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## **Iris and iridociliary melanoma : concepts in diagnosis and management**

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Part **I**

**DIAGNOSIS OF IRIS AND  
IRIDOCILIARY MELANOMA**





Chapter **2**

**Guidelines for diagnosis and treatment decision  
of suspected iris and iridociliary melanomas  
based on clinical risk factors and ultrasound  
biomicroscopic characteristics**

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## Abstract

**Purpose:** To evaluate the role of clinical risk factors and ultrasound biomicroscopic (UBM) characteristics in the diagnosis of iris melanoma.

**Methods:** A retrospective analysis of 117 patients with suspected iris melanoma managed according to guidelines developed in a referral center over a 14-year interval (1997 – 2010) with a minimum follow-up of 3 years (3 –14 years).

**Results:** Diagnosis of iris melanoma was made in 52 patients (44%) while 65 patients (56%) were observed. The clinical risk factors significantly associated with the diagnosis of iris melanoma were: presence of symptoms ( $P = 0.018$ ); largest basal tumor diameter  $> 3$  mm ( $P = < 0.001$ ); IOP  $> 21$ mmHg ( $P = 0.039$ ); secondary cataract ( $P = < 0.001$ ); and age  $> 48$  years ( $P = 0.046$ ). UBM characteristics significantly associated with the diagnosis of iris melanoma were: tumor thickness  $> 1$ mm ( $P = 0.006$ ); basal tumor diameter  $> 3$  mm ( $P = 0.042$ ); low reflectivity ( $P = 0.005$ ); tumor extension to anterior chamber angle ( $P = 0.049$ ); and presence of secondary cysts ( $P = 0.050$ ). Six patients (9%) in the observed group (65) showed tumor growth.

**Conclusion:** Clinical risk factors and ultrasound biomicroscopic characteristics included in these iris melanoma guidelines seem appropriate for differentiating between iris melanoma and naevus and are therefore helpful in deciding which cases need prompt treatment, also avoiding unnecessary treatment.

## Introduction

Iris and iridociliary naevi and melanomas are the most common primary tumors of the iris [1-3]. Iris naevi are benign but iris melanomas can be aggressive and may occasionally metastasize [4]. The metastatic rate is 5% at 10 years and 10% at 20 years of follow-up [5]. Moreover, any treatment for iris and iridociliary melanomas can cause serious visual morbidity. Even the conservative treatment with plaque brachytherapy can be associated with complications [7]. In addition, one study indicates that diagnostic errors occurred in 35% of patients who underwent enucleation for suspected iris melanoma [8]. In 1981, another study demonstrated that 87% of excised suspected iris melanomas were actually benign on histopathology [9]. Thus, differentiation between an iris naevus and melanoma is of utmost importance in avoiding unnecessary treatment. However, clinical differentiation remains difficult [6,8-11].

Traditionally, the clinical differentiation between an iris naevus and melanoma has been based on size, vascularity, secondary glaucoma and documented growth [1,2,4,12-15]. Many studies reported that a melanocytic iris lesion with a diameter exceeding 3mm and a thickness of >1mm with prominent vascularity, ectropion uveae, secondary cataract, secondary glaucoma and documented growth should be regarded as iris melanoma [10,16,17]. Char showed documented growth and intense vascularity of an iris tumor to be the most important reliable signs in the diagnosis of iris melanoma [18]. On the other hand, Territo reported the medial location and presence of pigment dispersion were the only clinical features associated with tumor growth [19].

A need was felt for identifying the clinical risk factors differentiating true iris melanomas from suspected iris naevi in daily practice. Therefore, in 1997, an Iris Melanoma Guidelines were developed for the Dutch Oncological and Orbital Society by the authors (RdK and JK) for ophthalmologists involved in ocular oncology services in the Netherlands, based on previous studies and their own experience [10,16,17]. These guidelines included twelve clinical features as shown in Table 1 (Appendix 1).

In the mean time, ultrasound biomicroscopy (UBM) was introduced and ancillary studies were started to evaluate the role of this investigation (UBM) in the diagnosis of iris and iridociliary melanomas [3,20,21]. Nine UBM characteristics of iris melanoma were also included in these Dutch Iris Melanoma Guidelines (Table 2) (Appendix 2).

