Correlation of Pathological Finding with Dose Distribution in a Case of Intraocular Choroidal Melanoma Treated by Stereotactic Radiosurgery

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Malignant melanoma is a radioresistant tumor and surgical resection has been established as a treatment of choice for large tumors. Recently, the effectiveness of stereotactic radiosurgery (SRS) for intraocular choroidal melanoma has been reported, but the proper radiation dose has not yet been established. We report a case of intraocular choroidal melanoma treated by SRS using a conventional linear accelerator as preoperative radiation therapy (RT) to prevent operation-induced metastases, and correlate the pathological finding in the resected specimen with the dose distribution obtained by SRS to establish the pathologically effective radiation dose.

Case report. A 65-year-old woman who complained of decreasing vision of the left eye was admitted to our hospital. An orbital postcontrast computed tomography (CT) done on admission demonstrated a slightly enhancing tumor, 16×16 mm in size, attached to the posterior wall of the left eyeball. Ophthalmoscopy revealed a brown tumor at the posterior part of the left eyeball. T1- and T2-weighted magnetic resonance (MR) images (Fig. 1) revealed a tumor of high and low signal intensities, respectively. Clinically, a malignant melanoma was highly suspected. Scintigraphy with gallium-67 revealed a high accumulation corresponding to the left intraocular lesion but did not demonstrate any other abnormal uptake suggesting distant metastases. The clinical stage was T3NOMO (Stage III; 1987, UICC).

SRS was chosen as a method of preoperative RT to prevent operation-induced metastases. At first, a head ring (BRW; Radionics, Inc., Burlington, MA, USA) was attached to the outer table of the cranium of the patient using a four-point fixation under local anesthesia. After achieving satisfactory akinesia of the left eyeball by injection of local anesthetic to the retrobulbar space, CT with contrast enhancement was performed with continuous 3-mm thick slices through the affected eye to the top of the skull to define the target for SRS planning. The tumor and the adjacent critical organs, such as the optic nerves, the optic chiasma, the brain stem and the major vessels, were marked according to the CT data and three-dimensional radiation planning was performed by a treatment planning workstation (X-Knife III software system; Radionics, Inc.).

The entire tumor was within the 80% isodose contour border. A marginal dose of 20 Gy with a central dose of 25 Gy with five arcs using a narrow beam collimator with a 3-cm diameter was planned (Fig. 2 and Fig. 3). This dose was decided on from doses previously reported as preoperative RT for intraocular choroidal melanoma. The average irradiation doses to the adjacent critical organs were as follows: the left optic nerve, 6.17 Gy; the right optic nerve, 0.12 Gy; the optic chiasma 0.096 Gy; and the brain stem, 0.051 Gy. All of these doses seemed to be tolerable. The dose volume histogram (DVH) of the left intraocular lesion is shown in Fig. 4. After completion of the 3D radiation planning, the patient was placed on the treatment couch to align the center of the tumor with the isocenter of the linear accelerator (Mevatron 77DX 67; Siemens, Germany), and a retrobulbar injection of local anesthetic was administered again for immobilization of the left eyeball during irradiation. Stercotactic irradiation was performed with combined rotations of the gantry and the treatment couch.

Two weeks after SRS, the left eyeball was surgically enucleated. The pathological examination (Fig. 5) revealed spindle B cell type tumors in the Callender classification (1) containing a high amount of melanin at the periphery of the tumor. Necrotic areas were observed mainly around the center of the tumor, and cystic changes were also observed. These pathologic changes were similar to those of tumors treated with iodine-125 brachytherapy (2). The distribution of necrotic areas in the tumor corresponded to the areas irradiated by more than 24.9 Gy in dose distributions obtained by SRS. Three years after the treatment, there was no local recurrence, nor was any distant metastases noted.

