melanoma is between 4 and 7 cases per million individuals and this rate has remained stable over the last twenty years (2,3). The 15-year melanoma-associated mortality rate in the US is between 40 and 50%, primarily due to liver metastasis (4). Eye-sparing treatments have replaced enucleation as the most common initial therapy for small and medium-sized choroidal melanomas. Radiotherapy serves an important role in organ conservation when treating patients with intraocular tumors and retained visual function. Plaque brachytherapy, stereotactic radiotherapy and proton beam radiotherapy are the most common treatments (5,6).

Gamma knife stereotactic radiosurgery (GK-SRS) was initially designed to treat brain targets with the skull rigidly fixed to the stereotactic coordinate frame. When these targets are around the eyes, the positioning and mobility of the eyes result in the use of GK-SRS to precisely position the eye for treatment challenging. Different approaches include the use of suction devices, retro- or parabulbar anesthesia and active fixation on a light point by the patient (7,8).

The present case study analyzes the use of a novel GK-SRS protocol and endo diode laser thermotherapy to treat a patient with intraocular melanoma at Taipei Medical University-Shuang Ho Hospital (New Taipei City, Taiwan, R.O.C). Furthermore, the precision and safety of GK-SRS as a primary treatment for uveal melanoma was evaluated. The patient provided informed written consent to participate in the present study and for the publication of patient data and photographs.

## Case report

*History.* A 57-year-old female without a history of underlying disease presented with increasing deviation of the right eye

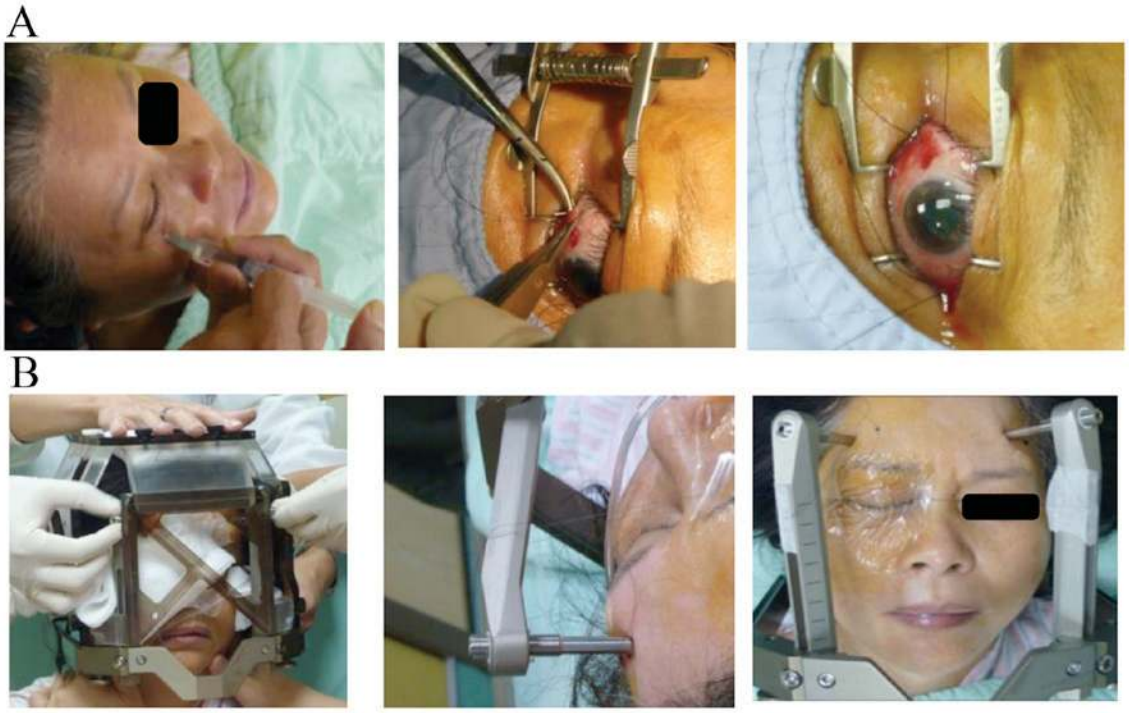


Figure 1. GK-SRS treatment procedure. Images of a 57-year old female patient with a right eye stage IIA choroidal melanoma. (A) Eyeball fixation. The treated eye was fixed with retrobulbar anesthesia, and two extraocular muscles were sutured. (B) Stereotactic frame fixation. The Leksell G frame was fixed to the patient's head with four pins placed into the skull and the sutured muscles were fixed to the frame.

