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Short-term efficacy of eye-saving treatment for medium and large T1-T4 choroidal melanomas in Ukrainian population as assessed by local tumor control

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Purpose. *To assess the efficacy of eye-saving treatment (involving transpupillary thermotherapy (TTT) combined with strontium-90 (Sr90)/ yttrium-90 (Yt90) brachytherapy (BT)) for medium and large CM in terms of local tumor control rate at 12 months after the initiation of treatment.*

Material and Methods: *This retrospective cohort study included 283 patients with CM who were treated at SI "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine" from 2007 to 2024. The study sample consisted of 125 men (44.2%) and 158 women (55.8%), with a mean age (standard deviation) of 54.2 (12.4) years. Short-term success was defined as evidence of complete tumor regression, partial tumor regression or stabilization of the tumor process at 12 months after the initiation of treatment. Short-term failure was defined as evidence of continued tumor growth, tumor recurrence (a tumor growing from the scar) or extrabulbar spread at 12 months after the initiation of treatment.*

Results: *Short-term treatment success was achieved in 274 patients (96.8%). Particularly, complete tumor regression was achieved in 86/274 patients (31.4%) or 86/283 patients (30.4%), partial tumor regression, in 165/274 (60.3%) or 165/283 (58.3%), and regression with stabilization of tumor size, in 23/274 (8.4%) or 23/283 (8.1%). Local treatment failure in the form of continued tumor growth was seen in 9/283 patients (3.2%) and led to enucleation.*

Conclusion: *More effective outcome of the eye-saving treatment (involving TTT combined with Sr90/ Yt90 BT) for CM may be expected in patients with T1 stage (tumor thickness of 3.1-6.0 mm and base diameter of 3.1-9.0 mm), T2 stage (3.1-9.0 mm; 3.1-15.0 mm), and T3 stage with category 4 tumor size (tumor thickness of 3.1-6.0 mm and base diameter of 15.1-18.0 mm) and category 5 tumor size (6.1-9.0 mm; 12.1-18.0 mm).*

Key words:

melanoma, choroidal melanoma, laser treatment, ophthalmology, oncology, ionizing radiation, radiation therapy

Introduction

The eye is the second most common site of melanoma (5.2%), and uveal melanoma (UM) accounts for 85% of ocular melanomas [1].

The outcome of treatment for UM depends mostly on its clinical signs, including primary size (especially tumor base diameter), pigmentation, location in the fundus (macular and optic nerve lesions, presence of extension into the ciliary body or extrascleral extension), cellular tumor type, tumor vascularization, and genetic and molecular changes (a high mytosis rate, loss of chromosomes 3 and 1p and/or gain of chromosomes 6p and 8q) [2-6].

In the most recent decade, plaque brachytherapy (BT) has emerged as a popular choice due to the eye-saving aspects of this treatment, and has been often combined with laser treatment, particularly transpupillary thermotherapy (TTT) [6-15].

The efficacy of BT for UM (particularly, choroidal melanoma (CM)) varies widely, with reported local failure rates between 0% and 27% [16-20].

The success rate of the TTT-only methodology developed at SI "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine" for small (T1) CM (measuring ≤ 3 mm in thickness and ≤ 12 mm in basal dimension) was 92.1% [21]. Additionally, the method of eye-saving treatment (involving TTT combined with strontium-90 (Sr90)/ yttrium-90 (Yt90) BT) for medium and large T1-T4 CM has been developed [22].

The purpose of this study was to assess the efficacy of eye-saving treatment (involving TTT combined with Sr90/Yt90 BT) for medium and large CM in terms of local tumor control rate at 12 months after the initiation of treatment.

Material and Methods

This retrospective cohort study included 283 patients with CM who were treated at SI "The Filatov Institute of

Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine" from 2007 to 2024. The study sample consisted of 125 men (44.2%) and 158 women (55.8%), with a mean age (standard deviation (SD)) of 54.2 (12.4) years (range, 20 to 86 years). The right eye was affected in 148 patients (52.3%), and the left eye in 135 patients (47.7%).