Discussion. Uveal melanoma is a relatively rare disease in Asian countries, but is the most common primary ocular malignancy in adults in Western countries. It occurs in approximately six to seven cases per million people per year according to US figures (3). Enucleation has been the standard treatment for

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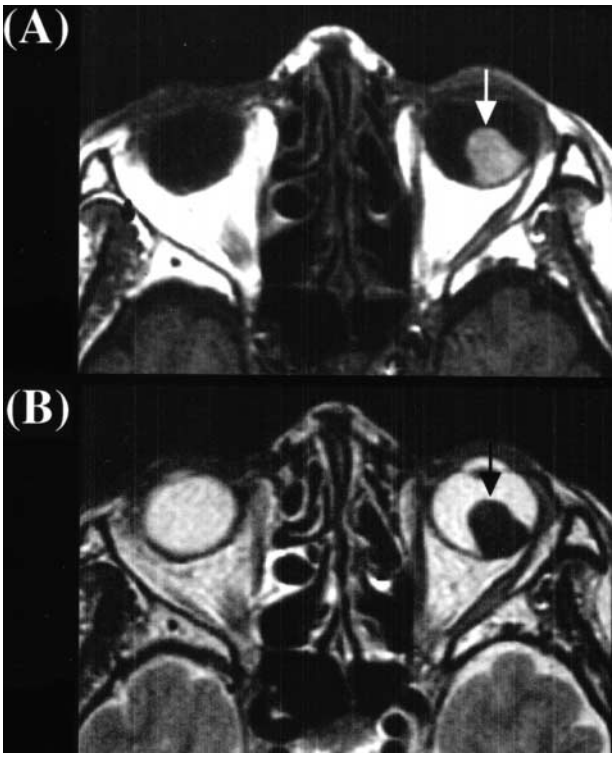

Fig. 1. (A) Axial T1- and (B) T2-weighted MR images showing the tumor (arrow) attached to the posterior wall of the left eyeball. Note high signal intensity on the T1-weighted image and low signal intensity on the T2-weigthed image.

intraocular melanomas for approximately 100 years. Among the conservative therapies, RT with proton beam irradiation and brachytherapy with various radioactive discs and plaques have been the most extensively evaluated (4–6). Recently, the effectiveness of SRS has been established as a new method of RT in patients with small intracranial lesions, including neoplasms and vascular malformations (7).

SRS was first defined by Lars Leksell, a Swedish neurosurgeon, in 1951. He described this treatment technique as a method of destroying intracranial targets using single high doses of ionizing radiation in stereotactically directed narrow beams. SRS can deliver high doses precisely to a very small treatment area and is now established as a treatment of choice for small intracranial lesions. However, studies supporting the use of SRS in the management of intraocular lesions are limited. To the best of our knowledge, there have been only a few reports concerning SRS for intraocular choroidal melanomas (8–11). All those reported cases were treated with a Gamma Knife unit and the only reported case treated with a conventional linear accelerator was by firactionated stereotactic radiotherapy (SRT) without special cones for beam collimation (12).

We performed SRS using a conventional linear accelerator equipped with a narrow beam collimator as preoperative RT. In general, the procedure adopted for the treatment of intraocular choroidal melanoma was similar to that used for the treatment of intracranial conditions, with the exception that complete akinesia of the ipsilateral eyeball was required throughout the entire procedure.

Immobilization of the ipsilateral eyeball throughout the entire procedure without drugs cannot be expected because of the long duration of the treatment. Some authors perform a peritomy and fix the four rectus muscles to the orbital border with silk sutures.