with initial pain in October, 2011. On physical examination, the patient's visual acuity was 0.8 in the right and left eye, and intraocular pressure was 15 mmHg in the right eye, within the normal range. A fundoscopic examination revealed a choroidal melanoma near the macula, surrounding the optic nerve fovea of the right eye. A B-scan demonstrated that the internal reflectivity was consistent with a uveal melanoma. An orbital magnetic resonance imaging (MRI) scan was performed, which revealed a small nodular lesion in the right choroid near the macula without extraorbital extension. The basal dimensions of the tumor were 9.5x8.9 mm and the thickness was 4.1 mm. A computed tomography (CT) scan was performed that demonstrated no evidence of lung or liver metastasis. Following the tumor survey, a right eye stage IIA (cT2aN0M0; according to the 7th edition of the American Joint Committee on Cancer staging manual) (9) choroidal melanoma with retained visual function was diagnosed through the aforementioned eye examinations and imaging tests (ophthalmoscopy, ultrasound, orbital MRI and CT). Subsequently, the patient underwent Leksell Gamma Knife Perfexion® stereotactic radiosurgery at Taipei Medical University-Shuang Ho Hospital.

*Eyeball fixation*. A prophylactic Levofloxacin ophthalmic solution was administered to prevent infection. Following the patient receiving retrobulbar anesthesia with long-acting marcaine (0.5%, 20 ml) to produce complete akinesia, the ophthalmologist sutured two extraocular muscles, on the basis of the tumor location (the medial rectus and lateral rectus).

*Stereotactic frame fixation*. A Leksell G stereotactic frame (Elekta Instrument AB, Stockholm, Sweden) was fixed to the patient's head using four pins. The frame provided the coordinate system for target localization. The midline of the stereotactic system was placed close to the eye to be treated. Subsequently, the threads of the two sutured muscles were fixed to the stereotactic frame to immobilize the eye throughout the procedure (Fig. 1).

*Imaging*. The stereotactic frame, with MRI and CT N-rod localizer boxes, was used to obtain MRI and CT data. High-resolution contrast-enhanced MRI scans (Signa HDx 1.5T MRI with a 1-mm slice interval) of the brain were acquired and the images were loaded to the gamma knife treatment planning system for Gamma Plan dose planning (Leksell GammaPlan® 9.0; Elekta Instrument AB). CT images were acquired using a Philips 16-slice CT scanner (Brilliance Big Bore; Philips Healthcare, Cleveland, OH, USA) with a 1-mm slice thickness (Fig. 2).

*Dose planning*. The gross volume of the melanoma was defined using the MRI scan sections in three-dimensional reconstructions: Axial, sagittal and coronal. A conformation treatment planning technique was used to apply conformal irradiation to the tumor and healthy tissue (the lens and optic nerve). The plan was designed to encompass the entire tumor volume with the prescribed dose to the periphery of the tumor. The tumor volume was 270.3 $mm^3$. The dose to the tumor margin was 30 Gy at the 55% isodose line (Figs. 2D and 3).

*Treatment*. During the treatment, the patient was maintained in a supine position, instead of the traditional prone position (Fig. 2G). The treatment was performed in one session. The beam-on time was 108.2 min. Following GK-SRS treatment, the stereotactic frame and the sutures were removed from the