This study is part of the research project "To Examine the Pathogenetic Mechanisms of the Clinical Effect of (Response to) Combination Treatment for Medium and Large Uveal Melanomas and Malignant Lesions of the Palpebral Conjunctiva, Semilunar Fold and Caruncle" (state registration number, 01224U00149).

Tumor stage was determined using the American Joint Commission on Cancer Tumor, Node and Metastases (TNM) classification scheme [23].

The eye-saving treatment with TTT plus Sr90/Yt90 BT for medium and large T1-T4 CM was performed in the following way: after TTT was delivered daily for four consecutive days, Sr90/Yt90 BT was performed in the form of beta-ray applicator suturing to the sclera in the projection of the tumor base [22]. The first follow-up visit was 3 months after the initiation of treatment and included measurement of tumor base diameter and thickness using ocular B-scan ultrasound and documenting tumor responses using ophthalmoscopy and fluorescein angiography (FA). If a residual tumor in the fundus with signs of activity was present, TTT sessions continued daily for four consecutive days (and followed by imaging-assisted measurement of tumor base diameter and thickness) every three months over a year.

Short-term treatment success was assessed at 12 months after the initiation of treatment. Short-term success was defined as evidence of complete tumor regression (no ophthalmoscopic, ocular B-scan ultrasound or FA evidence of tumor manifestations in the fundus), partial tumor regression (ophthalmoscopic and ocular B-scan ultrasound evidence of a residual tumor in the fundus at 12 months, with a consecutive reduction in tumor size every 3 months) or stabilization of the tumor process (B-scan ultrasound evidence of a 50% to 70% reduction in tumor size at 6 months with stabilization of tumor size over the following 6 months). Short-term failure was defined as evidence of continued tumor growth, tumor recurrence (a tumor growing from the scar) or extrabulbar spread. There was no evidence of metastasis both at baseline and at 12 months.

Data were analyzed using JASP software (version 0.18.1; the JASP Team, Amsterdam, the Netherlands). Mean and SD were calculated for quantitative data. Qualitative parameters were assigned numerical categories and in more than two groups were assessed by contingency tables and Pearson's chi square test [24].

Results

Tumors were classified into categories based on tumor size for the analysis of local outcomes of treatment (Table 1). Most patients had tumors of T2 and T3 stages, and tumor sizes were of categories 2 to 6 (247 patients or 87.3%). Table 2 presents outcomes in the fundus after the eye-saving treatment of medium and large T1-T4 CM. At 12 months, short-term treatment success was achieved in 274 patients (96.8%) (Table 2). Particularly, complete tumor regression was achieved in 86/274 patients (31.4%) or 86/283 patients (30.4%), partial tumor regression was achieved in 165/274 patients (60.3%) or 165/283 patients (58.3%), and regression with stabilization of tumor size was achieved in 23/274 patients (8.4%) or 23/283 patients (8.1%). Local treatment failure in the form of continued tumor growth was seen in 9/283 patients (3.2%) and led to enucleation.

Table 1. Distribution of patients among tumor stages and tumor-size categories

Tumor stage (T)	Tumor size		Tumor-size category	Number (percentage) of patients
	Thickness (mm)	Diameter (mm)		
T1	3.1-6.0	3-12	1	15 (5.3)
T2	3.1-6.0	9.1-15.0	2	94 (33.2)
	6.1-9.0	3.1-12.0	3	38 (13.4)
T3	3.1-6.0	15.1-18.0	4	17 (6.0)
	6.1-9.0	12.1-18.0	5	76 (26.9)
	9.1-12.0	3.1-18.0	6	22 (7.8)
	12.1-15.0	9.1-15.0	7	-
T4	3.1-12.0	>18.0	8	21 (7.4)
	12.1-15.0	15.1-18.0	9	-
Total				283 (100)

Table 2. Local outcome of eye-saving treatment for medium and large T1-T4 choroidal melanomas depending on tumor stage