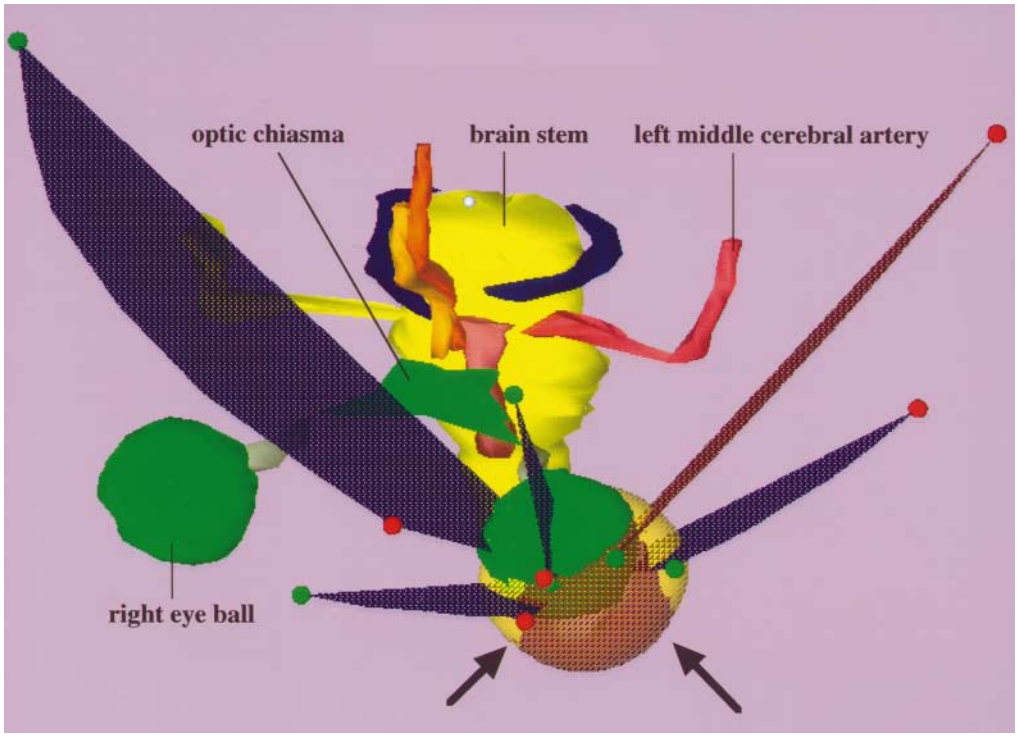

Fig. 2. Treatment configurations showing 80% isodose surface (arrows) for intraocular choroidal melanoma, associated five arcs and the adjacent organs. The green round areas indicate the eyeballs and the yellow area is the brain stem.

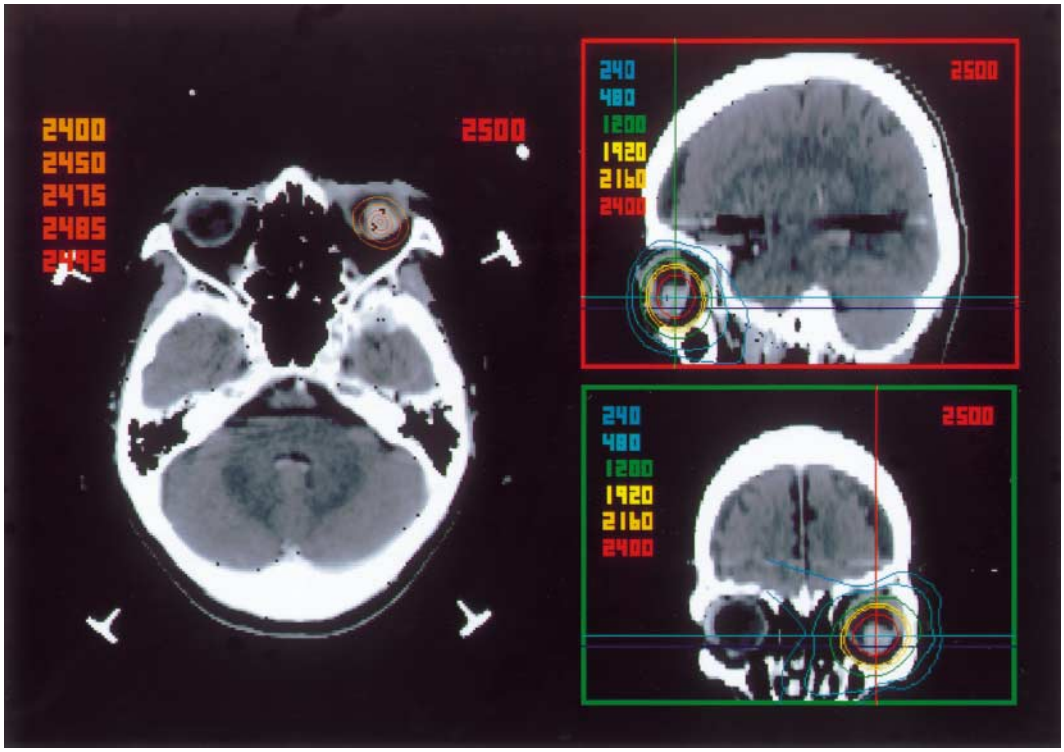

Fig. 3. The isodose profiles are defined on three directions. Values are the total dose in cGy.

Retrobulbar injection of local anesthetics is a simple and effective technique to enable the immobilization of the eyeball. However, the effectiveness of local anesthetics can be as short as a few hours. When it takes several hours to perform CT localization to stereotactic irradiation, two retrobulbar injections of local anesthetics are necessary, as in our patient. This may cause a change in the position of the tumor. We asked the patient to stare straight ahead both times to minimize the error of location of the eyeball. A non-invasive and reporducible method of immobilization of the eyeball should be developed for the future; indeed, some investigators have already proposed a new device for immobilization of the eyeball (13).