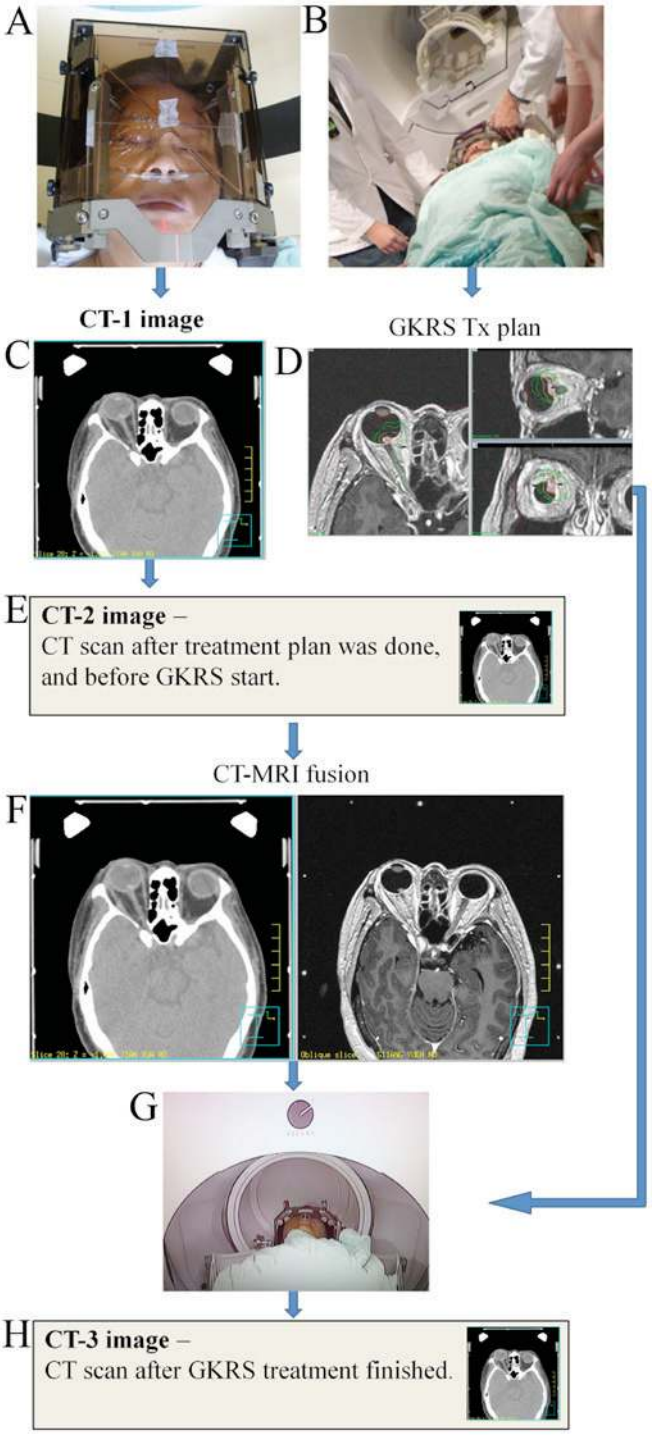


Figure 2. GK-SRS and verification procedure. Head frame coordinate indicators were used for (A) CT simulation and (B) MRI study. (C) CT-1 was performed immediately following the patient undergoing eye fixation and stereotactic frame immobilization. (D) MRI scans were loaded into the GK treatment planning system for dose planning. (E) To determine the precision of the eye fixation, CT-2 was performed following the treatment plan was completed, but prior to the start of the GK-SRS procedure. (F) CT-2 and the MRI scans were fused and evaluated across the axial, sagittal and coronal planes to analyze the reproducibility of the eye position. (G) The final GK treatment plan was approved and used for radiosurgery treatment. (H) CT-3 was performed immediately following GK-SRS. GK-SRS, gamma knife stereotactic radiosurgery; CT, computed tomography; MRI, magnetic resonance imaging.

patient. Ophthalmic Betamethasone (2 mg/g) and Neomycin (3.5 mg/g) ointments were prescribed to cover treated eye for symptom control twice daily. The patient was discharged on the following day.

*Tumor localization precision*. To determine the quality of the eye fixation technique and the localization precision of the orbital tumor, 3 sets of CT scans were performed on the patient. The first CT scan (CT-1) was performed immediately following eye fixation and stereotactic frame immobilization. The second CT scan (CT-2) was performed following completion of the treatment planning, but prior to the GK-SRS procedure (Fig. 2E). The third CT scan (CT-3) was performed immediately following the completion of the GK-SRS procedure (Fig. 2H). The three sets of CT images were fused on the basis of the stereotactic frame localizer position.

Owing to the time limitation on the treatment day, the CT-2 and MRI images were analyzed side by side by using Pinnacle$^3$ Auto-Planning software version 9.2 (Philips Healthcare), and evaluated from the axial, sagittal and coronal planes to determine the reproducibility of the eye position, and whether the frame and the head anatomy matched (Fig. 2F).

To additionally evaluate the accuracy of the eye fixation protocol, all 3 sets of CT scans were loaded into the gamma knife treatment planning system. The tumors, lens and optic nerves were contoured for all CT images. CT-2 and CT-3 were individually fused with CT-1, on the basis of on the localizer position. The fused images (Fig. 3A) and the raw data were exported from GK-SRS to the Computational Environment for Radiotherapy Research (CERR) treatment planning software (10), to compare the positioning error, dose volume histogram of the tumor and critical organs (Fig. 3B). The tumor volume and location deviation of the tumor, lens and optic nerves were analyzed. The MRI scans with the GK-SRS treatment planning dose distribution were fused with a different CT set. The targets were contoured by an experienced radiation oncologist for all MRI and CT sets and tumor coverage, referring to the proportion of target coverage by the prescription dose was calculated for all CT sets using the following formula: Coverage (%)=($TV_{PIV}$/TV) x100%. TV is the target volume, PIV is the prescription isodose volume, and $TV_{PIV}$ is the TV covered by the PIV.

*Statistical analyses*. On the basis of evaluation, targets were small and oval shaped following treatment. The gravity center point (GCP) was used to represent the evaluation point. The formula is as follows: $\bar{r}_{cg}=\frac{\sum \bar{r}_i m_i}{m_{total}}$, where $\bar{r}_{cg}$ indicates GCP, $\bar{r}_i$ indicates each point position, $m_i$ indicates each point mass, and $m_{total}$ indicates the total mass.

To determine the precision of the eye position used in the present case study, the 3 sets of CT images and the MRI images were fused according to the stereotactic frame. On the basis of the fused images, the position differences of the GCPs of the evaluation objects were calculated.

The deviations between CT-1 and CT-2 (Δ1) and between CT-1 and CT-3 (Δ2) were calculated using the following formula: $\Delta = \sqrt{\Delta x^2 + \Delta y^2 + \Delta z^2}$, where $\Delta x$, $\Delta y$ and $\Delta z$ represent the left-right, up-down and forward-back deviations, respectively.