Tumor-size category	Tumor stage (T)								
	T1, n=15		T2, n=132		T3, n=115		T4, n=21		Total number of patients/ percentage
	«+» n /%	«-» n/%	«+» n/%	«-» n/%	«+» n/%	«-» n/%	«+» n/%	«-» n/%	
1	15/100	-	-	-	-	-	-	-	15/5.3
2	-	-	94/71.2	-	-	-	-	-	94/33.2
3	-	-	38/28.8	-	-	-	-	-	38/13.4
4	-	-	-	-	17/14.7	-	-	-	17/6.0
5	-	-	-	-	74/64.4	2/1.7	-	-	76/26.9
6	-	-	-	-	19/16.6	3/2.6	-	-	22/7.8
7	-	-	-	-	-	-	-	-	-
8	-	-	-	-	-	-	17/81	4/19	21/7.4
9	-	-	-	-	-	-	-	-	-
Total	15/100	-	132/100	-	110/95.7	5/4.3	17/81	4/19	283/100

Note: +, treatment success; -, treatment failure; n /%, number of patients/ percentage for a particular tumor-size category

Of the 15 T1-stage patients with short-term treatment success, 12 (80.0%) had complete tumor regression and 3 (20.0%) had partial tumor regression. Of the 132 T2-stage patients with short-term treatment success, 49 (37.1%) had complete tumor regression, 77 (58.3%) partial tumor regression, and 6 (4.6%), regression with stabilization of tumor size. Additionally, of these patients, 43 (32.6%), 48 (36.4%) and 3 (2.3%), respectively, had category 2 tumor size, and 6 (4.5%), 29 (22.0%) and 3 (2.3%), respectively, category 3 tumor size. Of the 110 T3-stage patients with short-term treatment success, 21 (19.1%) had complete tumor regression, 75 (68.2%) partial tumor regression, and 14 (12.7%), regression with stabilization of tumor size. Of these patients, 5 (4.5%) and 12 (10.9%) respectively, had category 4 tumor size, 10 (9.1%), 52 (47.3%) and 12 (10.9%), category 5 tumor size, and 6 (5.5%), 11 (10.0%) and 2 (1.8%), respectively, category 6 tumor size. Among 115 T3-stage patients, 5 (4.3%) had treatment failure. Of the 17 T4-stage patients with short-term treatment success, 4 (23.5%) had complete tumor regression, 10 (58.8%) partial tumor regression, and 3 (17.7%), regression with stabilization of tumor size. Among 21 T4-stage patients, 4 (19.0%) had treatment failure. All T4-stage patients had category 8 tumor size. There was a significant difference among the groups in the tumor stage and tumor size category ($\chi 2 = 75.0$, $p = 0.00000$).

Discussion

Our method of eye-saving treatment (involving TTT combined with strontium-90 (Sr90)/ yttrium-90 (Yt90) BT) for medium and large T1-T4 CM enabled to achieve short-term treatment success in 274 of 283 patients with high local control rate of 96.8%.106Ru brachytherapy, when used in the treatment of UM, has been reported to provide local control rates of 62.6% to 94.0%, with the stabilization of the tumor process in 91.0% of cases at 5 years [6-20].

It should be noted that those authors analyzed mostly the results of treatment of medium CM (measuring ≤ 8.0 mm in thickness). They, however, practically have not analyzed the results of treatment depending on tumor stage (determined by tumor thickness and base diameter), which we believe to be important when assessing the efficacy of the treatment. Additionally, TTT is usually used to treat a residual tumor following plaque brachytherapy. In our combination treatment for CM, TTT is delivered daily for four consecutive days as a neoadjuvant treatment before brachytherapy to improve melanoma sensitivity to radiation, and to enable more effective therapeutic pathomorphosis after brachytherapy. Long-term results of the efficacy of our eye-saving treatment (involving TTT combined with Sr90/ Yt90 BT for medium and large T1-T4 CM will be presented in our future works.

