

RUTHENIUM-106 BRACHYTHERAPY FOR UVEAL MELANOMAS – PRELIMINARY RESULTS: A SINGLE INSTITUTIONAL EXPERIENCE*

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Abstract **OBJECTIVE:** To analyze the early response of uveal melanomas in patients treated with ruthenium-106 brachytherapy. **MATERIALS AND METHODS:** In the period between April 2002 and July 2003, 20 patients diagnosed with uveal melanoma were submitted to ruthenium-106 brachytherapy. The calculated dose delivered at the apex of the tumor ranged between 55 Gy and 100 Gy. Patients with lesions greater than 5 mm were submitted to transpupillary thermotherapy concomitantly with ophthalmic plaque insertion. **RESULTS:** As regards the lesions site, 75% of the lesions were located in the choroid, 15% in the iris, and the remainder 10% in the ciliary body. In a median 19-month-follow-up, the progression-free survival for brachytherapy was 69%, and 87% for associated brachytherapy and transpupillary thermotherapy. A significant tumor height reduction was observed after treatment. No patient was submitted to enucleation. **CONCLUSION:** Our preliminary results show that ruthenium-106 brachytherapy is an appropriate method for conservative treatment of patients with uveal melanomas in terms of local management, ocular and visual acuity preservation with an acceptable complications incidence rate.

Keywords: Uveal melanoma; Ruthenium plaque therapy; Conservative therapy; Brachytherapy.

Resumo *Braquiterapia com rutênio-106 em melanomas uveais – resultados preliminares: experiência uni-institucional.*

OBJETIVO: Analisar os resultados preliminares da braquiterapia com rutênio-106 em pacientes portadores de melanomas uveais. **MATERIAIS E MÉTODOS:** No período de abril de 2002 a julho de 2003, 20 pacientes com diagnóstico de melanoma uveal foram tratados com braquiterapia com rutênio-106. A dose calculada no ápice tumoral variou de 55 Gy a 100 Gy. Pacientes com lesões com altura maior que 5 mm foram submetidos a termoterapia transpupilar concomitante à colocação da placa oftálmica. **RESULTADOS:** Quanto à localização da lesão, esta se encontrava na coróide em 75% dos casos, na íris em 15% e no corpo ciliar em 10% dos pacientes. Com seguimento mediano de 19 meses, a sobrevida livre de progressão para a braquiterapia e para a associação com a termoterapia transpupilar foi de 69% e 87%, respectivamente. Observou-se redução significativa da altura tumoral após o tratamento. Nenhum dos pacientes foi submetido a enucleação. **CONCLUSÃO:** Nossos resultados preliminares mostram que a braquiterapia com rutênio-106 é uma opção adequada para o tratamento conservador de melanomas uveais em termos de controle local, manutenção do globo ocular e visão útil, com índice aceitável de complicações.

Unitermos: Melanoma uveal; Placa de rutênio; Tratamento conservador; Braquiterapia.

INTRODUCTION

Although rare, uveal melanoma is the most common primary intra-ocular malignancy in adults, with an approximate fre-

quency of six cases per million inhabitants per year in the United States^(1,2), seven cases per million inhabitants per year in the Western Europe⁽³⁾. Estimates for Brazil are not available.

Up to the eighties, the treatment for patients with uveal melanoma was surgical, consisting in enucleation, still the mainstay of therapeutical intervention for extensive lesions. However, other therapies aiming at preserving the vision and the ocular globe have been proposed since 1930⁽⁴⁾.

In 1930, Moore utilized radon seeds directly implanted into the ocular tumor of a patient⁽⁴⁾. In 1960, Stallard initiated the treatment for these tumors with cobalt-60 episcleral plaques. Since then, other iso-

topes like iodine-125, iridium-192, gold-198, paladium-103 and ruthenium-106 started being utilized⁽⁶⁻⁸⁾.

Randomized prospective studies like those developed by the Collaborative Ocular Melanoma Study (COMS) since 1986, showed that the mortality rate of patients with melanomas between 2.5 mm and 10 mm in elevation was similar when compared with the mortality rate for patients submitted to iodine-125 brachytherapy and to enucleation⁽⁶⁾. Yet, in 1986, Lommatzsch reported the utilization of ruthenium-106 beta-radiation for treatment of uveal melanomas with results comparable to those from other radioisotopes⁽⁷⁾. So, ocular brachytherapy started being used in pa-

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tients with uveal melanomas with up to 10 mm in elevation, allowing results similar to those from more radical procedures like enucleation, while preserving the visual acuity and the ocular globe.