Initially, anterior segment fluorescein angiographic features were included; however, as UBM replaced anterior segment fluorescein angiography, these features were subsequently excluded. These guidelines have been used in our Ocular Oncology Services since 1997, and based on this patients were diagnosed

**Table 1** Details of all the clinical risk factors in terms of frequency in two patients groups and results of univariate logistic regression analysis

| Number of variables | Clinical Risk Factors   | Treated Group (n=52) (%) | Observed Group (n=65) (%) | Univariate Odds Ratio | P-value | 95% CI of Odds Ratio |
|---------------------|---|--------------------------|---------------------------|-----------------------|---------|----------------------|
| 1                   | Patients has symptoms   | 25 (48)                  | 5 (7)                     | 11.1                  | < 0.001 | 3.8 – 32.2           |
| 2                   | Largest basal diameter is > 3mm   | 48 (92)                  | 31 (48)                   | 13.1                  | < 0.001 | 4.2 – 40.7           |
| 3                   | Abnormal tumor vessels  | 31 (60)                  | 19 (30)                   | 3.5                   | 0.001   | 1.6 – 7.7            |
| 4                   | Pigment dispersion  | 39 (75)                  | 19 (30)                   | 7.2                   | < 0.001 | 3.18 – 16.5          |
| 5                   | IOP > 21 mmHg in the tumor eye only   | 14 (27)                  | 1 (1)                     | 23.5                  | 0.003   | 2.9 – 186.5          |
| 6                   | Ectropion uveae   | 30 (38)                  | 30 (46)                   | 0.96                  | 0.933   | 0.4 – 2.0            |
| 7                   | Extension to anterior chamber angle   | 41 (79)                  | 23 (35)                   | 6.8                   | < 0.001 | 2.9 – 15.7           |
| 8                   | Secondary cataract (local lens opacity around the tumor in the tumor eye only)  | 35 (68)                  | 7 (11)                    | 17.0                  | < 0.001 | 6.4 – 45.2           |
| 9                   | Satellite lesions (seeding of melanoma cells away from the primary tumor)   | 18 (35)                  | 12 (18)                   | 2.3                   | 0.050   | 1.0 – 5.4            |
| 10                  | Tapioca appearance  | 7 (13)                   | 14 (21)                   | 0.56                  | 0.262   | 0.2 – 1.5            |
| 11                  | Decreased iris motility (localized decrease in iris motility adjacent to tumor, tested by throwing the slit-lamp light from different directions) | 25 (48)                  | 17 (26)                   | 2.6                   | 0.015   | 1.2 – 5.6            |
| 12                  | Age > 48 years  | 33 (63)                  | 49 (75)                   | 0.56                  | 0.164   | 0.2 – 1.2            |

**Table 2** Details of all the UBM characteristics in terms of frequency in two patients groups and results of univariate logistic regression analysis

| Number of variables | UBM Characteristics  | Treated Group (n=52) (%) | Observed Group (n=58) (%) | Univariate Odds Ratio | P- Value | 95% CI of Odds Ratio |
|---------------------|--|--------------------------|---------------------------|-----------------------|----------|----------------------|
| 1                   | Largest basal tumor dimension > 3mm                                  | 50 (96)                  | 19 (34)                   | 51.31                 | < 0.001  | 11.2 – 233.6         |
| 2                   | Tumor thickness > 1mm  | 51 (98)                  | 18 (31)                   | 113.33                | < 0.001  | 14.5 – 885.4         |
| 3                   | Irregular tumor structure  | 39 (75)                  | 12 (21)                   | 0.087                 | < 0.001  | 0.03 – 0.2           |
| 4                   | Indistinct tumor boundary with irregular outline                     | 39 (75)                  | 11 (19)                   | 12.81                 | < 0.001  | 5.1 – 31.7           |
| 5                   | Secondary iris cysts of pigment epithelium                           | 30 (57)                  | 4 (7)                     | 18.40                 | < 0.001  | 5.8 – 58.4           |
| 6                   | Non-intact posterior iris pigment epithelium                         | 39 (75)                  | 11 (19)                   | 12.81                 | < 0.001  | 5.1– 31.7            |
| 7                   | Low internal reflectivity (major part of tumor has low reflectivity) | 44 (85)                  | 12 (20)                   | 21.08                 | < 0.001  | 7.8 – 56.4           |
| 8                   | Ciliary body involvement   | 37 (71)                  | 12 (20)                   | 9.45                  | < 0.001  | 3.9 – 22.6           |
| 9                   | Anterior chamber angle extension                                     | 18 (35)                  | 1 (2)                     | 30.17                 | 0.001    | 3.8 – 236.2          |



and managed as two groups: one cohort of patients was diagnosed as iris melanoma and treated promptly; a second cohort was diagnosed as having iris naevus and observed.