The Digital Imaging and Communications in Medicine-radiation therapy data for each patient in the GK treatment planning system was transferred to the CERR radiation therapy treatment planning software for plan

Table I. Summary of the GK-SRS treatment plan for patient with choroidal melanoma.

| Tumor volume, $mm^3$ | Marginal dose, Gy | Maximal dose, Gy | Prescribed isodose line, % | Beam-on time, min | Optic nerve maximal dose, Gy |
|---|---|---|---|---|---|
| 270.5 | 30.0 | 54.5 | 55 | 108.2 | 38.9 |

GK-SRS, gamma knife stereotactic radiosurgery.

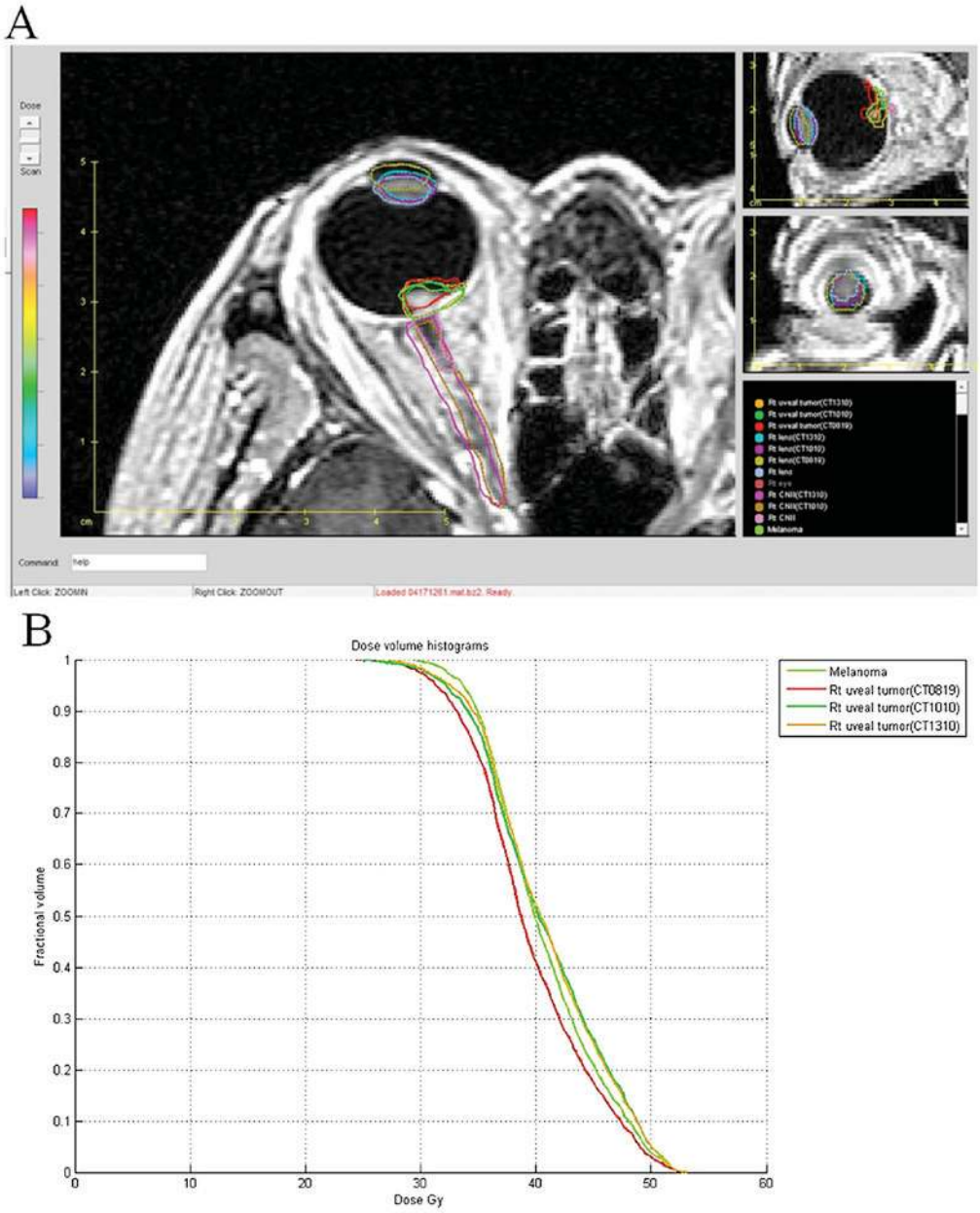


Figure 3. Eye movement analysis. The tumor was contoured in the 3 sets of CT images on the GK treatment planning system and exported to the CERR software. (A) The MRI scans with the GK-SRS treatment planning dose distribution were fused with different CT sets, on the basis of the localizer position. (B) The dose volume histogram of the tumor for the 3 sets of CT scans was evaluated. GK-SRS, gamma knife stereotactic radiosurgery; CT, computed tomography; MRI, magnetic resonance imaging; CERR, Computational Environment for Radiotherapy Research.

evaluation (10). Tumor volume, tumor location deviation, lens deviation and the dose volume histogram of the tumor, on the basis of the MRI scan and the 3 sets of CT images, were analyzed.