Amongst the radioisotopes most frequently utilized in ocular brachytherapy, cobalt-60 is a gamma-radiation emitter with 1.25 MeV energy and 5.2-year half-life, whose main disadvantages are the higher radiation exposure of the medical team and higher radiation dose in adjacent organs, and iodine-125, a gamma-radiation emitter with 0.028 MeV energy and a relatively short 59.6-day half-life. As regards ruthenium-106, this isotope presents as main characteristic the beta-radiation emission, allowing higher dose concentration in the tumor, and lower dose in adjacent areas. Besides, the medical team involved in the procedure is submitted to lower exposure to radiation, and organs in risk receive lower radiation doses, consequently optimizing the radiological protection^(3,8).

Considering that ruthenium-106 is a beta-radiation emitter, it is best indicated in the treatment of small melanomas, with up to 6 mm in elevation and a long half-life, allowing longer periods of use and therefore lower cost compared with other isotopes. Ruthenium radiation dose calculation is performed with basis on tables provided by the manufacturer, and otherwise expensive computer planning systems are not necessary⁽⁹⁾ (Figure 1).

Main complications associated with brachytherapy are: retinopathy, cataract, neovascular glaucoma and maculopathy which may occur in 9% to 27% of cases in a three-year period. Main influencing factors which seem to be related with such complications are tumor elevation, TMN stadium, and the proximity of the tumor with the fovea and optic disc⁽¹⁰⁾.

Most recently, transpupillary thermotherapy has started being utilized. It is a form of therapy utilizing infrared laser diode for inducing hyperthermia with a variation between 45°C to 60°C. This therapeutic modality is exclusively indicated in cases of small melanomas in conjunction with brachytherapy allowing the treatment of lesions > 5 mm, or even as an adjuvant therapy in cases where regression is not achieved or where there is a regression of the disease⁽¹¹⁾. Transpupillary thermotherapy is characterized by a deep penetration with an immediate cytotoxic effect, resulting in necrosis of the tumor up to 6 mm in depth in experiments with animals, and 4.7 mm in melanomas of the choroid in humans⁽¹²⁾.

The ideal therapy for ocular melanomas still remains controversial, and ocular brachytherapy and external radiotherapy with proton beam are adequate therapeutic options aiming at preserving the ocular globe and the vision^(13,14).

So, the present study is aimed at analyzing the preliminary results from ruthenium-

106 brachytherapy in patients with uveal melanoma.

MATERIALS AND METHODS

This is a retrospective study performed on 20 cases of patients with unilateral uveal melanoma, referred to the Radiotherapy Unit by the Department of Ophthalmology of Universidade Federal de São Paulo, for being submitted to ocular brachytherapy, in the period between April 2002 and July 2003.

The diagnosis was made by clinical and ophthalmological examinations. Fluorescein angiography and ocular ultrasound A- and B-scans were requested. Both modes were employed for evaluating the tumors elevation. For evaluation of the tumors localized in the iris and ciliary body ultrasonic biomicroscopy was performed.

The staging of patients aiming at characterizing the absence of metastatic lesions included chest x-ray, abdominal ultrasound, hemogram and biochemical analysis. The patients were staged according to TNM⁽¹⁵⁾ and COMS⁽¹⁶⁻¹⁸⁾ criteria.

For the present study, the following inclusion criteria were taken into consideration: diagnosis of unilateral melanoma of the choroid, iris or ciliary body; tumor ≤ 6 mm in elevation; base diameter ≤ 16 mm; patients with age ≥ 21 years. Patient's informed consent. Exclusion criteria were the following: diagnosis of another malignancy; patients undergoing immunosuppressive therapy; patients incapable of returning for follow-up; patients with severe co-morbidities; multifocal or diffuse lesions with scleral infiltration; previously treated patients; patients with metastasis; lesions that cannot be delimited by ocular ultrasound.

Bebig GmbH (Berlin, Germany) ruthenium-106 ophthalmic plaques were utilized. The main feature of these plaques is beta-radiation emission, with maximum 3.54 MeV energy, and half-life of 365 days.