We performed an analysis of the initial scoring on the basis of our iris melanoma guidelines and correlated our management decisions with outcomes in terms of treatment and observation. We set out to determine whether: (1) patients in the treated group did have a melanoma; (2) tumors in the observation group indeed behaved as iris naevi; and (3) to study the rate of tumor growth in the observation group. The goal of this study was to determine whether we had indeed identified the important diagnostic clinical risk factors and UBM characteristics of iris and iridociliary melanomas.

## Materials and Methods

A total of 117 patients referred to the Ophthalmic Oncology Service of the Leiden University Medical Centre with a diagnosis of suspected iris and iridociliary melanomas from 1997 to 2007 were included in this study. These patients were managed according to the Dutch Iris Melanoma Guidelines. The last date of inclusion was December 31<sup>st</sup>, 2007, as patients with a minimum follow-up of three years were only included. Diffuse melanomas, causing heterochromia and diffuse iris infiltration, without obvious iris thickening, were excluded from this study. The reason is that several risk factors included in these guidelines can not be estimated for diffuse melanomas. All patients underwent complete ophthalmic examination at their first visit, including tumor measurements, transpupillary transillumination, gonioscopy, tonometry, fundoscopy and assessment for the presence of secondary cataract after mydriasis. All lesions were documented by clinical photography and UBM examinations. Before and including 2006, all primary and follow-up UBM examinations were performed at the Department of Ophthalmology, Nijmegen, with a 50-MHz probe manufactured by Humphrey Instruments (California, USA). From 2007 onwards, these scans were performed at the LUMC using the Lin 50 UBM probe manufactured by Quantel Medical Aviso (France). The iris melanoma proforma were filled-out for every patient according to the clinical and UBM examination findings. The forms for the UBM findings were filled-out independently of the clinical findings to avoid bias. If three of the clinical risk factors 1-5 were positive (considered the most important factors), a prompt treatment decision was taken. The risk factors 2,4,6,7 and 8 were taken as predictors of growth [17]. Based on these findings patients were divided into the following groups: (1) patients diagnosed as having iris melanoma and treated (treatment cohort); (2) patients

diagnosed as suspected iris naevus and observed at regular follow-up visits (the observation cohort). The latter patient cohort had regular follow-up examinations at six months and then once a year. Assessments included complete ophthalmic examination, comparing the lesion with previous slit-lamp photographs and UBM examination.

The clinical records of all patients were reviewed and data were extracted from the data-base. In the treated iris and iridociliary melanoma group, the method of treatment (excision, enucleation or Ruthenium-106 plaque radiation), date of treatment and the histology report of any excised lesions were also analyzed. For the observed group, we focused on whether the lesion grew or stayed stable, the period of observation after which growth was documented and the histology if the lesion was excised.

The descriptive statistics were computed for all clinical risk factors and UBM characteristics for both the treated and observed cohorts. All risk factors influencing a decision to treat were assessed by univariate and multivariate logistic regression analysis. The Receiver Operating Characteristic (ROC) curves were plotted and the area under the curve was calculated [22]. The rate of tumor growth in the observation group was estimated by Kaplan-Meier analysis.

