

# **Requirement of additional treatment for intraocular tumors following plaque radiotherapy**

*Thesis*

Submitted for partial fulfillment of Master Degree in  
Ophthalmology

By:

**Mohamed Gamal Ali Galal**  
M.B.,B.Ch.

Supervised by

***Prof Dr/ Bahaa El-Din Abdullah Ali***

Professor of Ophthalmology  
Faculty of Medicine, Ain Shams University

***Ass Prof Dr/ Hisham Mohamed Khairy  
Abdel Dayem***

Assistant Professor of Ophthalmology  
Faculty of Medicine, Ain Shams University

***Prof Dr/ Mohamed Mostafa Lotayef***

Professor of Radiation therapy  
National Cancer Institute, Cairo University

Faculty of medicine  
Ain Shams University

Cairo 2011

## **ACKNOWLEDGMENT**

First of all thanks to **GOD** for blessing this work until it has come to light as a part of His generous help throughout my life.

I would like to express my deepest gratitude and thanks to ***Prof Dr/Bahaa El-Din Abdullah Ali***, Professor of Ophthalmology, Faculty of Medicine, Ain Shams University for his close observation and valuable remarks which provided me with the best guide during my preparation for this thesis

I am deeply indebted to ***Prof Dr/ Mohamed Mostafa Lotayef***, Professor of Radiation therapy National Cancer Institute, Cairo University, and ***Ass Prof Dr/ Hisham Mohamed Khairy Abdel Dayem***, Assistant Professor of Ophthalmology Faculty of Medicine, Ain Shams University for their supervision, help and the great effort they have done during the preparation and revision of the whole work.

Also special thanks to my family, colleagues and friends for their help in this work.

## *CONTENTS*

	<b>Page</b>
<b>INTRODUCTION.....</b>	<b>1</b>
<b>AIM OF THE WORK.....</b>	<b>3</b>
<b>REVIEW OF LITERATURE.....</b>	<b>4</b>
<b>PATIENTS &amp; METHODS .....</b>	<b>57</b>
<b>RESULTS .....</b>	<b>64</b>
<b>DISCUSSION .....</b>	<b>96</b>
<b>SUMMARY .....</b>	<b>102</b>
<b>CONCLUSION.....</b>	<b>105</b>
<b>REFERENCES.....</b>	<b>106</b>
<b>ARABIC SUMMARY .....</b>	

## *LIST OF FIGURES*

<b>Fig. No.</b>	<b>Title</b>	<b>Page</b>
<b>1</b>	Iris painting.	<b>4</b>
<b>2</b>	Trichrome stain of the anterior segment showing the normal anatomy of the iris, angle, and ciliary body. Note the dilator and sphincter muscle of the iris and ciliary body muscle (red). The ciliary body appears with hyalinization of the stroma (blue).	<b>6</b>
<b>3</b>	Iris melanoma. Darkly melanotic iris tumor has a thick central nodule.	<b>13</b>
<b>4</b>	Iris melanoma. Amelanotic iris tumor contains prominent intrinsic blood vessels. Note peaking of the pupil toward the tumor and focal ectropion iridis.	<b>13</b>
<b>5</b>	U/S biomicroscopy of iridociliary melanoma. Image shows the solid nature of the lesion and involvement of the CB.	<b>18</b>
<b>6</b>	External indicators of underlying CB melanoma. (A) Sentinel blood vessels on the sclera overlying a CB melanoma.(B) Trans-scleral extension of an iridociliary melanoma. Note that the anterior margin of the intraocular tumor is in the peripheral iris.	<b>17</b>
<b>7</b>	Typical shapes of CM. (A) Dome-shaped choroidal melanoma. (B) Mushroom-shaped CM.	<b>18</b>
<b>8</b>	U/S of CM. (A) B-scan of dome-shaped CM (B) B-scan of mushroom-shaped CM.	<b>20</b>
<b>9</b>	Secondary exudative RD.	<b>20</b>
<b>10</b>	FA of dome-shaped choroidal melanoma. (A) Early phase frame shows filling of both retinal and intratumoral arteries. (B) Late phase frame shows nonuniform hyperfluorescent staining of tumor.	<b>21</b>