*Eye fixation analysis*. The treatment plan and tumor volumes measured for the 3 sets of CT and MRI scans are listed in Tables I and II. Table III presents the GCP coordinates and the deviations for tumor and lens between the different sets of

Table II. Summary of tumor volume according to MRI and 3 sets of CT scans.

| MRI, $mm^3$ | CT-1, $mm^3$ | CT-2, $mm^3$ | CT-3, $mm^3$ |
|---|---|---|---|
| 270.5 | 266.1 | 262.3 | 266.9 |

MRI, magnetic resonance imaging; CT, computed tomography.

CT images. On the basis of the GCP position differences, the deviations of the tumor and lens were <0.110 mm in the CT-1, CT-2 and CT-3 images.

Dose distributions and tumor coverage with the prescribed dose were calculated and evaluated for the 3 sets of CT images. The tumor coverage is listed in Table IV. The analysis of the dosimetric consequences in these cases revealed that the tumor was covered with isodose curves >95%.

The tumor deviations between CT-1 and CT-2, and between CT-1 and CT-3 were 0.099 mm and 0.109 mm, respectively. The lens deviation between CT-1 and CT-2, and between CT-1 and CT-3 were 0.107 mm and 0.089 mm, respectively. The dose distributions and the coverage of the tumor with the prescribed dose were calculated. The tumor coverage, on the basis of the MRI, CT-1, CT-2 and CT-3 scans were 99.7, 97.4, 98.1 and 98.3%, respectively.

*Postoperative course*. The patient tolerated the procedure well. The follow-up fundoscopic examination, performed 1 month after GK-SRS, revealed hyperpigmentation of the tumor surface, distinct borders of the tumor margins and tumor shrinkage (Fig. 4). However, 3 months after the gamma knife procedure, the patient complained of decreased vision in the right eye with a visual acuity of 0.03. Subsequently, a B-scan and mydriatic fundus examination revealed persistent right eye vitreous hemorrhage. The patient underwent a trans pars plana vitrectomy for a dense non-clearing vitreous opacity of right eye. During this surgery, the ophthalmologist applied endo diode laser thermotherapy (wavelength, 810 nm) to a choroid tumor that involved the optic nerve and achieved safe margins (2 mm/500-1,000 mW/spot; 1 min/spot; total, 30 spots), until the tumor turned from white to gray. Samples taken by needle aspiration from the vitreous fluid were fixed in 10% neutral buffered formalin for 24-48 h at room temperature, embedded in paraffin and sectioned to 4-5-$\mu$m. The immunohistochemical staining of the cell block cytology revealed positive staining for HMB45, a monoclonal antibody used to confirm melanoma, using an anti-HMB45 primary antibody (cat. no. 282M-95; dilution, 1:20; Thermo Fisher Scientific. Inc.), incubating the samples with this primary antibody for 2 h at 36˚C. The ultraView Universal Alkaline Phosphatase Red Detection kit (Ventana Medical Systems, Inc., Tucson, AZ, USA) was used to detect the anti-HMB45 primary antibody. The immunohistochemical staining result was also positive for Ki67, which is a cellular marker for proliferation, using an anti-Ki67 antibody (cat. no. RM-9106-S; dilution, 1:200; Thermo Fisher Scientific, Inc.), incubating samples with this antibody for 48 min at 36˚C, The ultraView Universal DAB Detection kit (Ventana Medical Systems, Inc.) was used to detect the anti-Ki67 primary antibody. An Olympus BX41 light microscope (Olympus Corporation, Tokyo, Japan) was used to visualize results at a magnification of x400 (Fig. 5), demonstrated sparse malignant cell nests with rich melanin-pigment compatible with malignant melanoma.

*Follow-up assessment*. This patient underwent a complete ophthalmological diagnostic investigation and follow-up evaluation following GK-SRS that included visual acuity testing (Snellen charts), indirect ophthalmoscopy and color fundus photos every 3 months after treatment for 3 years. A head MRI was performed every 3 months for 1 year, and then every 6 months for 2 years for tumor evaluation. Furthermore, liver ultrasonography and chest X-ray were conducted every 6 months for 3 years to detect early metastasis.

At 37 months after LGK-SRS and 32 months after vitrectomy, follow-up MRI scans revealed tumor shrinkage (9.5x8.9 to 7.2x6.4 mm) and a decrease in tumor thickness (4.1-3.0 mm) (Fig. 6). The patient remained free of metastatic disease. The best-corrected visual acuity decreased from 1.0, at the time of uveal melanoma diagnosis, to 0.03, prior to vitrectomy, and 0.2, following vitrectomy.

