Iris and iridociliary melanoma : concepts in diagnosis and management

Razzaq, L.

Appendix

Patient Sticker

Appendix 1

Leiden University Medical Center, Leiden
Department of Ophthalmology

Guidelines for the diagnosis and treatment of iris melanoma
Doctor: …… Date: ……..

Most Important clinical risk factors:

1.	Patient has symptoms	Yes / No
2.	Basal diameter of tumor > 3mm.	Yes / No
3.	Abnormal tumor vessels	Yes / No
4.	Pigment dispersion	Yes / No
5.	IOP > 21 mmHg	Yes / No
6.	Ectropion Uveae	Yes / No
7.	Extension to anterior chamber angle	Yes / No
8.	Secondary cataract	Yes / No

Prognostic Factors:

9.	Satellite lesions	Yes / No
10.	Tapioca appearance	Yes / No
11.	Decreased iris motility	Yes / No
12.	Age > 48 years	Yes / No

Examination:

1. *Fluorescein Angiography of Anterior Segment:*

a.	Fluorescence completely blocked	Yes / No
b.	Geographic vasculature	Yes / No
c.	Early leakage	Yes / No
d.	Late leakage	Yes / No
e.	Abnormal vessels	Yes / No

2. *Ultrasound biomicroscopy (UBM)*

i.	Characteristics of iris melanoma	Yes / No
ii.	Ciliary body extension	Yes / No

Factors 1 – 5 Yes: 77.7% chance of having Iris melanoma; Prompt treatment
Factors 1 – 5 No: 2.3% chance of having iris melanoma; Observation
Factors: 4+6+7+8 Yes: 74.1% chance of tumor growth in 5years
Factors: 4+6+7+8 No : 1.1% chance of tumor growth in 5years
a + b Yes: Signs of benign tumor
c + d + e Yes: Signs of malignant tumor
i + ii Yes: Signs of iris melanoma

Developed and Based on: JW Harbour, JJ Augsburger et al. Initial management and follow-up of melanocytic iris tumors. Ophthalmology, 1995(102): 1987-1993; van Klink F., de Keizer RJ, Jager MJ, Kakebeeke-Kemme HM. Iris nevi and melanomas: a clinical follow-up study. Doc.Ophthalmol. 1992;82:49-55.

Patient Sticker

Appendix 2

University Medical Center, St. Radboud, Nijmegen
Leiden University Medical Center, Leiden

Department of Ophthalmology

Ultrasound biomicroscopy (UBM) characteristics for the diagnosis of iris melanoma
Doctor: …… Date: ……..

UBM Characteristics favoring the diagnosis of iris melanoma:

1.	Largest basal tumor dimension > 3mm	Yes / No
2.	Tumor thickness > 1mm	Yes / No
3.	Irregular tumor structure	Yes / No
4.	Indistinct tumor boundary with irregular outline	Yes / No
5.	Secondary iris pigment epithelium cysts	Yes / No
6.	Non-intact posterior iris pigment epithelium	Yes / No
7.	Low internal reflectivity	Yes / No
8.	Ciliary body extension	Yes / No
9.	Tumor extension to anterior chamber angle	Yes / No

Based on UBM schedule developed by Dr. A.M. Verbeek
University Medical Center, St. Radboud, Nijmegen.

Patient Sticker

Appendix 3

Leiden University Medical Center
Department of Ophthalmology

New modified guidelines for the diagnosis and treatment of iris melanoma
Doctor: …… Date: ……..

Clinical Risk factors:

1. Symptoms	Yes / No
2. Basal diameter of tumor > 3mm.	Yes / No
3. IOP > 21 mmHg	Yes / No
4. Secondary cataract	Yes / No
5. Age > 48 years	Yes / No

Clinical risk factors 1- 5 Yes: 99.31 % probability of having melanoma
Clinical risk factors 1- 5 No: 0.69 % probability of having melanoma

UBM Characteristics:

1. Tumor thickness > 1mm.	Yes / No
2. Basal tumor diameter > 3mm.	Yes / No
3. Low reflectivity	Yes / No
4. Anterior chamber angle extension	Yes / No
5. Secondary iris cysts	Yes / No

UBM characteristics 1- 5 Yes: 99.76 % probability of having melanoma
UBM characteristics 1- 5 No: 0.24 % probability of having melanoma

For the other possible combinations of positive and negative factors, probability of having melanoma can be computed on the basis of formula given in next pages.

Based on the results of study described in chapter 2 of this thesis (October 2011).