<b>11</b>	FA of mushroom-shaped choroidal melanoma. (A) Early laminar venous phase frame shows filling of intratumoral blood vessels. (B) Late phase frame shows intense generalized staining of apical nodule and associated subretinal fluid.	<b>21</b>
<b>12</b>	Sonograms show typical CM. Several vessels can be detected on color Doppler sonogram.	<b>22</b>
<b>13</b>	Histopathology of posterior uveal melanoma. (A) Spindle cell melanoma. (B) Epithelioid cell melanoma. (C) Mixed-cell melanoma. (D) Vascular loops and networks that separate lobules of choroidal melanoma.	<b>25</b>
<b>14</b>	Leukocoria.	<b>32</b>
<b>15</b>	(A) Ocular fundus aspect of RB, (B) U/S of RB.	<b>32</b>
<b>16</b>	(A) MRI pattern of RB with optic nerve involvement(sagittal enhanced T1-weighted sequence). (B)Aspect of trilateral RB (MRI).	<b>33</b>
<b>17</b>	Histopathology of retinoblastoma. (A) Flexner-Wintersteiner rosettes. (B) Homer Wright rosettes. (C) Fleurettes.	<b>34</b>
<b>18</b>	Standard COMS-type gold plaque with three I-125 seeds. Typically all the slots are filled with seeds.	<b>39</b>
<b>19</b>	For different applications there are 16 plaque types available. Uveal and choroidal melanomas: CCA, CCB, CCC, CCD and CGD. Retinoblastoma: CCX, CCY, CCZ and CXS. CB melanomas or melanomas close to the iris: CIA, CIB, CIB-2. Tumors close to the optical nerve: COB, COD, COE and COC.	<b>44</b>
<b>20</b>	Ru-106 plaques have a small penumbra, minimal side-scatter, and a rapid drop-off in radiation intensity.	<b>46</b>
<b>21</b>	Schematic of Ru-106 plaque shows that the silver radiation window, under which the radioactive part sits, is only 0.1 mm thick.	<b>47</b>

<b>22</b>	X-ray film showing the radiation field created by an I-125 plaque.	<b>48</b>
<b>23</b>	Loss of eyelashes.	<b>50</b>
<b>24</b>	Punctate keratitis.	<b>51</b>
<b>25</b>	Rubeosis iridis and neovascular glaucoma may develop following radiation to the anterior segment.	<b>52</b>
<b>26</b>	Radiation induced cataract.	<b>53</b>
<b>27</b>	A) Characteristic ophthalmoscopic features of non-proliferative radiation retinopathy, brachytherapy. (B) Retinal capillary non-perfusion in the macula and microaneurysms are most evident on the FA. (C) CME on the OCT.	<b>55</b>
<b>28</b>	Typical appearance of radiation optic neuropathy. Note optic disc swelling with surrounding exudates and hemorrhages.	<b>56</b>
<b>29</b>	Plaque simulator program (Retinal Diagram).	<b>58</b>
<b>30</b>	Plaque simulator program (Treatment plan screen).	<b>59</b>
<b>31</b>	Plaque simulator program (Isodose plot screen).	<b>59</b>
<b>32</b>	RU 106 plaques.	<b>60</b>
<b>33</b>	Adult and child percentage in the study.	<b>64</b>
<b>34</b>	Male and female percentage in the study	<b>64</b>
<b>35</b>	Patient received single treatment versus patient received additional treatment according to age group.	<b>65</b>
<b>36</b>	Number of cases with no additional treatment and number of cases treated with additional treatment either TTT or surgical resection	<b>67</b>
<b>37</b>	Percent of each tumor in the study.	<b>71</b>

<b>38</b>	Comparison between the two study groups about distance from ONH and macula.	<b>74</b>
<b>39</b>	Duration of plaque application in each study group.	<b>77</b>
<b>40</b>	Mean dose rate in patients with single treatment (plaque) and patients with additional treatment.	<b>79</b>
<b>41</b>	Change in tumor height before and after treatment in both study groups.	<b>82</b>
<b>42</b>	Comparison of tumor height before and after treatment between the two study groups.	<b>84</b>
<b>43</b>	Comparison of complications between both study groups.	<b>93</b>



## *LIST OF TABLES*

<b>Table No.</b>	<b>Title</b>	<b>Page</b>
<b>1</b>	Staging of uveal melanoma (TNM).	<b>26</b>
<b>2</b>	COMS classification of uveal melanoma	<b>26</b>
<b>3</b>	International classification of retinoblastoma.	<b>35</b>
<b>4</b>	Reese-Ellsworth's classification	<b>36</b>
<b>5</b>	Characteristics of radioisotopes used for episcleral brachytherapy.	<b>45</b>
<b>6</b>	Description of dimensions of RU plaques used in study	<b>61</b>
<b>7</b>	Description of personal characteristics of all study patients	<b>64</b>
<b>8</b>	Description and comparison of personal characteristics among cases with the two different lines of treatment.	<b>66</b>
<b>9</b>	Description of number and percentage of sessions in patients treated with TTT.	<b>69</b>
<b>10</b>	indications for TTT additional treatment	<b>69</b>
<b>11</b>	Description of site of affected eye and tumor type among all study patients.	<b>70</b>
<b>12</b>	Comparison of affected eye and tumor type among cases with different lines of treatment.	<b>72</b>
<b>13</b>	Description of distance of tumor from optic nerve and from macula among all study patients.	<b>73</b>
<b>14</b>	Description and comparison of distance of tumor from optic nerve and from macula in between cases with different lines of treatment.	<b>73</b>