Two plaque models were employed: COB (round notched) and CCB (round), both with 20 mm in diameter (Figure 2). Patients with lesions proximal to the optic nerve were submitted to brachytherapy with the COB plaque, while in the other the CCB plaque was utilized. Patients with

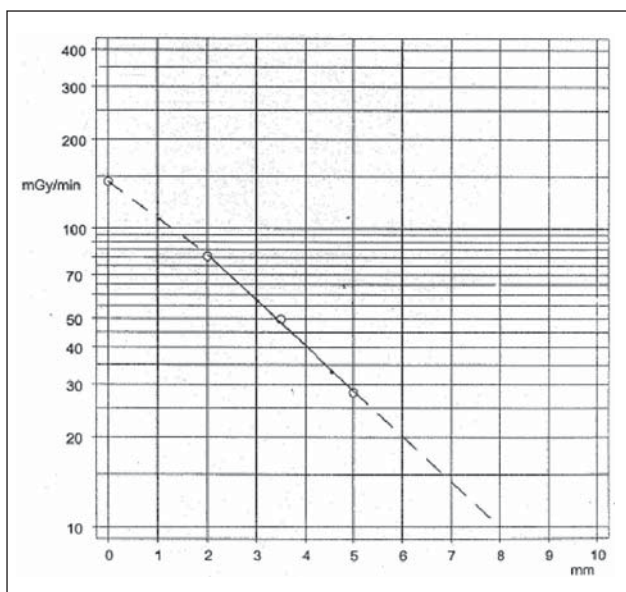


Figure 1. Calculation of radiation dose, illustrating the dose rate in mGy/min × depth in mm.



Figure 2. RU-106 plaque models: CCB (round) and COB (round notched).

lesions with more than 5 mm in elevation (five patients) were submitted to transpupillary thermotherapy delivered to the apex of the tumor, associated with placement of the ophthalmic plaque. The prescribed radiation dose was calculated on the apex of the lesion, from the inner face of the sclera.

The present study covered the following aspects: demographic data (age and sex of patients), tumor characteristics (lesion site, affected eye, TNM and COMS staging, tumor elevation), and treatment characteristics (type of plaque, radiation dose to the apex, base and sclera).

After the treatment, the patients were clinically evaluated every three months

during the first two years of follow-up, with the purpose of verifying the local management, progression-free survival, the lesion elevation, rate of preservation of the ocular globe, visual acuity and presence of metastases and complications. Ocular ultrasound and fluorescein angiography were performed every three months, and chest x-ray and abdominal ultrasound, every six months. The local management was defined as stabilization or decrease in the lesion elevation at imaging study in comparison with the pre-treatment study. The presence of lesions in other sites was defined as metastasis. Progression-free survival corresponds to absence of local or distance failure. Treatment-related adverse effects were considered as complications. The follow-up period started in the date of the plaque placement.

Parameters regarding demographic, tumor and therapy characteristics, rate of preservation of the ocular globe, presence of metastasis and complications were submitted for a descriptive analysis.

With the purpose of comparing numerical variables in relation to the local management, lesion elevation before and after the therapy, and visual acuity, summary measures were calculated and box-plots

were constructed. The *t*-test was employed for evaluating variables related to local management and visual acuity, and the paired *t*-test for comparing pre- and post-therapy tumor elevation. Contingency tables were elaborated, and the Fisher's exact test was employed for evaluating.

Kaplan-Meier curves were constructed to estimate survival curves of interest in relation to the progression-free survival.

In all of the tests, the null hypothesis rejection level was fixed in 0.05 or 5% ($p < 0.05$), significant values being marked with an asterisk, and the non-significant values, with (NS).

RESULTS

The patients' ages ranged between 29 and 80 years (median, 56 years). The majority of patients were Caucasian (95%), and women (70%) (Table 1).

As regards tumor characteristics, the right eye was involved in 45%, and the left eye in 55% of cases. Choroid and/or ciliary body melanomas were diagnosed in 85% of patients, and iris melanoma in 15%. The lesion elevation ranged between 1.14 mm and 6 mm (median, 3.45 mm) (Table 1). TMN staging demonstrated 20% of pa-

Table 1 Demographic and evolutive characteristics of patients submitted to ruthenium brachytherapy.