Conclusion

Therefore, our eye-saving treatment (involving TTT combined with Sr90/ Yt90 BT) for medium and large T1-T4 CM was effective with a local tumor control rate of 96.8% at one year. The treatment technology developed enabled an eye-saving treatment not only for medium CM of T1 (tumor thickness of 3.1-6.0 mm and base diameter of 3.1-9.0 mm), T2 (tumor thickness of 3.1-9.0 mm and base diameter of 3.1-15.0 mm), and T3 stages (tumor thickness of 3.1-6.0 mm and base diameter of 15.1-18.0 mm), but

also for large CM of T3 stage (tumor thickness of 6.1-9.0 mm and base diameter of 12.1-18.0 mm).

References

1. Chang AE, Karnell LH, Menck HR. The National Cancer Data Base report on cutaneous and noncutaneous melanoma: a summary of 84,836 cases from the past decade. The American College of Surgeons Commission on Cancer and the American Cancer Society. Cancer. 1998 Oct 15;83(8):1664-78. doi: 10.1002/(sici)1097-0142(19981015)83:8<1664::aid-cncr23>3.0.co;2-g.
2. Singh AD, Shields CL, Shields JA. Prognostic factors in uveal melanoma. Melanoma Res. 2001 Jun;11(3):255-63. doi: 10.1097/00008390-200106000-00007.
3. Ewens KG, Kanetsky PA, Richards-Yutz J, Al-Dahmash S, De Luca MC, Bianciotto CG, Shields CL, Ganguly A. Genomic profile of 320 uveal melanoma cases: chromosome 8p-loss and metastatic outcome. Invest Ophthalmol Vis Sci. 2013 Aug 23;54(8):5721-9. doi: 10.1167/iovs.13-12195.
4. Damato B, Dopierala JA, Coupland SE. Genotypic profiling of 452 choroidal melanomas with multiplex ligation-dependent probe amplification. ClinCancerRes. 2010 Dec 15;16(24):6083-92. doi: 10.1158/1078-0432.CCR-10-2076.
5. Damato B. Progress in the management of patients with uveal melanoma. The 2012 Ashton Lecture. Eye (Lond). 2012 Sep;26(9):1157-72. doi: 10.1038/eye.2012.126.
6. Shields CL, Say EAT, Hasanreisoglu M, Saktanasate J, Lawson BM, Landy JE, Badami AU, Sivalingam MD, Mashayekhi A, Shields JA, Ganguly A. Cytogenetic Abnormalities in Uveal Melanoma Based on Tumor Features and Size in 1059 Patients: The 2016 W. Richard Green Lecture. Ophthalmology. 2017 May;124(5):609-618. doi: 10.1016/j.ophtha.2016.12.026.
7. Bartlema YM, Oosterhuis JA, Journée-De Korver JG, Tjho-Heslinga RE, Keunen JE. Combined plaque radiotherapy and transpupillary thermotherapy in choroidal melanoma: 5 years' experience. Br J Ophthalmol. 2003 Nov;87(11):1370-3. doi: 10.1136/bjo.87.11.1370.
8. Blasi MA, Laguardia M, Tagliaferri L, Scupola A, Villano A, Caputo CG, Pagliara MM. Brachytherapy alone or with neoadjuvant photodynamic therapy for amelanotic choroidal melanoma: Functional Outcomes and Local Tumor Control. Retina. 2016 Nov;36(11):2205-2212. doi: 10.1097/IAE.0000000000001048
9. Damato B, Patel I, Campbell IR, Mayles HM, Errington RD. Local tumor control after 106Ru brachytherapy of choroidal melanoma. Int J RadiatOncolBiol Phys. 2005 Oct 1;63(2):385-91. doi: 10.1016/j.ijrobp.2005.02.017.
10. Damato B, Patel I, Campbell IR, Mayles HM, Errington RD. Visual acuity after Ruthenium(106) brachytherapy of choroidal melanomas. Int J RadiatOncolBiol Phys. 2005 Oct 1;63(2):392-400. doi:10.1016/j.ijrobp.2005.02.059.
11. Damato B. Treatment of primary intraocular melanoma. Expert Rev Anticancer Ther. 2006 Apr;6(4):493-506. doi: 10.1586/14737140.6.4.493.
