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# Complications of local beta radiation of uveal melanomas

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**Abstract.** The results of local beta ray radiation of 295 eyes containing a uveal melanoma (including 74 melanomas of the anterior choroid and ciliary body) are presented with special respect to the complications of treatment. The most frequent complications were radiation retinopathy and optic neuropathy. Complications known to occur from other radiation methods, such as dry eye syndrome, loss of cilia, and scleral necrosis, did not occur in our series. The incidence of radiation cataract, as compared to the treatment with $^{60}$Co plaques, was lower in our series. An average of 700 Gy delivered to the scleral base of the tumor was needed for uveal melanomas which could be destroyed. This radiation dose resulted in a 10% incidence of radiation retinopathy.

## Introduction

Ever since the pioneering work of Stallard (1960, 1966) local radiation of uveal melanomas has been available for the treatment of these tumors. As in the days of Stallard, the most commonly used radiation source is still $^{60}$Co, which is a high-energy gamma radiation source. Based on the physical properties of $^{60}$Co, a wide variety of complications are encountered with this radiation source. Large series have been reported by MacFaul and Bedford (1970), MacFaul (1977), Shields (1977), Shields et al. (1982), Rotman et al. (1977, 1983), Zografos and Gailloud (1979, 1983) and Zygulska-Mach et al. (1983). Ruthenium ($^{106}$Ru/$^{106}$Rh) plaques have been introduced in the treatment of choroidal melanomas by Lommatzsch (1974, 1979, 1983). They deliver beta rays with an energy of 3.54 Mev (79%), 3.0 Mev (8%), 2.4 Mev (11%) and 2.0 Mev (2%). Based on the reports of Lommatzsch (1974, 1979, 1983), $^{106}$Ru/$^{106}$Rh plaques were used in the present study for the treatment of intraocular tumors.

## Materials and methods

From August 1979 to September 1984, 312 patients with a malignant melanoma of the choroid or ciliary body were treated with $^{106}$Ru/$^{106}$Rh plaques. In 295 patients, local radiation with a $^{106}$Ru/$^{106}$Rh plaque was the first treatment modality used for the melanoma, and the statistical data presented in this paper are based on these 295 patients.

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The mean tumor prominence was 5.75 mm (SD = 2.7 mm; maximum value 15.3 mm). These data were derived from ultrasonographic evaluations where 1 μs was considered equal to 0.766 mm in tumor tissue. Of these tumors, 32.3% were in the range of 0 to 3.8 mm, 50.2% in the range of 3.8 to 7.7 mm, 15.5% 7.7–11.5 mm and 2% in the range of 11.5 to 15.3 mm. We did not calculate the total tumor volume because of the difficulties in evaluating tumor dimensions objectively. The tumor diameters ranged from 20° to 90° on the fundus. To date, the mean follow-up period for these patients has been 1.3 years; (SD = 1.12 years; maximum follow-up after starting treatment, 5 years).

In addition to the original indications for ruthenium therapy given by Lommatzsch (1983), patients with ciliary body melanomas have also been treated (Foerster et al. 1983).

The radiation dose delivered to the sclera (scleral contact dose, SCD) in all 295 patients averaged 700 Gy. In most tumors this SCD was delivered within 1 week. As the isodose distribution cannot be calculated in polychromatic beta-ray sources (Schmidt 1977), the radiation dose at the tumor apex was not considered in the present paper, but special attention was paid to the maximal tumor height in the ultrasonogram. After discharge from the hospital, follow-up examinations, including photographic and ultrasonographic evaluation, were done at regular intervals. All data are computerized and on file in the tumor registry of the West German Tumor Center in Essen.

## Results

The majority of tumors showed slow, uncomplicated regression within 1 year. In a minority of cases one or more of the following complications occurred: surgical complications, complications of the anterior segment, vitreous hemorrhages, radiation retinopathy, and radiation-induced optic neuropathy. Complications reported for patients treated with other radiation modalities, such as loss of cilia, the dry eye syndrome, or scleral necrosis, were not seen in this group of patients.