Patient	Age (years)	Sex	Eye	Elevation (mm)	Plaque	Time (days)	Apex dose (cGy)	Final elevation (mm)	Complication
1	46	Male	Left	3.35	CCB	2	9.475	0.68	No
2	48	Female	Right	4.80	COB	3	7.379	0.00	Visual worsening
3	63	Female	Right	1.14	CCB	2	10.488	0.89	No
4	62	Female	Left	3.50	CCB	3	9.072	3.30	No
5	46	Male	Right	3.80	CCB	3	8.986	3.10	No
6	29	Female	Right	1.68	CCB	2	9.532	1.60	No
7	46	Female	Left	6.00	CCB	4	5.932	1.80	No
8	33	Female	Right	3.40	COB	2	8.064	0.00	Visual worsening
9	46	Male	Left	3.37	COB	2	7.891	0.00	Visual worsening
10	64	Female	Left	5.50	CCB	5	8.280	4.00	No
11	48	Female	Right	5.20	CCB	4	8.502	3.90	No
12	55	Male	Left	3.00	COB	3	8.493	3.00	No
13	57	Female	Left	3.41	CCB	4	8.582	2.54	No
14	75	Male	Right	5.40	CCB	5	6.278	4.60	Infectious
15	79	Female	Left	3.80	CCB	4	7.142	2.90	No
16	80	Female	Left	6.00	COB	4	5.587	6.30	No
17	62	Female	Left	1.92	CCB	2	8.493	1.36	No
18	80	Male	Left	2.40	CCB	3	8.680	2.60	Visual worsening
19	54	Female	Right	1.57	CCB	3	8.432	1.50	No
20	59	Female	Right	3.70	CCB	5	8.160	3.50	No

CCB, round plaque; COB, round notched plaque.

tients staged as T1, and 80% as T2. According to COMS criteria, 10% of lesions were small-sized, and the remaining 90%, intermediate. As regards the therapy, the radiation dose to the apex ranged between 55.8 Gy and 104.8 Gy (median, 84.6 Gy). The median of the radiation-dose to the tumor base and sclera was respectively 248.3 Gy and 319.4 Gy. The CCB plaque was utilized in 75% of cases. The follow-up period ranged between 9 and 23 months (median, 19 months).

During the clinical follow-up, an increase in the tumor dimensions was observed in five cases (25%). Of these patients, three were submitted to adjuvant transpupillary thermotherapy, and currently are under follow-up, with no evidence of disease progression. Two patients could not undergo transpupillary thermotherapy because of the lesion localization. One of them is under observation, and enucleation is scheduled for the other. Table 2 shows the local management with brachytherapy and associated with transpupillary thermotherapy. The initial elevation of the lesion

($p = 0.883$), the prescribed radiation-dose to the tumor apex ($p = 0.879$) and the lesion localization ($p = 1.000$) did not constitute significant factors for the local management of the disease. The progression-free survival with brachytherapy and with adjuvant transpupillary thermotherapy may be observed in Kaplan-Meier survival curves (Figure 3). One patient progressed to death nine months after therapy due to unrelated causes. Comparing the initial elevation of the lesion with the elevation after the therapy, a significant reduction ($p = 0.001$) was observed (Figure 4). No patient was submitted to enucleation. As regards visual acuity at the moment of the latest evaluation, 70% of patients presented a visual acuity higher than 20/200, and 30% presented visual acuity equivalent or lower than 20/200. The prescribed radiation dose to the tumor base and sclera did not constitute a prognosis factor of significance for the visual acuity.

During the follow-up period distant metastases were not detected. Complications were observed in 25% of cases. In

four patients, visual acuity worsening was observed in one patient, and another presented infectious complication.

DISCUSSION

Results regarding demographic compare favorably with previous studies published in the literature, demonstrating a predominance of uveal melanoma in Caucasian patients with median age of 60 years. Singh and Tophan, in an epidemiological analysis of melanomas in the United States reported a 97.8% incidence in Caucasian individuals. In this same study, the ages of the population studied ranged between 6 and 100 years, 59.4 year for men, and 61.5 for women (median, 59.4 years). As regards sex, uveal melanoma seems to present a slightly high incidence in men. Notwithstanding this fact has not been observed in the present study, this may be justified by the low number of patients in comparison with studies performed for incidence evaluation⁽¹⁾.

In the analysis of the tumor characteristics, melanomas most frequently were located in the choroid. Also, a higher number of cases of iris melanomas were observed in the present study in relation to the literature where the reported incidence achieves only 2%–3% for lesions localized in this topography⁽¹⁹⁾. The mild predominance in the left eye observed in the present

Table 2 Local management after brachytherapy and brachytherapy with transpupillary thermotherapy.