Formula for computing probability of having iris melanoma on the basis of clinical risk factors:

1/(1+exp(-6.496 + 1.965 x complaints +3.007 x diameter + 3.145 x IOP + 2.666 x Secondary cataract - 1.33 x age))

Variable		Parameter coding
Symptoms	No	1
	Yes	0
Diameter > 3mm	No	1
	Yes	0
IOP > 21mmhg.	No	1
	Yes	0
Secondary cataract	No	1
	Yes	0
Age > 48	No	1
	Yes	0

Risk factor	B
complaints	-1.965
Diameter	-3.007
IOP	-3.415
Secondary cataract	-2.666
Age	1.330
Constant	6.496

For example, if a patient has symptoms and the diameter of lesion is > 3mm: then these two factors has parameter coding '0' for Yes.
All other factors are '1' for No, as given in coding table.
Then above formula becomes:
1/(1+exp(-6.496 + 0+0 + 3.145 x 1 + 2.666 x 1 - 1.33 x 1)) = 0.88
It means that probability of having melanoma is 88%

Formula for computing probability of having iris melanoma on the basis of UBM characteristics:

1/(1+exp(-7.001 + 3.377 x thickness + 1.753x diameter + 1.607 x iris cysts + 2.093 x reflectivity +4.175 x AC extension))

		Parameter coding
AC angle extension	No	1
	Yes	0
Thickness	< 1mm	1
	> 1mm	0
Diameter	< 3mm	1
	> 3mm	0
Iris cysts	No	1
	Yes	0
Reflectivity	High	1
	Low	0

Risk Factor	B
Thickness	-3.377
Diameter	-1.753
Iris cysts	-1.607
Reflectivity	-2.093
AC angle extension	-4.175
Constant	7.001

For example, if a patient has thickness > 1mm and diameter of lesion > 3mm. on UBM, then these two factors has parameter coding '0' for Yes and all other factors are '1' for No, as given in coding table.

Above formula then becomes:

1/(1+exp(-7.001 + 0 + 0 + 1.607 x 1 + 2.093 x 1 +4.175 x 1)) = 0.77

It means that probability of having melanoma is 77%

Appendix: Figures

Figure 1 Ruthenium CIA plaque designed for iris melanoma

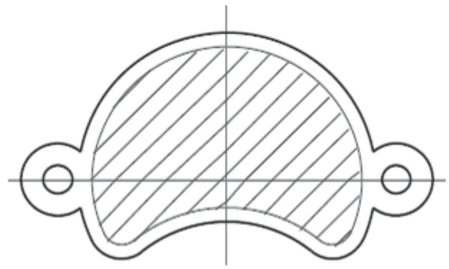


Figure 2 Few study patients with iris melanoma treated with Ruthenium plaque therapy. Left side 3 pictures showing tumor before treatment, Right side the same tumors after the treatment