An appropriate radiation dose for intraocular choroidal melanomas has not yet been established. It must be effective for the local control of the tumor. On the other hand, it must avoid the occurrence of complications on adjacent structures as much as possible. We used 25 Gy as a central dose and 20 Gy as a marginal dose. This dose was used previously as preoperative RT for intraocular choroidal melanoma (14). The radiation dose was similar to the dose used for intracranial malignant tumors. However, this dose was lower compared with that reported by other investigators for intraocular choroidal melanoma. Rennie and colleagues administered 70 Gy to the periphery of the tumor in 14 patients with posterior uveal melanomas and regression of the tumor was observed in 13 patients, but significant radiation-induced adverse reactions were noted in 13 patients (9). Devlin and colleagues delivered a dose of 50 Gy to the marginal dose (50%) without complications (10). Marchini and colleagues reported that local tumor control may be obtainable using an SRS dose of 40–45 Gy, which would, hopefully, reduce the rate of complication (11).

These reported cases were treated with radical RT. We believe that preoperative RT needs a lower radiation dose than that of radical RT. Recently, Hsiung and colleagues reported three patients effectively treated with linac-based SRS with a total dose of 20 Gy as radical RT (15). But, in our study, the pathological findings in the resected specimen showed that a marginal dose of 20 Gy with a central dose of 25 Gy was not enough to achieve full necrosis in the tumor, though the period from SRS to enucleation was only 2 weeks. We think that a dose of more than 24.9 Gy may be necessary to obtain necrosis in this tumor. We should not forget the aim of irradiation of uveal melanomas is not the induction of total necrosis but the total blocking of tumor growth.

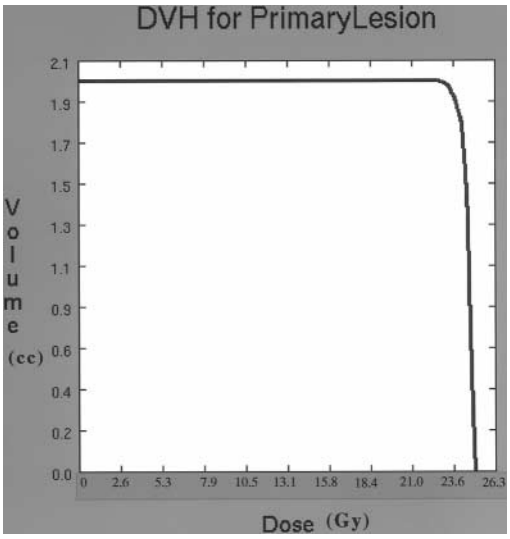

Fig. 4. Dose volume histogram of the left intraocular choroidal melanoma.

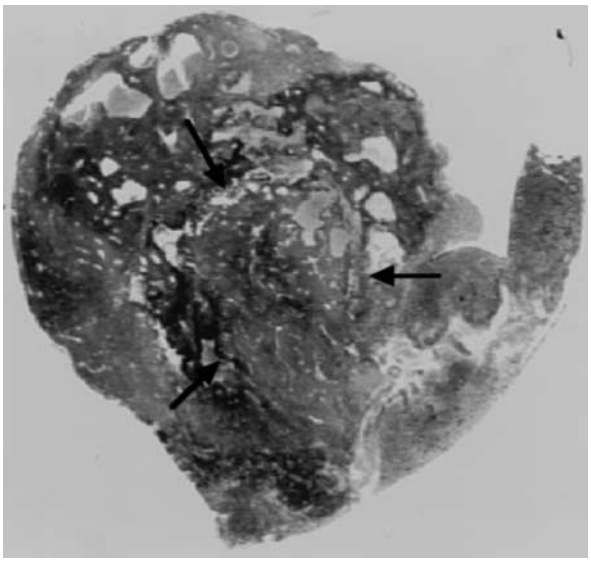

Fig. 5. Pathological examination reveals necrotic areas (arrows) mainly around the center of the tumor, corresponding to the areas irradiated by more than 24.9 Gy in the tumor.

It is also important to remember that the consequence of irradiation is of course the risk of late side effects. SRS may contribute to the radiacal treatment of choice for introcular choroidal melanoma, although further studies may still be needed to resolve problems regarding both the appropriate radiaiton dose that adequately treats the tumor with minimum complicaitons and the immobilization method of the ipsilateral eyeball.

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