Treatment	Local management		Failure		Total	
	N	Rate	N	Rate	N	Rate
Brachytherapy	15	75%	5	25%	20	100%
Brachytherapy + TTT	18	90%	2	10%	20	100%

TTT, transpupillary thermotherapy.

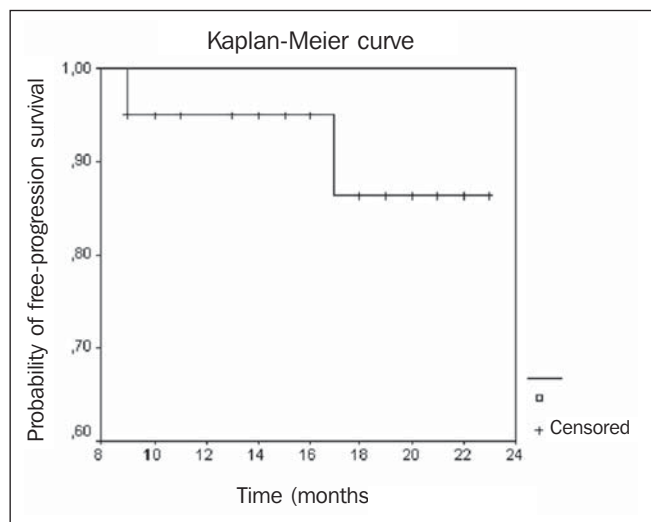


Figure 3. Kaplan-Meier estimation of progression-free survival in patients submitted to ruthenium-106 brachytherapy and adjuvant transpupillary thermotherapy.

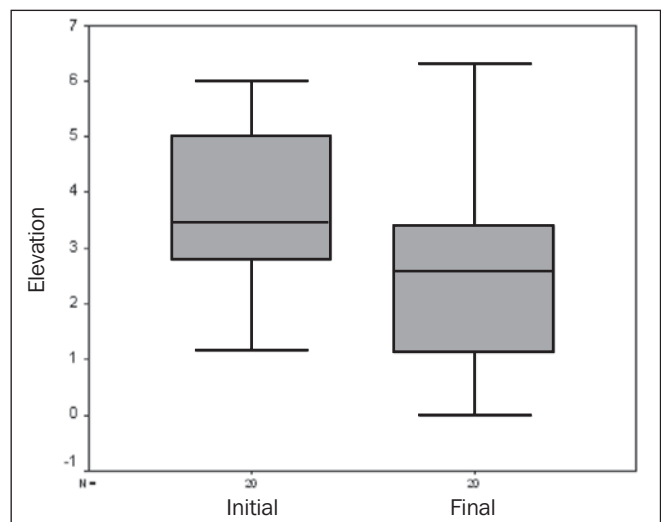


Figure 4. Initial tumor elevation in relation to the final elevation.

study also is reported by some studies in the literature. Hermann et al. observed that in 56% of cases, the tumors were localized in the left eye⁽²⁰⁾. However, this difference was not observed in studies involving a higher number of cases⁽¹⁸⁾.

All of the lesions were staged as T1 or T2N0M0 by the TNM (6th edition)⁽¹⁵⁾, and as intermediate by the COMS. In other publications about the employment of ruthenium-106 in melanomas therapy, a predominance of tumors staged as T1 and T2 also is observed. This is due the fact that ruthenium-106 is a Beta-radiation emitter with low penetrability, besides not being indicated for more extensive lesions. Also, it may be added that the majority of studies was based on the staging method recommended by the International Union Against Cancer (UICC) in 1997⁽²¹⁾, classifying choroid melanomas with > 5 mm in elevation and/or >15 mm in diameter as T3. According to the TMN 6th edition, only those lesions with > 16 mm in its larger diameter and/or > 10 mm in elevation would be classified as T3. So, considering the new staging, one can say that the incidence of T1 and T2 tumors described in the literature probably is higher. This also can be confirmed by the comparison between the median elevation of the lesions in the present study (3.45 mm) and that reported in the literature, ranging from 3 mm to 5.2 mm^(22,23).

The most utilized plaque was the round-shaped CCB. The greatest majority of studies performed with ruthenium-106 plaques do not describe the plaque models. In the present study, the CCB model was utilized in the treatment of patients with central lesions, proximal to the optic nerve, while the COB plaque was utilized in the remaining. As regards the lesions localization, the literature reports a lower incidence of central lesions in comparison with paracentral, peripheral or yet ciliary body and iris lesions. In the study performed by the COMS, lesions at 0–2 mm from the optic disc corresponded to only 14.9% of cases⁽²⁴⁾. On the other hand, in other publications, central lesions were observed in 35% of cases, these results being similar to the ones from the present analysis⁽¹⁷⁾.