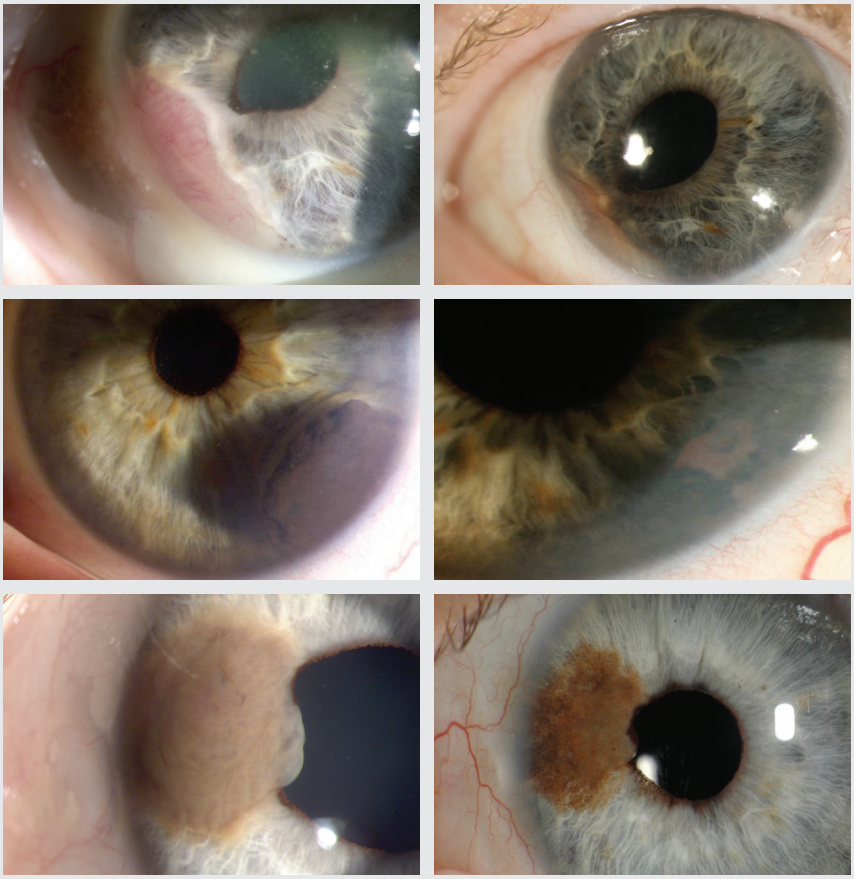
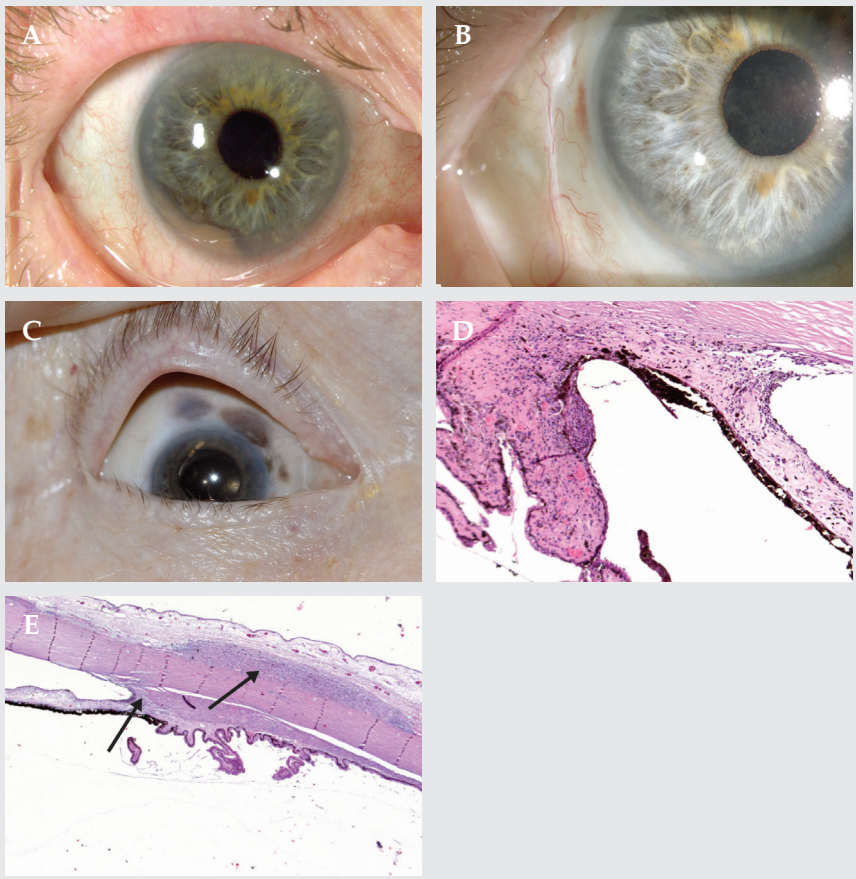


Figure 3 **A**: One study patient having iris melanoma in inferotemporal quadrant of right eye before treatment **B**: Same iris melanoma one year after treatment with Ru-106. **C**: After 3 years patient showed recurrent tumor and extrascleral extension. **D**: Histology of irradiated area showing viable cells. The chamber angle is closed by fibrosis and covered with a thin layer of vital un-pigmented melanoma cells. (original magnification: x10) **E**: Histology showing melanoma cells on the iris surface, in the opposite chamber angle, in the trabecular meshwork and extrascleral extension. (original magnification: x2.5).



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List of Publications

List of publications

Ruthenium plaque radiation for iris and iridociliary melanomas: development of dry eyes?
Razzaq L, de Keizer RJ
Br J Ophthalmol. 2010 Nov; 94: 1549-50. Published online: 2010 June 1.