### *Surgical complications*

Surgical complications were related to the surgical procedure of suturing the plaque to the sclera. Complications just as hematomas of the subtenoid space or small

retrobulbar hematomas are, of course, not specifically related to $^{106}Ru/^{106}Rh$ plaques. As $^{106}Ru/^{106}Rh$ is a beta-ray source with low tissue penetration, it is very important to avoid the development of a gap between the plaque and sclera by accumulation of blood. During the operation, even very small episcleral vessels should be coagulated and the plaque should be sutured tightly to the sclera.

Complications may result from disturbances of the optic nerve perfusion. Careful observation of the central retinal artery is mandatory when treating tumors adjacent to the optic disc (Fig. 1). Nevertheless, occlussion of the central retinal artery following placement of the plaque was seen in one patient.

*Short-term postradiation complications*

Immediate or delayed (mean interval 4.9 months) radiation-induced anterior uveitis was seen in 4.4% (13/295) of the patients. In nearly all the inflammatory response of the anterior segment was transitory. Complete seclusion of the pupil with acute glaucoma requiring surgical intervention occurred in one patient. Of the patients, 13.9% (41/295) developed transitory exudative retinal detachment. Exudative detachments of the retina (or and increase in the size of preexisting retinal detachments) should not be considered as true complications unless they lead to severe deterioration of central vision in patients with peripheral tumors. Exudative retinal detachment is a sign of acute radiation damage to the blood vessels. Choroidal detachments are rare and most likely not caused by the radiation itself but by mechanical obstruction of the vortical veins.

Extensive tumor necrosis following radiation may cause subsequent hemorrhages into the tumor mass, vitreous hemorrhages and panuveitislike findings (Fig. 2). Hemorrhages into the tumor were found in 11.2% of the cases (33/295); persistent vitreous hemorrhages occurred in 6.8% of our cases (20/295).

*Long-term complications*

The most common long-term complication of the anterior segment was radiation-induced cataract formation. To date, no cataract formation has been noted in patients with choroidal melanomas. However, 10.8% of the patients with ciliary body melanomas (8/74) developed cataract after receiving a mean SCD of 443 Gy. The cataract consisted of vacuoles in the subcapsular space of the radiation sector, and these vacuoles may progress to a mature cataract. In one patient, cataract extraction was performed after subtotal tumor regression. The mean interval between radiation and cataract formation was 15.5 months (minimum 0.64 month; maximum 50 months).

The two most frequent and potentially dangerous long-term complications were radiation damage either to the retina or optic nerve. Only radiation damage to the retina not within the tumor site should be considered as radiation retinopathy. These changes consisted of focal capillary nonperfusion, microaneurysms of the retinal capillaries, preferably at the posterior pole, cotton-wool spots, intraretinal hemorrhages, occlusion of larger retinal vessels, central retinal vein occlusions, and forward new vessel formation.

Radiation retinopathy (Figs. 3 and 4) was found in 10.5% of the patients (31/295). It occurred between 1.4 and 33.8 months after radiation, with a mean of 14.5 months. Radiation retinopathy was more frequent in tumors at the posterior pole. In one case central retinal vein thrombosis developed, which was treated with photocoagulation. The mean scleral contact dose in the patients with radiation retinopathy was 700 Gy, which is in the same range as the mean SCD used in patients in whom the tumor was totally destroyed.

