

## ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

# Current management of choroidal melanoma in Serbia

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**Introduction/Objective** Uveal melanoma is the most common primary malignant intraocular tumor in adults, and approximately 90% of uveal melanomas originate from the choroid. Nowadays, different treatment options for choroidal melanoma are available and an increasing tendency toward eye-sparing therapies is evident. The aim of this paper is to analyze the current treatment of choroidal melanoma in Serbia.

**Methods** This was a retrospective, observational study. Included patients were those with choroidal melanoma diagnosed at the Clinic for Eye Disease, Clinical Center of Serbia in Belgrade, between January 2014 and December 2016. Information on patients' age and gender and suggested and performed therapy was analyzed.

**Results** During the observation period, a diagnosis of choroidal melanoma was established in 148 patients, 71 (48%) males and 77 (52%) females. Recommended treatment was enucleation in 108 (72.9%), brachytherapy in 24 (16.2%), and proton beam radiation in 16 (10.8%) patients. Fifteen (10.1%) patients did not accept the suggested therapy, 10 (6.8%) patients refused any treatment at all, and five patients insisted on enucleation instead of advised eye-sparing therapies.

**Conclusion** In our country, choroidal melanoma is usually detected late, when the possibility of an efficient local treatment with preservation of the eye and its function is limited and when the patient's prognosis is poor. A periodic fundus examination in mydriasis in persons after the age of 50 years plays an important role in early diagnosis of a disease.

**Keywords:** choroidal melanoma; treatment; Serbia

**INTRODUCTION**

Uveal melanoma is the most common primary malignant intraocular tumor in adults. Standardized annual incidence rates of a tumor increase from less than two per million in the south to more than eight per million in the north of Europe [1]. Approximately 90% of uveal melanomas originate from the choroid [2].

Careful clinical fundus examination with a dilated pupill is the most important element in the diagnosis of choroidal melanoma, accompanied by ancillary methods such as ultrasonography, fluorescein angiography, or optical coherence tomography. Despite the fact that the main oncologic principle of histological or cytological evaluation of the lesion is not routinely performed in the diagnosis of choroidal melanoma, the diagnosis of the tumor is highly accurate [3].

Nowadays, the treatment of choroidal melanoma is the main challenge. The main goal of local tumor treatment is to eradicate the tumor locally in order to prevent further tumor dissemination. In addition, the effort is made to preserve the eye and the best possible visual function.

Individual approach to choroidal melanoma treatment is necessary. Characteristics of each tumor and diseased eye, the visual function, the

patient's general health and its expectations and preferences, the characteristics and availability of the treatment modalities have to be taken into consideration in deciding on melanoma treatment. Nowadays, different treatment options for choroidal melanoma are available, and an increasing tendency toward eye-sparing therapies is evident.

The aim of this paper is to analyze the current treatment of choroidal melanoma in Serbia.

**METHODS**

This was a retrospective observational study. Included patients were those with choroidal melanoma diagnosed at the Clinic for Eye Diseases, Clinical Center of Serbia in Belgrade, between January 2014 and December 2016. At the Clinic, all patients with presumed intraocular tumor are presented to the Consultation Group, which, after detailed patient examination and analysis of his medical papers, recommends treatment. The final decision on therapy is made in consultation with the fully informed patient. The data on patients were obtained from the Consultation Group registry. Information on patients' age and gender, and suggested and performed therapy was analyzed.

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## RESULTS

During this three-year observation period, a diagnosis of choroidal melanoma was established in 148 patients, 71 (48%) males and 77 (52%) females. In 39.2% of patients, the diagnosis of choroidal melanoma was established in the seventh decade of the patient's life. The mean age at diagnosis for all the patients was 62.5 years – 62.7 for males and 62.4 for females.

The recommended treatment was enucleation in 108 (72.9%), brachytherapy in 24 (16.2%), and proton beam radiation in 16 (10.8%) patients. Enucleation was advised to 45 males and 63 females, brachytherapy to 15 males and nine females, and proton beam radiation to 11 males and five females.

Fifteen (10.1%) patients did not accept the suggested therapy, 10 (6.8%) patients, of whom seven males and three females, refused any treatment at all. Two patients insisted on enucleation instead of the advised brachytherapy, and three patients wanted enucleation instead of the recommended proton beam radiation; these five patients were treated according to their wishes.

## DISCUSSION

The Clinic for Eye Diseases, Clinical Center of Serbia in Belgrade, has a special unit for ophthalmology-oncology, the only one of its kind in our country. The great majority of patients with intraocular tumors from Serbia are treated in this unit, and records from it can be considered representative for our population.

A standardized incidence rate for uveal melanoma in Central Europe is four to six per million [1]. This rate remains stable. At the Clinic for Eye Diseases of the Clinical Center of Serbia, in the period from 1986 to 2005, the average of 48.7 new cases of uveal melanoma per year were registered [4]. We registered 49.3 new cases of choroidal melanoma per year. Our findings point out that the incidence of choroidal melanoma in Serbia is in accordance with the incidence of this tumor in Central Europe and that it is relatively stable.