## Discussion

Ocular melanoma typically affects Europeans and rarely occurs among Asian, African-American or Hispanic populations (1,11). Cheng and Hsu (12) identified that the incidence of ocular melanoma in Taiwan was 0.39/million. Furthermore, Chinese patients with uveal melanoma were typically younger compared with Western patients (12). The choroid is the most common site of involvement, followed by the ciliary body and the iris (13). In spite of the low incidence of uveal melanoma, the management of patients with this condition remains a therapeutic challenge for oncologists and surgeons (13).

Historically, uveal melanoma was treated with enucleation; however, enucleation was hypothesized to promote tumor cells that metastasize due to elevated intraocular pressure and tumor disruption (14). Novel techniques have been developed for orbital preservation including transpupillary thermotherapy, brachytherapy, local tumor resection, proton beam irradiation and stereotactic radiosurgery (5,6,15); however, the use of endo diode laser thermotherapy has rarely been studied. The Collaborative Ocular Melanoma Study randomly assigned 1,317 patients with medium-sized choroidal melanomas (apical height, between 2.5 and 10.0 mm; basal diameter, between 5 and 16 mm) to receive either enucleation or iodine-125 brachytherapy. No difference was identified with regard to the 5-year survival rates between enucleation and brachytherapy (81 and 82%, respectively; P=0.48) (16). Plaque brachytherapy has evolved into a promising alternative to enucleation because it provides successful local control with only a moderate decrease in visual acuity (16).

GK-SRS was developed by the Swedish neurosurgeon Lars Leksell for intracranial lesion treatment (17). This technique is engineered to deliver a single dose of ionizing radiation to a small target with a steep dose fall-off at the margins. These characteristics are crucial for irradiating intraocular tumors while sparing normal peritumoral tissue (17). In 1987,

Table III. GCP coordinates and the deviations between the tumor and lens across the different CT image sets.

| | CT-1 ($x$, $y$, $z$) | CT-2 ($x$, $y$, $z$) | CT-3 ($x$, $y$, $z$) | Δ1, mm | Δ2, mm |
|---|---|---|---|---|---|
| Tumor | (-2.109, 4.398, -1.964) | (-2.047, 4.271, -1.933) | (-2.076, 4.282, -1.891) | 0.099 | 0.109 |
| Lens | (-2.528, 5.904, -1.459) | (-2.449, 5.764, -1.460) | (-2.444, 5.805, -1.479) | 0.107 | 0.089 |

GCP, gravity center point; CT, computed tomography.

Table IV. Summary of the tumor coverage at the prescribed isodose.

| Prescription dose, Gy | MRI, % | CT-1, % | CT-2, % | CT-3, % |
|---|---|---|---|---|
| 30 | 99.7 | 97.4 | 98.1 | 98.3 |

MRI, magnetic resonance imaging; CT, computed tomography.

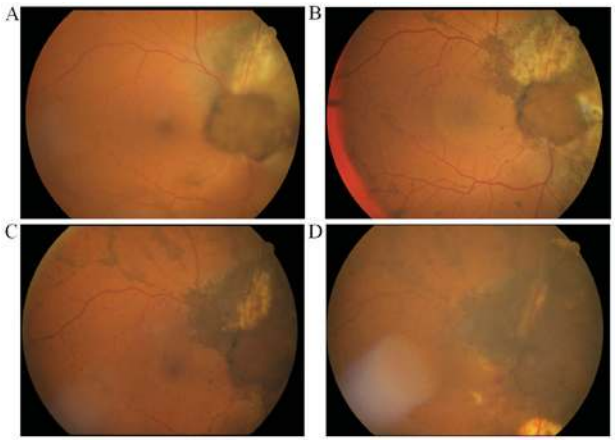


Figure 4. Fundoscopic views of the choroidal melanoma. (A) At diagnosis; (B) 4 months after GK-SRS; (C) 3 months after trans pars plana vitrectomy and endo diode laser thermotherapy (oculus dexter); and (D) 20 months after GK-SRS, following the resolution of the serous retinal detachment, tumor surface hyperpigmentation, tumor margin distinct borders and tumor shrinkage. GK-SRS, gamma knife stereotactic radiosurgery.

Rand *et al* (18) used GK-SRS with a single dose of 60-90 Gy delivered at 90% isodose to treat six rabbits with eye melanoma and an overall regression was demonstrated. Long-term SRS results regarding uveal melanoma via GK-SRS reveal satisfying tumor control with rates of approximately 90% (19-21).