## Results

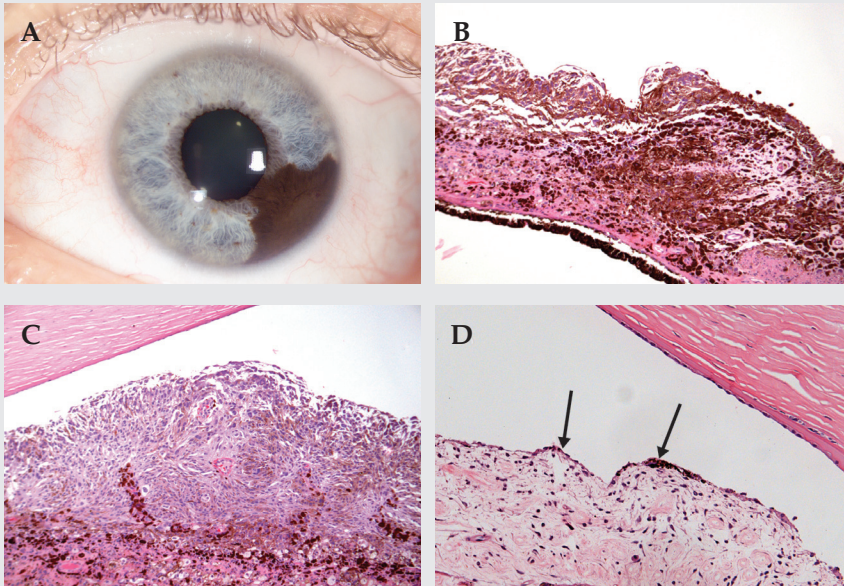
The cohort comprised 117 patients examined and/or treated between January 1997 and December 2007, for a suspected iris or iridociliary melanocytic tumor. Following the guidelines, 52 (44%) patients were diagnosed as melanomas and treated (treated cohort) while 65 (56%) patients were observed initially as suspected iris naevi (observation cohort).

Of the 52 treated patients, 36 (69%) patients received Ruthenium (Ru-106) plaque therapy and the remaining 16 patients (31%) underwent surgery (iridectomy or iridocyclectomy in 9 and enucleation in 7) (Figure 1). All 36 tumors that received Ru-106 plaque radiotherapy showed tumor regression (Figure 2). Of the 16 tumors that underwent excision or enucleation, eight were classified histopathologically as spindle cell melanomas, seven as spindle and epithelioid cell (mixed cell) melanomas and one as iris naevus. Metastasis occurred in three of these 52 patients (5.7%); two of them had undergone enucleation and one had been treated with Ru-106 plaque therapy. All the treated patients are still having follow-up examination at our clinic.

Six (5%) out of total 117 patients died. Two (1.7%) died of distant metastasis, both belonged to the treated group, and four because of other causes.

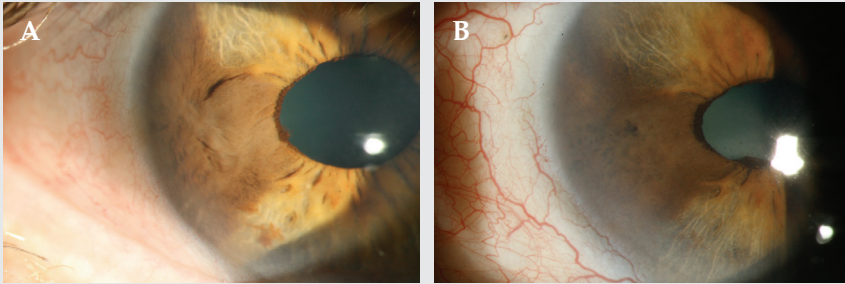
The sixty-five patients in the observed group had a follow-up ranging from 3 to

**Figure 1** **A:** Iris melanoma in the inferonasal quadrant, with tumor extending into anterior chamber angle 360° on gonioscopy, underwent enucleation. **B:** Photomicrograph of the iris showing melanoma cells in and on the iris (Inferonasal iris). (Hematoxylin and eosin, original magnification: x 10), **C:** Photomicrograph of the iris on the other side (temporal iris) also showing melanoma cells as it is a case of ring melanoma. (Hematoxylin and eosin, original magnification; x 10), **D:** Iris melanoma seedings on the temporal iris marked with arrows. (Hematoxylin and eosin, original magnification: x 20)



14 years (median: 6.5 years). Of these patients, 59 (91%) tumors remained unchanged until the last follow-up examination, whereas six lesions (9%) showed growth. The time interval from initial examination to detection of growth in these six lesions was 2 - 4.5 years (median: 3 years). The details of clinical risk factors and UBM characteristics in these patients are shown in Table 3&4. In these six patients, the tumor was treated with a Ru-106 plaque in four, iridectomy in one and one lesion is still being observed because growth was subtle. Histopathology of the one lesion that was excised showed spindle cell melanoma (Figure 3). The 10-year probability of lesion enlargement was 13.9% (95% CI: 0 - 3.31%) (Figure 4).