The ruthenium-106 plaque time of permanence ranged between two and five days

(median, three days), and was directly proportional to the prescribed radiation-dose delivered to the tumor apex, and inversely proportional to the plaque activity. The prescribed dose delivered to the tumor apex ranged between 55 Gy and 105 Gy (median, 85 Gy), and to the base, the prescribed dose ranged between 148 Gy and 450 Gy. The dose delivered to the sclera ranged between 191 Gy and 578 Gy. The radiation dose to be prescribed to the tumor apex with ruthenium-106 is still to be defined in the literature. In an analysis of several studies in the literature about the use of ruthenium plaque for treatment of melanomas, one can observe that most of times the dose ranges between 80 Gy and 100 Gy, but studies with doses from 60 Gy to 160 Gy may be found. Rouberol et al. have treated 213 patients affected by choroid and ciliary body melanoma with a 60 Gy dose⁽²⁵⁾. Shields et al., in a study about visual acuity in 1,106 patients with uveal melanoma submitted to brachytherapy with iodine-125, ruthenium-106, cobalt-60 or iridium-192, have described a median dose of 90.9 Gy to the apex, and 330 Gy to the tumor base⁽²⁶⁾. Seregard, in a meta-analysis with 1,066 patients treated with ruthenium-106 has observed a dose to the apex ranging between 80 Gy and 100 Gy⁽²⁷⁾. A study describing the Dutch experiment with ruthenium for uveal melanoma utilized doses up to 160 Gy delivered to the tumor apex, and doses to the sclera from 220 Gy to 950 Gy⁽³⁾. Hermann et al., analyzing the effect of the dose-assignment in relation to results from ruthenium-106 plaque brachytherapy, utilized doses of 120 Gy to the apex of the tumor⁽²⁰⁾. Shields et al., in a study with concomitant transpupillary thermotherapy and brachytherapy, describe a dose to the apex ranging between 55 Gy and 124 Gy (median, 90 Gy), and 254 Gy to the base⁽¹¹⁾. As regards radiation dose to be utilized, the American Brachytherapy Society recommends the dose of 85 Gy to the apex of the lesion when iodine-125 is utilized as radioisotope⁽¹⁴⁾. However, these same guidelines recommend a dose from 120 Gy to 160 Gy aiming at maximizing the healing effect when ruthenium-106 is utilized. Meanwhile, the American Brachytherapy Society suggests that this large dose gradient may result in high doses to the sclera, which may

cause a higher number of complications⁽¹⁴⁾. In a randomized prospective study developed by the COMS utilizing iodine-125 in the treatment of choroid melanomas, in 49.9% of cases, the dose to the apex was 85.1 Gy to 120 Gy, and in 41.3% of patients the dose to the sclera ranged between 293 Gy and 409.9 Gy⁽²⁷⁾. So, studies evaluating dose-assignment excepted, the doses utilized in the present study are compatible with data in the literature regarding prescribed radiation dose to the apex of the lesion, to the tumor base and sclera.

Our results in relation to local management and progression-free survival compare to previous studies, despite the difficulty to evaluate retrospective data from different centers, considering variations in follow-up periods, tumors dimensions and doses delivered. Summanen et al., evaluating 100 patients treated with ruthenium-106, have observed local failure in 19% of cases with 0.1 to 2.7 years of follow-up (median, 0.7 year)⁽²⁸⁾. This leads to the conclusion that local failures occur precociously, especially in the first years of follow-up, and are very significant for the interpretation of our results. Studies with similar follow-up periods demonstrate a complete tumor regression in 57.1% of cases and local recidivation in 31% of patients⁽²⁹⁾. Foerster et al., evaluating the ruthenium therapy in 100 patients affected by uveal melanoma, have observed local recidivation of 12%, with a median two-year follow-up period⁽³⁰⁾. Seregard, in a review of the Swedish experiment with transpupillary thermotherapy as an adjunct to ruthenium brachytherapy, has observed in a 20-month follow-up period that in 70.3% of cases there was a partial or complete regression of the lesion, a result very similar to the 75% local management observed in the present study⁽³¹⁾.