12. Forte R, Cennamo G, Staibano S, De Rosa G. Echographic examination with new generation contrast agent of choroidal malignant melanomas. Acta Ophthalmol Scand. 2005 Jun;83(3):347-54.doi:10.1111/j.1600-0420.2005.00428.x.
13. Shields CL, Shields JA, Cater J, Gündüz K, Miyamoto C, Micaily B, Brady LW. Plaque radiotherapy for uveal melanoma: long-term visual outcome in 1106 consecutive patients. ArchOphthalmol. 2000 Sep;118(9):1219-28. doi: 10.1001/archopht.118.9.1219.
14. Shields CL, Cater J, Shields JA, Chao A, Krema H, Materin M, Brady LW. Combined plaque radiotherapy and transpupillary thermotherapy for choroidal melanoma: tumor control and treatment complications in 270 consecutive patients. Arch Ophthalmol. 2002 Jul;120(7):933-40. doi: 10.1001/archopht.120.7.933.
15. Shields CL, Kaliki S, Furuta M, Mashayekhi A, Shields JA. Clinical spectrum and prognosis of uveal melanoma based on age at presentation in 8,033 cases. Retina. 2012 Jul;32(7):1363-72. doi: 10.1097/IAE.0b013e31824d09a8.
16. Singh AD, Turell ME, Topham AK. Uveal melanoma: trends in incidence, treatment, and survival. Ophthalmology. 2011 Sep;118(9):1881-5. doi: 10.1016/j.ophtha.2011.01.040.
17. Spagnolo F, Caltabiano G, Queirolo P. Uveal melanoma. Cancer Treat Rev. 2012 Aug;38(5):549-53. doi: 10.1016/j.ctrv.2012.01.002.
18. Wang Z, Nabhan M, Schild SE, Stafford SL, Petersen IA, Foote RL, Murad MH. Charged particle radiation therapy for uveal melanoma: a systematic review and meta-analysis. Int J RadiatOncolBiol Phys. 2013 May 1;86(1):18-26. doi: 10.1016/j.ijrobp.2012.08.026.
19. Leonard KL, Gagne NL, Mignano JE, Duker JS, Bannon EA, Rivard MJ. A 17-year retrospective study of institutional results for eye plaque brachytherapy of uveal melanoma using (125)I, (103)Pd, and (131)Cs and historical perspective. Brachytherapy. 2011 Jul-Aug;10(4):331-9. doi: 10.1016/j.brachy.2011.01.006.
20. Foti PV, Longo A, Reibaldi M, Russo A, Privitera G, Spatola C, Raffaele L, Salamone V, Farina R, Palmucci S, Musumeci A, Caltabiano R, Ragusa M, Mariotti C, Avitabile T, Milone P, Ettorre GC. Uveal melanoma: quantitative evaluation of diffusion-weighted MR imaging in the response assessment after proton-beam therapy, long-term follow-up. Radiol Med. 2017 Feb;122(2):131-139. doi: 10.1007/s11547-016-0697-3.
21. Information Bulletin No. 22 based on Pat. of Ukraine №102,890 issued 25.11.2015. Method for treatment of T1 choroidal melanoma. Authors: Pasyechnikova NV, Naumenko VO, Poliakova SI, Tsukanova IV. Patent Holder: State Institution "Filatov Institute of Eye Diseases and Tissue Therapy", NAMS of Ukraine.
22. Copyright Registration Certificate for a Work No. 135,100 issued on April 15, 2025. Method for treatment of T2-T3 choroidal melanoma with transpupillary therapy combined with Sr90/Yt90 brachytherapy. Authors: Pasyechnikova NV, Maletskiy AP, Poliakova SI, Chabotariov IeP, Tsukanova IV, Drumi DA.
23. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th Edition of the AJCC Cancer Staging Manual and the Future of TNM. Ann Surg Oncol. 2010 Jun;17(6):1471-4. doi: 10.1245/s10434-010-0985-4.
24. Buhl A, Zofel P. [SPSS Version 10—Introduction to modern data analysis]. Addison-Wesley: München, Germany; 2000. German.

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Abbreviations: *CM, choroidal melanoma; TTT, transpupillary thermotherapy; UM, uveal melanoma*