**Figure 2** Iris melanoma in one of patient in treated group before (A) and after treatment (B) with Ruthenium plaque therapy



**Table 3** Clinical risk factors details of six tumors in the observed group who showed growth during follow-up

| Number of variables | Clinical risk factors               | Patients in observed Group who showed growth of tumor (n = 6) |
|---------------------|-------------------------------------|---|
| 1                   | Patients has symptoms               | 0 / 6   |
| 2                   | Largest basal diameter is > 3mm     | 3 / 6   |
| 3                   | Abnormal tumor vessels              | 3 / 6   |
| 4                   | Pigment dispersion                  | 3 / 6   |
| 5                   | IOP > 21 mmHg in the tumor eye only | 0 / 6   |
| 6                   | Ectropion uveae                     | 5 / 6   |
| 7                   | Extension to anterior chamber angle | 3 / 6   |
| 8                   | Secondary cataract                  | 1 / 6   |
| 9                   | Satellite lesions                   | 1 / 6   |
| 10                  | Tapioca appearance                  | 1 / 6   |
| 11                  | Decreased iris motility             | 3 / 6   |
| 12                  | Age > 48 years                      | 4 / 6   |

**Table 4** UBM characteristics of six tumors in the observed group which showed growth during follow-up

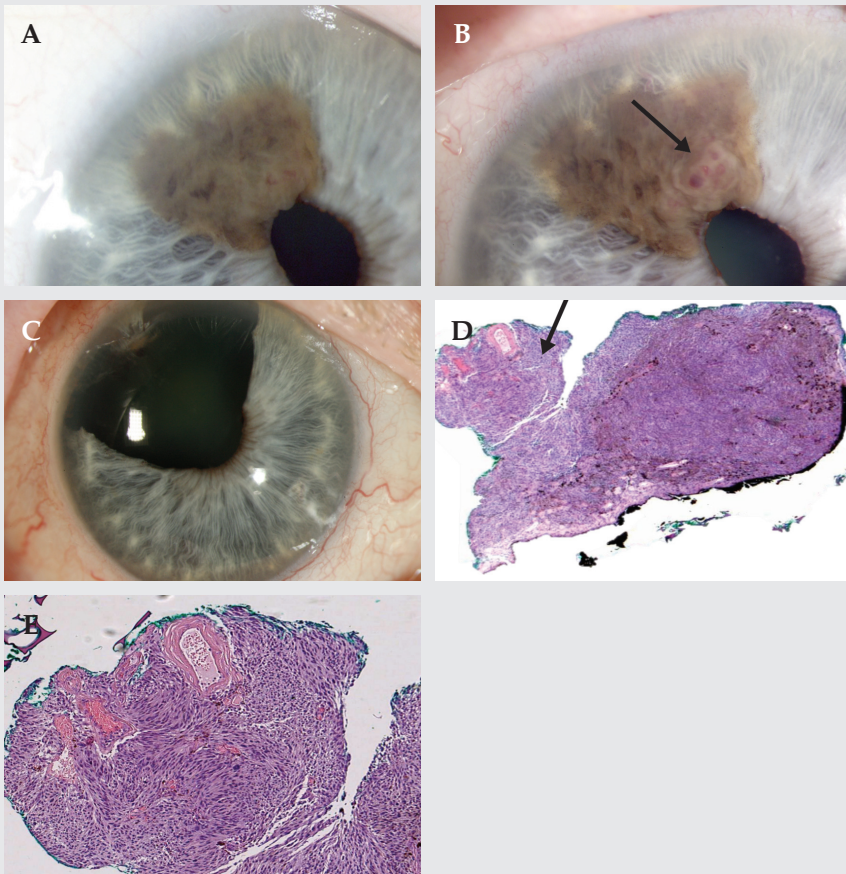
| Number of variables | UBM characteristics                 | Patients in observed Group who showed growth of tumor (n = 6) |
|---------------------|-------------------------------------|---|
| 1                   | Largest basal tumor dimension > 3mm | 4 / 6   |
| 2                   | Tumor thickness > 1mm               | 4 / 6   |
| 3                   | Irregular tumor structure           | 4 / 6   |
| 4                   | Indistinct tumor boundary           | 4 / 6   |
| 5                   | Secondary iris cysts                | 2 / 6   |
| 6                   | Non-intact iris pigment epithelium  | 2 / 6   |
| 7                   | Low internal reflectivity           | 1 / 6   |
| 8                   | Ciliary body involvement            | 3 / 6   |
| 9                   | Anterior chamber angle extension    | 0/ 6  |

A 2 × 2 contingency table was computed for evaluating the association between clinical data in the two cohorts (i.e. treated, observed) and clinical outcome (i.e. melanomas, suspected naevi) (Table 5). This table shows the association between rows (groups) and columns (outcomes) by using the Fisher's exact test (p-value: <0.0001).