<b>15</b>	Type of RU 106 plaque and duration of application of plaque used among all study patients.	<b>75</b>
<b>16</b>	Comparison of type and duration of application of plaque used among cases with additional treatment.	<b>76</b>
<b>17</b>	Radiation dose and dose rate given among all study patients.	<b>78</b>
<b>18</b>	Comparison of dose and dose rate given in between cases with different lines of treatment.	<b>78</b>
<b>19</b>	Tumor height before and after treatment and the amount of change in it among all study patients.	<b>80</b>
<b>20</b>	Description and comparison of tumor height before, after treatment and the amount of change in it in between cases with different lines of treatment.	<b>81</b>
<b>21</b>	Tumor base before and after treatment and the amount of change in it among all study patients.	<b>83</b>
<b>22</b>	Description and comparison of tumor base before, after treatment and the amount of change in it in between cases with different lines of treatment.	<b>84</b>
<b>23</b>	Tumor height before and after treatment among single treatment cases.	<b>85</b>
<b>24</b>	Tumor base before and after treatment among single treatment cases.	<b>85</b>
<b>25</b>	Tumor height before and after treatment among multiple treatment cases.	<b>86</b>
<b>26</b>	Tumor base before and after treatment among multiple treatment cases.	<b>86</b>
<b>27</b>	Post treatment complications among all study patients after 9 month of last treatment	<b>87</b>

<b>28</b>	post treatment complications among all study patients after 18 month of last treatment procedure	<b>88</b>
<b>29</b>	Post treatment complications among cases with different lines of treatment after 9 month	<b>90</b>
<b>30</b>	Treatment complications among cases with different lines of treatment after 18 month	<b>92</b>
<b>31</b>	Number and percent of tumors required secondary enucleation according to tumor type	<b>94</b>
<b>32</b>	Relation between mean radiation dose and occurrence of papillopathy and retinopathy	<b>95</b>

## **List OF ABBEREVIATIONS**

<b>CB</b>	: Ciliary body
<b>cGy</b>	: Centi-Gray
<b>CM</b>	: Choroidal melanoma
<b>CME</b>	: Cystoid macular edema
<b>COMS</b>	: Collaborative Ocular Melanoma Study Group
<b>CT</b>	: Computed tomography
<b>EBRT</b>	: External beam radiation therapy
<b>FA</b>	: Florescence angiography
<b>Gy</b>	: Gray (unit of radiation measurement = 100 rad)
<b>HVL</b>	: Half -value layer
<b>LM</b>	: Lymph node
<b>I<sup>125</sup></b>	: Iodine 125
<b>IOP</b>	: Intraocular pressure
<b>MRI</b>	: Magnetic resonance imaging
<b>N</b>	: Number
<b>NS</b>	: Non significant
<b>OCT</b>	: Ocular coherence tomography
<b>P-value</b>	: Probability value
<b>Pd<sup>103</sup></b>	: Palladium 103
<b>RB</b>	: Retinoblastoma
<b>RU<sup>106</sup></b>	: Ruthenium 106
<b>RPE</b>	: Retinal pigment epithelium

<b>RD</b>	: Retinal detachment
<b>S</b>	: Significant
<b>SD</b>	: Standard deviation
<b>TTT</b>	: Transpupillary thermotherapy
<b>U/S</b>	: Ultrasound
<b>VF</b>	: Visual field

## **AIM OF THE WORK**

The purpose of this study is to analyze the results of treatment of intra-ocular tumors with plaque radiation therapy alone and cases that required other line of treatment adjuvant with radiation therapy.

# INTRODUCTION

Malignant eye tumors present 0.2 % of all malignant tumors diagnosed, but it is a direct reason of death for one in each 3 patients. (*Paunksnis et al., 2009*) During the past century, the prognosis of patients with ocular tumors has continuously improved owing to early diagnoses and advances in treatment strategy. (*Galluzzi et al., 2003*)

For more than a century, enucleation has been the standard treatment for intra ocular tumors. However, concerns about enucleation, especially possible tumor spread caused by manipulation of the eye during surgery, plus vision loss and the poor cosmetic outcome; have made clinical advances focusing on intraocular tumor control enabling increased globe conservation while minimizing the risk to the patient by introducing irradiation therapy as a popular alternative. (*Chryssanthi et al., 2008, Scott et al., 1999, Shields JA & Shields Cl., 1994*)

The most commonly used forms of radiation therapy are ophthalmic plaque brachytherapy and external beam radiotherapy (EBRT). (*Finger, 2009*) Radiation may conserve a useful level of vision, depending on the size of the tumour and its location with respect to the optic disc and macula. (*Chryssanthi et al., 2008*)

Radioactive plaque brachytherapy has been successfully utilized, but its applicability is presently limited to anterior lesions smaller than 8–10 mm. (*Allan et al., 2007*)