In 4.1% of the cases (12/295) optic neuropathy was

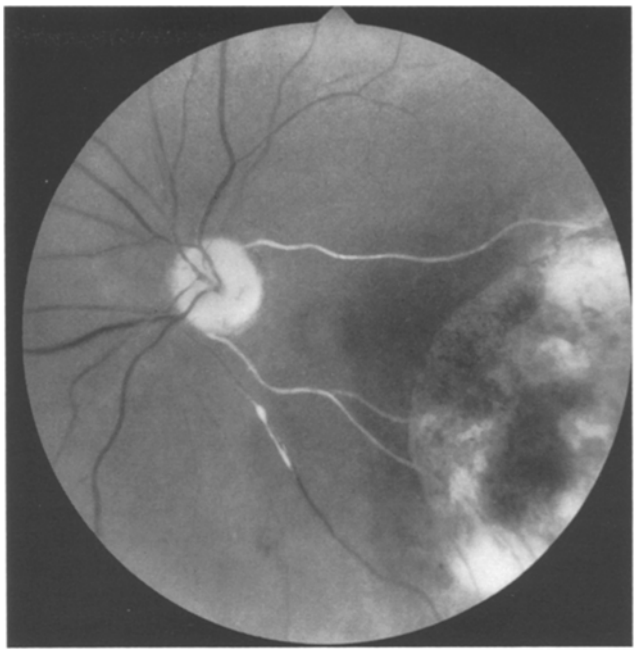

**Fig. 1.** Vascular occlusion of retinal vessels of a 61-year-old female patient after ruthenium therapy

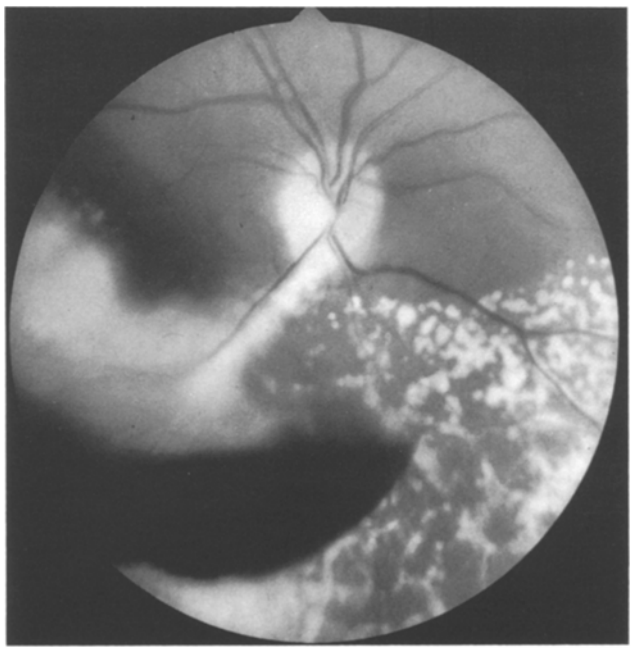

**Fig. 2.** Fundus of a 36-year-old female patient harboring a uveal melanoma in the lower temporal quadrant. The patient developed preretinal hemorrhages and extensive lipid exudates 15 months after ruthenium therapy

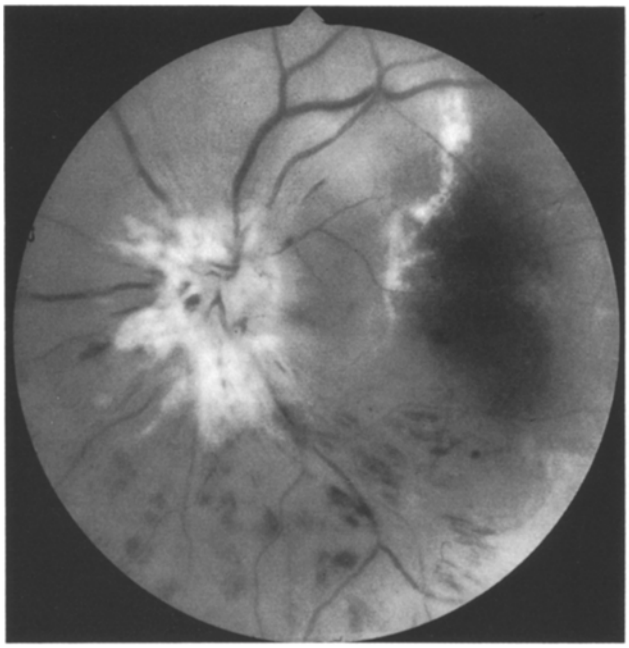

**Fig. 3.** Radiation retinopathy in a 60-year-old patient 11 months after ruthenium plaque therapy of a uveal melanoma of 40° diameter in the temporal quadrant with cotton-wool spots, hemorrhages, and extensive edema and lipid exudates in the area adjacent to the tumor