To ensure the treatment precision of GK-SRS, eyeball immobilization and tumor imaging are two important steps in the treatment protocol. Different eye-immobilization systems for eye melanoma have been described previously (22,23). Mueller *et al* (24) used a retrobulbar injection of a long-acting anesthetic agent to achieve complete akinesia during treatment and performed a second MRI scan to validate post-treatment tumor position. Langmann *et al* (21) and Modorati *et al* (19) immobilized the globe using retrobulbar anesthesia, and by suturing the extraocular muscles. Due to the application and subsequent resorption of the anesthetic liquid, whether the eye would be displaced within the orbit during the treatment was investigated. Based on the present case study, by retrospectively evaluating the tumor and lens deviations in the present case on the basis of the CT images obtained during treatment, the accuracy of the eye positioning was analyzed. The deviations between the pre- and post-treatment positions were ≤0.1 mm for all data points investigated. The analysis of the dosimetric consequences in these cases revealed that the tumor remained covered by >97% isodose curves. Therefore, retrobulbar anesthesia and two extraocular muscle sutures are feasible and efficacious methods for orbital tumor radiosurgery.

Logani *et al* (20) demonstrated that ocular melanoma cell lines are radioresistant *in vitro*, particularly at lower doses; however, ocular melanoma cell lines may be responsive to a single high dose delivered using stereotactic radiosurgery or brachytherapy. As such, their initial report revealed that higher doses ranging between 90 and 50 Gy at the tumor margins were prescribed (18). However, secondary side effects including neovascular glaucoma, radiation retinopathy, optic neuropathy and maculopathy were common; therefore, the irradiation dose was decreased over time (19,24,25). Langmann *et al* (25) demonstrated that if the mean margin dose was decreased to between 52.1 and 41.5 Gy, a lower complication rate of neovascular glucoma was noted with the similar local control rate. Modorati *et al* (19) demonstrated that a decrease in dose (to between 50 and 35 Gy) at the tumor margin was not significantly associated with survival probability, but was associated with decreased radiation-induced side effects. Mueller *et al* (24) demonstrated that the current treatment for uveal melanoma was performed using 25 Gy at a 50% isodose. Previous studies have revealed decreased rates of radiogenic side effects due to the lowering of the total irradiation dose to ~40 Gy and 35 Gy at 50% isodose (19,25). In the present case study, 30 Gy at the 55% isodose line was administered to the tumor margin.

In the present case study, as the tumor was located close to the optic nerve, the maximal dose to the optic nerve was 38.9 Gy. During the 15-month follow-up period, ophthalmoscopy revealed tumor shrinkage and serous retinal detachment disappearance. However, vitreous hemorrhage occurred 5 months after treatment. The patient subsequently received trans pars plana vitrectomy for dense non-clearing vitreous opacity of the right eye. The management of the vitreous hemorrhage using this technique in eyes with previously irradiated uveal melanoma appears to be safe, without increased risk of intraocular, local, orbital or systemic dissemination of the tumor (26).

Enucleation and fine-needle lesion biopsy are direct ways of acquiring tissue for additional analysis; however, the

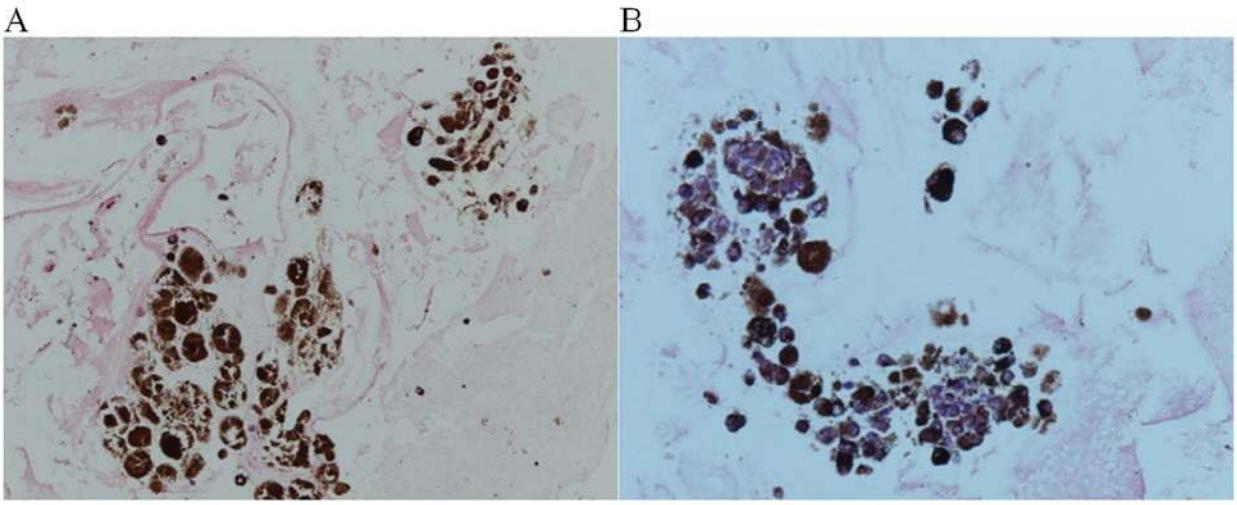


Figure 5. Cytology findings. Vitreous fluid cytology (oculus dexter) revealed sparse malignant cell nests with rich melanin-pigment compatible with malignant melanoma. Immunostaining revealed (A) HMB45 (+) and (B) Ki-67 (+ for some cells) (magnification, x400).