Ruthenium plaque radiation therapy for iris and iridociliary melanomas
Razzaq L, Keunen JEE, Schalij-Delfos N, Creutzberg CL, Ketelaars M, de Keizer RJ
Acta Ophthalmol. 2010 Jul 29. [Epub ahead of print]

Iris melanoma in a child treated with iridectomy and a phakic iris repair implant lens: a case report of 8 years postoperative follow-up
de Keizer RJ, Razzaq L, Tassignon MJ, Verbeek AM
Br J Ophthalmol. 2010 Jul; 94(7):953-4.

Anterior segment imaging of iris melanocytic lesions
Razzaq L, Van der Spek KE, Luyten GPM, de Keizer RJ
Eur J Ophthalmol. 2011 Sep-Oct ;21(5):608-14.

Transscleral excision of suprauveal mesectodermal iridociliary leiomyoma Without postoperative iris defect: Correlation with UBM, MRI and histopathology
Razzaq L, Semenova EA, Marinkovic M, de Keizer RJ, Van Duinen SG, Luyten GPM.
Accepted in Arch of Ophthalmol. 2011 Feb.

Clinical and pathologic characteristics of biopsy proven iris melanoma: A multicenter international study
Khan S, Finger PT, Yu G, Razzaq L, Jager MJ, de Keizer RJW, Sandkull P, Seregard S, Gologorsky D, Schefler AC, Murray TG, Kivela T, Giuliari GP, McGowan H, Simpson ER, Corriveau C, Coupland SE, Damato BE
Arch of Ophthalmol. Published online September 12, 2011.

Guidelines for diagnosis and treatment decision of suspected iris and iridociliary melanomas based on clinical risk factors and ultrasound biomicroscopic characteristics
Razzaq L, Keunen JEE, van Zwet EW, Luyten GPM, de Keizer RJ.
Submitted.

Corneal endothelial cell density after Ruthenium plaque radiation therapy for iris melanoma patients
Razzaq L, Jager MJ, Luyten GPM, Marinkovic M, de Keizer RJ
Submitted.

Fuchs adenoma of the choroid simulating a choroidal hemangioma
Razzaq L, Marinkovic M, Swart W, van Duinen SG, Luyten GPM.
Submitted.

Incidence of retinoblastoma in the Netherlands 1950 - 2010: A shift in the proportion of hereditary retinoblastoma
Bosscha MI, Razzaq L, Dommering CJ, van Leeuwen FE, Moll AC
Submitted.

Changes in contrast sensitivity functions and visual acuity in patients with pre-senile and senile cataract
Razzaq L, Afzal F.
Dissertation accepted by College of Physicians and Surgeons, Karachi, Pakistan. 2009 Aug.

The BRAF, GNAQ and GNA11 mutations in iris melanomas and histopathological correlation
Razzaq L, Versluis M, Jager MJ, Luyten GPM, de Keizer RJW, van der Velden PA.
Manuscript in preparation.

Curriculum Vitae

Curriculum Vitae

The author of this thesis, Lubna Razzaq, was born on September 29th, 1975 in Islamabad, Pakistan. She completed her secondary school education at the Federal School and College Islamabad, standing first in her college and 5th in the Federal Board of secondary education in 1993. She received her Bachelors in Medicine and Bachelors in Surgery (MBBS) degree in 1999 from Rawalpindi Medical College, Rawalpindi, Pakistan, securing the position among the top ten of 250 students. While attending the eye ward during her medical school, she observed how small procedures, such as cataract surgery, bring big changes in one's life; she therefore opted for Ophthalmology as her future field. She passed her Fellowship part 1 Ophthalmology examination in 2000. In 2001, after passing the Federal Public Service Commission Examination, she became Registrar in Ophthalmology. Initially, she worked at the Jinnah Postgraduate Medical Center, Karachi (2001- 2002) and then at the Pakistan Institute of Medical Sciences, Islamabad, Pakistan (2003-2007), where she completed her ophthalmic training. In December 2007, she began her PhD study on ocular melanomas under the supervision of Professor Dr. Gré P.M. Luyten and Prof. Dr. Rob J.W. de Keizer at Leiden University Medical Center, the Netherlands. During her research, she also had the opportunity to increase her clinical knowledge and skills in Ocular Oncology. Meanwhile, she passed the Fellowship of the Royal College of Surgeons in Ophthalmology, Edinburgh, United Kingdom, Part 1 & 2 in 2009 and Part B (7 of 8 sections) in June 2011. The results of her PhD research are presented in this thesis. After finishing her PhD, she is going to start working as clinical ophthalmologist.

Besides working in Ophthalmology, she is the wife of Burhan-ud-din Qureshi and the mother of two sons, Mohid and Mahad.