Comparison of the clinical risk factors in the treated group (n = 52) and the observed group (n = 65) is shown in Table 1. The substantial difference between the two groups is noted in risk factors no. 1 – 5 and 7, 8 and 9. All UBM variables showed significant differences, as shown in Table 2.

In addition, univariate logistic regression for clinical risk factors showed that each of the variables 1-5 was significantly associated with the diagnosis of iris melanomas. Of the remaining factors, anterior chamber angle extension of tumor and secondary cataract were most significant (Table 1). Multivariate logistic regression of these features using forward stepwise selection defined as important factors: presence of symptoms, diameter >3mm, IOP >21mmHg, secondary cataract and age at onset >48 years (Table 6). The ROC curve for these clinical factors based on multivariate logistic regression showed the area under curve (AUC) 0.93 (93%) and 95% CI of 0.875 – 0.976 (Figure 5).

**Figure 3** Example of one tumor in observed group, which showed growth. **A:** At first visit, **B:** After 3 years of follow-up tumor enlarged with a more prominent vascular growth on the surface of the tumor (marked with arrow), **C:** After local excision, **D:** Iridectomy specimen showing the iris melanoma, the arrow indicates the recent outgrowth with the large blood vessels. (Hematoxylin and eosin, Original magnification: x 2.5), **E:** Detail of recent outgrowth showing spindle cells with oval nuclei (Hematoxylin and eosin, original magnification: x 40)



**Figure 4** Kaplan-Meier curve showing probability of enlargement of 65 observed iris melanocytic tumors as a function of follow-up time period



**Table 5** 2 X 2 Contingency table to see the association between groups (treated, observed) and columns (outcome: melanomas, naevi)

| Group / Outcome | Iris Melanomas | Suspected Iris Naevi | Total |
|-----------------|----------------|----------------------|-------|
| Treated         | 51             | 1                    | 52    |
| Observed        | 5              | 60                   | 65    |
| Total           | 56             | 61                   | 117   |
| P- value        | <0.001         |                      |       |

Univariate logistic regression of UBM characteristics showed that all the factors were significantly associated with the diagnosis of malignant melanoma and the clinical decision to treat (Table 2). Multivariate logistic regression using forward stepwise selection of UBM variables showed that thickness >1mm, basal dimension >3mm, low reflectivity, tumor extension to the anterior chamber angle and presence of secondary cysts were the most important characteristics

associated with malignancy (Table 7). The ROC curve for these UBM characteristics based on multivariate regression showed AUC of 0.96 (96%) and 95% CI of 0.935 – 0.994 (Figure 6).

**Table 6** Results of Multivariate logistic regression of clinical risk factors using forward stepwise selection

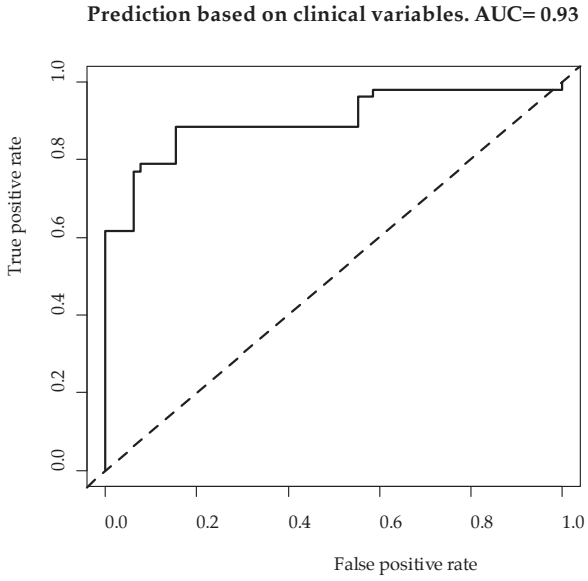
| Clinical risk Factors | Odds ratio | P-value | 95% CI of Odds ratio |
|-----------------------|------------|---------|----------------------|
| Symptoms              | 0.14       | 0.018   | 0.02 – 0.71          |
| Diameter > 3mm.       | 0.04       | < 0.001 | 0.00 – 0.26          |
| IOP > 21 mmHg         | 0.03       | 0.039   | 0.00 – 0.84          |
| Secondary cataract    | 0.07       | < 0.001 | 0.01 – 0.25          |
| Age > 48 years        | 3.77       | 0.046   | 1.02 – 13.98         |