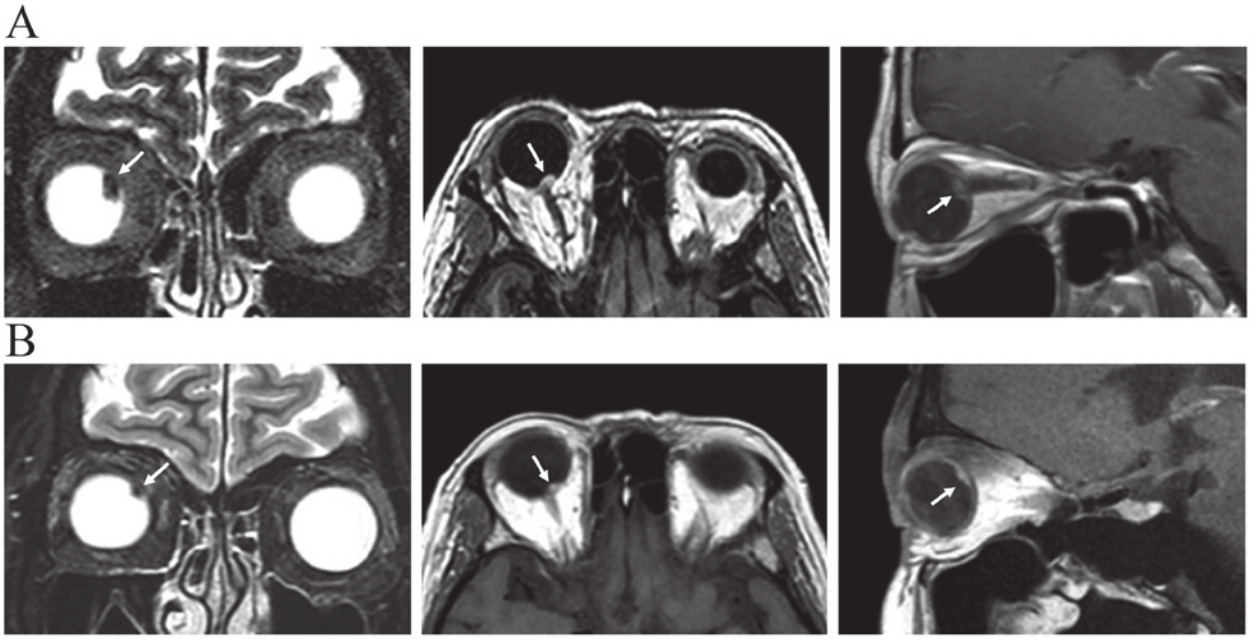


Figure 6. MRI images of a patient with choroidal melanoma. (A) Prior to treatment; and (B) 38 months after GK-SRS; the images revealed tumor shrinkage and a decrease in thickness. Left, coronal short tau inversion recovery image; middle, axial T1 image; and right, sagittal T1 image. MRI, magnetic resonance imaging; GK-SRS, gamma knife stereotactic radiosurgery.

former method sacrifices the affected eye and the latter may lead to tumor metastasis. Fine-needle biopsy of the vitreous humor is a relatively safe procedure, but it has decreased success rates (27). In the present case study, vitreous fluid was selected during the pars plana vitrectomy and the pathological examination revealed sparse malignant cell nests with rich melanin-pigment compatible with malignant melanoma.

Thermotherapy uses the principle of intermediate-level hyperthermia between 45 and 60˚C (28). Nuijs-Beems *et al* (28) demonstrated that the temperature range was optimal for the destruction of cells throughout the full thickness of the tumor. Intermediate-level hyperthermia differs from photocoagulation, in that the latter heats the tissue to temperatures >60˚C with resultant destruction of the cells in the outer layers of the tumor. The outer layer cells form a reflective surface and do not allow additional penetration of the heat into the mass. In thermotherapy, the spot size is larger (≤6 vs. <1 mm) and the duration of exposure is increased (1-10 min vs. 0.5-1 sec) compared with that of photocoagulation (28). To achieve improved local tumor control in the present case study, endo diode laser thermotherapy was initially administered to the choroid tumor, which involved the optic nerve, and achieved safe margins (28). At the regular follow-up assessment, an MRI scan revealed tumor shrinkage and no metastatic disease.

GK-SRS, used in the present case study, is a relatively non-invasive, organ-conserving and brief single fraction treatment for intraocular tumor, compared with enucleation and plaque brachytherapy. The present study hypothesizes

that eye fixation with retrobulbar anesthesia and two extraocular muscles suture is a feasible and efficacious method for radiosurgery within 6 h. Furthermore, endo diode laser thermotherapy is a safe and effective procedure for patients with uveal melanoma. On the basis of the present case report, additional clinical trials and studies are required.

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