Lommatzsch et al., analyzing 141 patients submitted to ruthenium brachytherapy at a dose of 100 Gy, have observed a disease-free survival rate corresponding to 89.6% in five years⁽³²⁾. Seregard, in a meta-analysis involving 1,066 patients treated with ruthenium at doses between 80 Gy and 100 Gy, has observed a disease-free survival of 86% in five years⁽²⁷⁾. In the present study, once the progression-free survival of patients submitted to brachytherapy and

transpupillary thermotherapy is analyzed, one may observe that our results are similar to those in the literature, with a longer follow-up period and higher number of cases.

Studies evaluating the dose-assignment effect on the local management show controversial results. Tjho-Heslinga et al., utilizing a dose to apex of 160 Gy in 101 patients affected by uveal melanoma, have observed complete and partial remission in respectively 62.6% and 31.3% of cases, these results being slightly superior to those described in the literature with the usual doses. In the present study, transpupillary thermotherapy also was utilized in 25 patients, allowing a reduction in the radiation dose and, consequently, in the risk of retinopathy⁽³⁾. However, in another study with a 120 Gy dose to the apex of the lesion in patients with choroid melanomas, the benefit from the dose-assignment to the survival has not been observed⁽²⁰⁾.

In a literature review, elevation and larger basal diameter of the tumor, dose delivered to the tumor apex and retinal detachment play a significant role in relation to the local management and disease-free survival⁽²⁷⁾. In the present study, factors like lesion elevation, radiation dose, and tumor localization did not affect the local management of the disease. This may have occurred because of the number of patients and number of failures observed, since this is a rare malignant neoplasm. Also, it may be added that the concomitant employment of transpupillary thermotherapy and brachytherapy in patients with lesions > 5 mm may have contributed to the favorable and similar results of patients with larger lesions who received lower radiation dose to the apex of their tumors.

The post-therapy tumor elevation was significantly lower than that before the treatment, evidencing that the therapy was effective, allowing a decrease in the tumor thickness of about 65% of the initial elevation. In a literature review in terms of reduction of tumor elevation after ruthenium brachytherapy, a reduction around 3%/month is observed, and the majority of lesions do not present a complete regression, stabilizing at a constant value around 61% of the initial elevation after approximately 24 months⁽²³⁾. In our series, results concern-

ing enucleation and visual acuity are slightly better than those in the literature. Quivey et al. have observed that 58% of 239 patients treated with iodine plaques maintained a vision $\geq 20/200$ ⁽³³⁾. The COMS Report no. 16 has evaluated the visual acuity of patients three years after iodine brachytherapy and observed an enucleation rate of 6.2% and visual acuity $\leq 20/200$ in 43% of cases. In this same study, after a 24-month follow-up, compared with our series, 4% of the patients had been enucleated, and 33% presented visual acuity $\leq 20/200$ ⁽²⁴⁾. In another analysis of visual acuity after brachytherapy, Shields et al. have observed that in 51% of cases the visual acuity was $\leq 20/200$ ⁽²⁶⁾. Notwithstanding our results have shown that the prescribed radiation dose does not affect the visual acuity, probably because of the number of cases, the factors that seem to be related to the visual acuity after the therapy are: the isotope utilized, the presence of diabetes, the tumor elevation, the lesion localization, the type of plaque utilized, and the presence of retinal detachment⁽²⁴⁾.

The presence of metastasis is observed in about 10%-20% of patients with uveal melanoma, and is related mainly to the tumor size⁽³⁴⁾. In our series, the presence of metastasis was not observed. This may be explained by the fact that the present study includes only patients at the initial phase of the disease, with tumors ≤ 6 mm in elevation.

Analyzing this series as a whole, despite the short follow-up period and the small number of patients, our results show that ruthenium brachytherapy allowed a good local management of the disease and a reasonable progression-free survival in the studied population. Notwithstanding enucleation would be the therapy indicated in our institution, the use of this radioisotope allowed, in all of the cases, the preservation of the ocular globe, and the maintenance of the visual acuity at a certain extent.

This is the first study about the use of ruthenium in our country, and we consider that this radioisotope may be exclusively utilized in the treatment of uveal melanomas with up to 5 mm in elevation, while patients with lesion with more than 6 mm

in elevation are candidates to brachytherapy with other radioisotopes. In cases of melanomas with 5 mm to 6 mm in elevation, ruthenium brachytherapy must, if possible, be associated with transpupillary thermotherapy.

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