**Table 7** Results of Multivariate logistic regression of UBM characteristics using forward stepwise selection

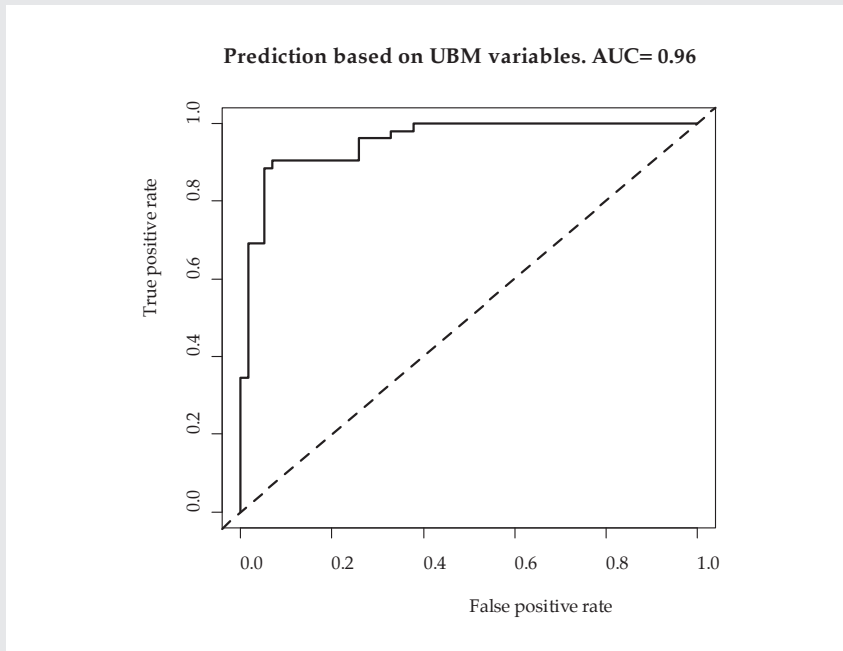
| UBM characteristics                       | Odds ratio | P-value | 95% CI of Odds ratio |
|---|------------|---------|----------------------|
| Thickness >1mm                            | 0.03       | 0.006   | 0.00 – 0.38          |
| Basal tumor diameter >3mm                 | 0.17       | 0.042   | 0.02 – 1.09          |
| Low reflectivity                          | 0.12       | 0.005   | 0.02 – 0.53          |
| Tumor extension to anterior chamber angle | 0.01       | 0.049   | 0.00 – 0.98          |
| Presence of secondary cysts               | 0.20       | 0.050   | 0.03 – 1.05          |



**Figure 5** ROC curve for most significant clinical risk factors identified on multivariate logistic regression analysis: secondary cataract, diameter >3mm, presence of complaints, IOP >20mmHg and age at onset >48 years, showing the AUC of 0.93 (95% CI: 0.875 – 0.976)



**Figure 6** ROC curve for most significant UBM characteristics identified on multivariate logistic regression analysis: thickness >1mm, low reflectivity, basal dimension >3mm, anterior chamber extension and presence of secondary cysts, showing the AUC of 0.96 (95% CI: 0.935 – 0.994)



## Discussion

The aim of patient management is always to treat the truly malignant melanomas and to avoid unnecessary treatment of naevi. However, making a reliable diagnosis of iris or iridociliary melanomas and differentiating it from iris naevi remained clinically difficult because of absence of clear-cut diagnostic features, the low rate of tumor growth and distant metastasis [6,9,11]. Furthermore, performing a diagnostic biopsy of iris tumors carries a risk for melanoma cells dissemination and subsequent growth in addition to other complications, and is therefore best avoided. According to two different studies, 78 - 87% of all suspected iris melanomas undergoing excision are histologically proven to be

benign [8, 9, 12]. On the other hand, Kersten and coworkers concluded that although melanocytic iris lesions have excellent prognosis, they should not be considered benign or distinct from posterior melanomas [4].