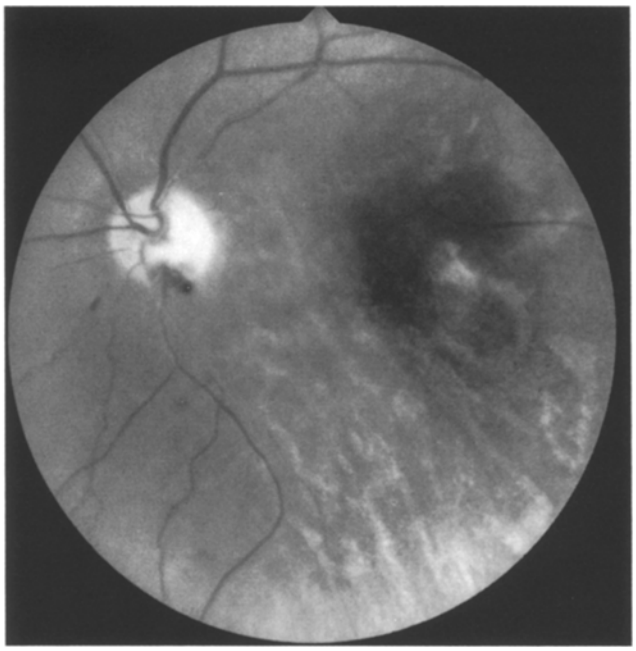

**Fig. 4.** The same patient as in Fig. 3 1 year later showing atrophic changes of retinal pigment epithelium, choriocapillaris, and optic nerve