We found more female than male patients with choroidal melanoma, which is unexpected. In a study of 1,824 patients with uveal melanoma in Serbia over a 55-year-long period, Latković [4] found a slight preponderance of males, which is in accordance with the literature data.

In a 40-year-long study in the USA, the mean age of patients at diagnosis of uveal melanoma was 61.4 years [5]. The mean age of our patients at diagnosis was 62.5 years. Our patients were older than patients with uveal melanoma diagnosed in Serbia between 1951 and 2005, with a mean age of 54.95 years [4]. Andreoli et al. [6] stated that the mean age at diagnosis has increased over the last 37 years.

The percentage of uveal melanoma cases managed primarily by radiotherapy increased by 62% between the 1973–1977 and 2006–2012 time periods according to the Surveillance, Epidemiology and End Results database in

the USA [5]. In the USA in the 1973–1975 period, 93.8% of patients with uveal melanoma were treated only by surgery, but in 2006–2008 period, just 28.3% of patients were treated surgically. Primary enucleation was performed in 33% of 2,384 patients with uveal melanoma between 1996 and 2011 in the United Kingdom [7].

Unfortunately for 73% of patients with choroidal melanoma in Serbia, enucleation is still the initial treatment of a tumor. It means that in time of melanoma, the prognosis of the visual function is poor, the tumor is voluminous, and secondary changes like total retinal ablation or secondary glaucoma are present. The situation is worse in female patients. Enucleation is recommended in 83% of female and in 63% of male patients with choroidal melanoma.

In our country, only 16% of choroidal melanoma is diagnosed when the tumor is relatively small and the eye is in a relatively good condition with useful function, and when brachytherapy is advisable.

Various clinical, histopathologic, genetic, and molecular parameters are discussed and recognized as predictors of metastatic disease and survival in choroidal melanoma. The tumor size is a parameter with considerable influence on melanoma prognosis. A study of 8,033 uveal melanomas found metastases at 10 years' follow-up in 12% of patients with small melanoma and in 49% of patients with large melanoma, and the authors concluded that the increase of the thickness of the tumor leads to an increase in the risk of metastasis occurrence [8]. It has been shown that with each 1 mm increase in tumor thickness as measured by ultrasonography the risk of metastasis increases by 5% [9].

The fact is that tumor size is the only parameter important for melanoma prognosis on which we can have some influence. Diagnosis of small choroidal melanoma provides the best possible prevention of metastases development and gives a possibility to apply an eye-conserving treatment with the potential of saving useful vision.

In Finland, 13% of patients with uveal melanoma were entirely asymptomatic at the time of diagnosis [10], and in the United Kingdom as much as 30.2% of patients were free of symptoms on referral [7]. A delay of less than four months from the onset of symptoms to treatment may not always represent a serious hazard [10].

## CONCLUSION

The importance and benefits of early diagnosis and treatment of choroidal melanoma are obvious. Unfortunately, in our country, the tumor is usually detected late, when the possibility of efficient local treatment with preservation of the eye and its function is limited and when patient's prognosis is poor.

It is important to provide proper information about choroidal melanoma to the general population and to insist on the importance of early diagnosis of the disease. A periodic fundus examination in mydriasis in persons after the age of 50 years is of great importance. Special attention must be given to women.

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## Лечење меланома хороидеје у Србији данас

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### САЖЕТАК

**Увод/Циљ** Меланом увеје је најчешћи примарни малигни интраокуларни тумор одраслих, а око 90% меланома увеје су меланоми хороидеје. Данас постоје различите могућности за лечење меланома хороидеје, а све чешће се примењују поступци који поред ефикасне локалне терапије тумора омогућавају очување ока.

Циљ рада је био да се анализира како се меланом хороидеје лечи данас у Србији.

**Методe** У ретроспективну студију посматрања укључени су болесници код којих је дијагноза постављена у периоду од јануара 2014. до децембра 2016. Анализирани су подаци о полу и узрасту оболелих и о предложеној и спроведеној терапији меланома хороидеје.

**Резултати** Дијагноза меланома хороидеје је постављена код 148 болесника – 71 (48%) мушкарца и 77 (52%) жена. Препоручена терапија је била енуклеација код 108 (72,9%) болесника, брахитерапија код 24 (16,2%) и терапија усмереним снопом протона код 16 (10,8%). Петнаест (10,1%) болесника није прихватило саветовану терапију, десет (6,8%) је одбило било какву терапију, а пет је инсистирало на енуклеацији уместо предложене зрачне терапије.

**Закључак** Меланом хороидеје се обично дијагностикује касно, могућности за ефикасну локалну терапију тумора уз очување ока и његове функције су ограничене и животна прогноза оболелог је озбиљна.

**Кључне речи:** меланом хороидеје; терапија; Србија