Shields, Harbour and others have published reports regarding the clinical, diagnostic and prognostic features of iris melanomas but did not evaluate clinical features such as decreased iris motility and satellite lesions; in addition, UBM features were not taken into account because this equipment was not available at that time [10, 16, 17, 23, 24].

After UBM became available, several reports established the role of ultrasound biomicroscopy in the diagnosis of iris and iridociliary melanomas [7, 25-30]. Most of these clinical studies retrospectively analyzed the presence or absence of various characteristics in observed and treated patients.

We present the results gathered over a 14-year period (1997- 2010) during which all patients with iris and iridociliary melanocytic tumors were managed according to the Dutch Iris Melanoma guidelines which included all clinical risk factors and UBM characteristics of iris and iridociliary melanomas. We have now performed a analysis to determine whether our guidelines for iris melanoma was indeed working and justified use by the Dutch Society for Ocular Oncology Services. The main strength of this study is the inclusion of all patients referred to our national center for a suspected melanocytic iris and iridociliary tumors with a long and complete follow-up of a maximum of 14 years and evaluation of both clinical risk factors and UBM characteristics. All clinical risk factors known to be prognostic for iris or iridociliary melanomas were taken into account and we also included some that had not yet been evaluated by others [17].

A limitation of our study is the relatively small number of patients. Also the number of iris naevi (65) followed in the observation cohort only marginally exceeded the treated iris melanomas group (52), which does not correspond to the increased incidence of iris naevi compared to iris melanomas. This is probably due to the fact that in our academic ocular oncology clinic we only see suspected iris melanocytic lesions, while typical iris naevi are seen by local ophthalmologists. Another limitation is that not all the melanomas in the treated group were confirmed histologically because most were treated by plaque radiotherapy. But this is in accordance with the changing trend of iris melanomas treatment with radiotherapy during the last two decades [31,32,33,34]. In addition, all the tumors showed regression after radiation, which supports the fact that malignant tumors were treated.

This study confirms that most of the clinical risk factors included in our guidelines for the diagnosis of iris melanomas were present more often in the treated cohort. The first five important risk factors showed a high odds ratio for the decision to treat on the univariate logistic regression analysis. The clinical

variables that did not show significant differences between the treated and observed group were ectropion uveae, decreased iris motility and age >48 years. Our study also showed that all the UBM characteristics favoring a diagnosis of iris melanoma included in our study were most often present in the treated group. All the UBM characteristics showed high odds ratio on the univariate logistic regression analysis, while the multivariate analysis showed that largest basal dimension >3 mm, tumor thickness >1 mm, secondary iris cysts, low internal reflectivity and anterior chamber angle extension of the tumor proved to be the most significant factors associated with a diagnosis of melanoma. When such characteristics are present, prompt treatment is indicated.

The assumption that all the tumors in the treated group were melanoma was supported by the histological finding that 15/16 tumors were classified as melanomas (94%) and only one as naevus (6%). The 36 patients treated with radiation also showed regression of their tumors, probably reflecting the malignant nature of their tumor. The results of Ruthenium brachytherapy for these tumors regression were shown in one other study [35]. The growth rate in the observed group was low (i.e. 10-year probability of enlargement was 14%) and comparable to other studies [17]. In total, six lesions showed growth, one of which was treated with excision and was histologically proven to be a melanoma. The other four were treated by plaque therapy, and all showed regression. The metastatic rate in our study was 5.7%, which correlated with other studies; patients who developed metastasis were in the treated group [4,5].

Although it was previously reported that it is a challenge to differentiate between iris naevi and melanoma, the ROC curves in this study showed a high AUC for both the clinical (93%) and UBM features (96%) included in our iris melanoma guidelines, which makes these guidelines a sensitive tool for diagnosing iris and iridociliary melanomas.

In conclusion, our study provides a comprehensive analysis of all clinical risk factors and UBM characteristics associated with the diagnosis of iris melanoma and may help ophthalmologists to differentiate between iris and iridociliary naevus from melanoma.

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