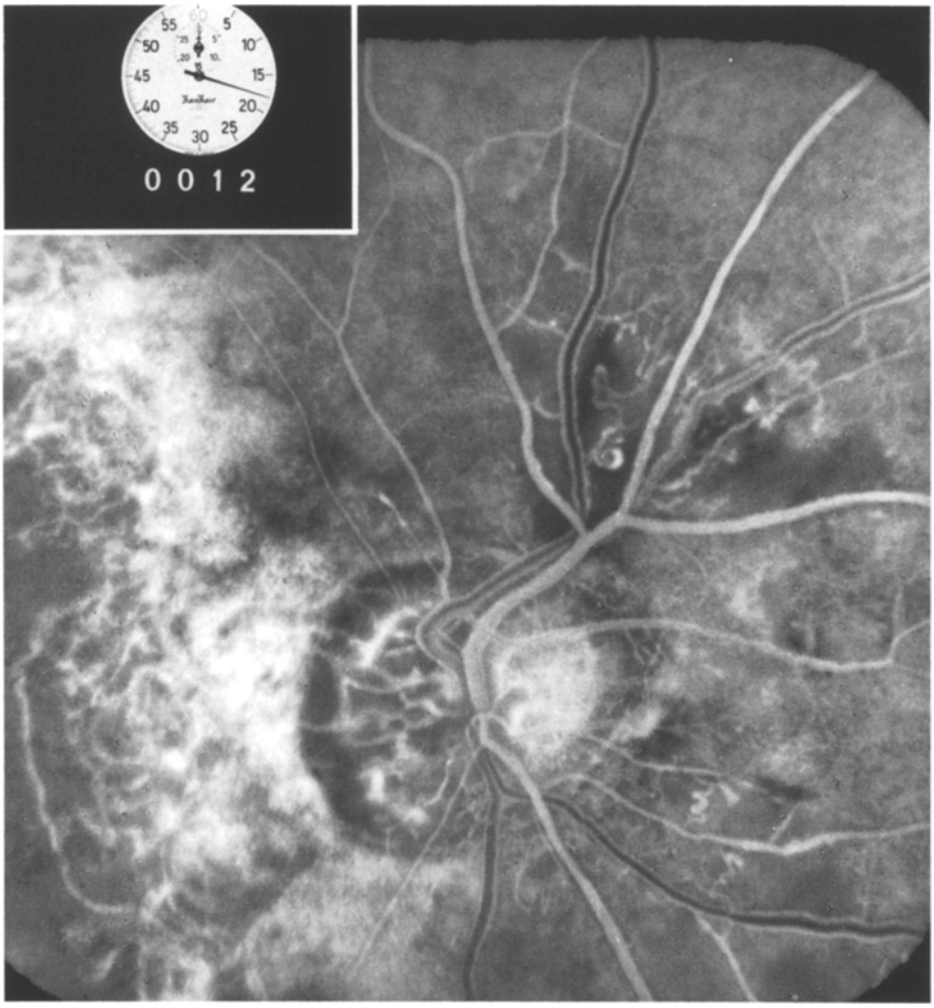


**Fig. 5.** Temporal optic atrophy 7 months after ruthenium therapy in a 45-year-old patient with uveal melanoma of 40° diameter in the macula with capillary nonperfusion without exudation

**Table 1.** Ruthenium plaque therapy of uveal melanomas

| | All patients ($n=295$) | Ciliary body tumors ($n=74$) |
|---|---|---|
| Mean age | 55.4 years | 54.8 years |
| Mean follow-up | 1.3 years | 1.23 years |
| Maximum follow-up | 5.2 years | 4.2 years |
| Mean tumor prominence | 5.7 mm | 7.9 mm |

**Table 2.** Results of ruthenium plaque therapy of uveal melanomas

| | All patients ($n=295$) | Ciliary body tumors ($n=74$) |
|---|---|---|
| Tumor destroyed | 11.9% | 11% |
| Tumor remnants | 75% | 69% |
| Recurrent tumor growth | 19% | 26% |
| Enucleation | 11% | 17.6% |
| Metastatic disease | 2% | 2.7% |

**Table 3.** Sequence of treatment modalities in ruthenium plaque therapy

| | All patients ($n=295$) | Ciliary body tumors ($n=74$) |
|---|---|---|
| Ruthenium once | 83% | 77% |
| Ruthenium twice | 16.3% | 23% |
| Ruthenium three times | 0.7% | 0% |
| Additional photocoagulation | 12.2% | 2.7% |

**Table 4.** Complications of ruthenium plaque therapy

| | All patients ($n=295$) | Ciliary body tumors ($n=74$) |
|---|---|---|
| Radiation uveitis | 4.4% | 14.9% |
| Cataract | 2.7% | 10.8% |
| Glaucoma | 2.4% | 6.8% |
| Vitreous hemorrhages | 6.8% | 5.4% |
| Increasing retinal detachment | 13.9% | 9.5% |
| Lipid exudates | 6.4% | 2.7% |
| Radiation retinopathy | 10.5% | 4.1% |
| Optic neuropathy | 4.1% | 1.4% |
| Neovascularizations | 3.1% | 1.4% |

noted (Fig. 5). In all cases the central tumor margin was within a circle of 20° surrounding the optic nerve head. No statistically significant relationship between radiation dose delivered to the tumor base and radiation-induced optic neuropathy was observed.

To date, rubeosis iridis has not been observed in the series. Secondary glaucoma as a radiation complication was rare. It occurred only in two patients with choroidal melanomas and in 6.8% of ciliary body melanomas (5/74). In 2 of 7 cases with secondary glaucoma, enucleation had to be performed because of these complications. However, in cases with radiation retinopathy or in radiation-induced optic neuropathy, no enucleation had to be performed. Enucleation was necessary in 10.8% of the cases (32/295) after a mean interval of 10.8 months (range 1.5 to 50.9 months). The most frequent cause was uncontrolled tumor growth, which was found in 25.7% of the patients with ciliary body tumors (19/74) compared with 16.9% (36/221) of the choroidal melanomas. Retinal neovascularization occurred in 2.6% of the cases (9/295) after 25.8 months (mean time). In one case photocoagulation was necessary.

## Discussion

The main advantage of using $^{106}Ru/^{106}Rh$ plaques is that a high contact dose can be delivered to the tumor base while sparing the radiosensitive intraocular and surrounding orbital tissues. The dose delivered to the lens periphery in an emmetropic eye, in which the anterior margin of the plaque overlies the pars plana, is less than 5% of the dose at the tumor base. Consequently in this series of patients, a significant decrease in cataract formation was observed. It should be emphasized that cataract formation in this series occurred exclusively in ciliary body tumors and not in patients with choroidal melanoma. The follow-up time is still insufficient to permit final conclusions, as radiation cataract can occur 10–15 years after radiation therapy. The series of Lommatzsch (1983), with a follow-up of up to 16 years, suggests that the long-term incidence of radiation cataract is no higher. All other local radiation modalities have shown a higher incidence of cataract (Rotman et al. 1977; Zografos and Gailloud 1979; Shields et al. 1982).

The serious complications in this series and in other series (Brown et al. 1982a, b) were radiation retinopathy and radiation-induced optic neuropathy. Radiation-induced changes, such as vascular occlusion or atrophy of the retinal pigment epithelium, choroid or retina overlying the plaque, were not considered to be radiation retinopathy. In this study radiation retinopathy was defined as radiation effects in the retina and choroid not within the tumor site. Radiation retinopathy may be a self-limiting disease requiring no therapy (Brown et al. 1982a; Noble and Kupersmith 1984). The hemorrhages, cotton-wool spots and lipid exudates may disappear, leaving only an atrophic scar.

In this series, the mean scleral contact dose in those patients in whom the tumor could be destroyed was 700 Gy. This resulted in a chorioretinal scar without any ultrasonically detectable tumor remnants. The incidence of radiation retinopathy was 10.5%. The mean scleral contact dose in those patients was 650 Gy. If sufficient tumor-regression results are to be obtained, it seems inevitable that the incidence of radiation retinopathy will be this high. The incidence in this series, however, was definitely lower compared with $^{60}Co$ plaque therapy (MacFaul and Bedford 1970; Zografos and Gailloud 1979; Shields et al. 1982; Rotman et al. 1983; Zografos and Gailloud 1983; Zygulska-Mach et al. 1983).

Radiation-induced optic neuropathy shows vascular phenomena that are similar to radiation retinopathy. It occurs in patients with tumors at the posterior pole and is rare in those with ciliary body tumors. No treatment is possible, and all patients suffer from severe deterioration of visual function.

$^{125}I$ plaques were introduced by teams headed by Packer and Rotman (Rotman et al. 1977; Packer and Rotman

1980; Rotman et al. 1983) when looking for low-energy gamma radiation sources as alternative to $^{60}Co$ plaques. In their series, rubeosis iridis was the most common complication in treating large tumors, a complication not encountered in ruthenium treatment. Radiation cataract and radiation retinopathy occurred more frequently than in ruthenium therapy.

Recently, Gragoudas et al. (1985) have published their follow-up data on the treatment of malignant melanomas of the uvea with external beam radiation using protons. Their complication rate seems to be lower compared with our data and the data published on other local treatment modalities. Only 1 of 241 eyes treated had to be enucleated because of continous tumor growth. Although the success rate is outstanding, the data still need confirmation (Fine 1985).

The results presented seem to indicate that ruthenium therapy is a valuable tool in the treatment of uveal melanomas and an alternative to enucleation. Even though the follow-up period is short, the rate of complications seems to be lower than in any other local treatment modality.

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