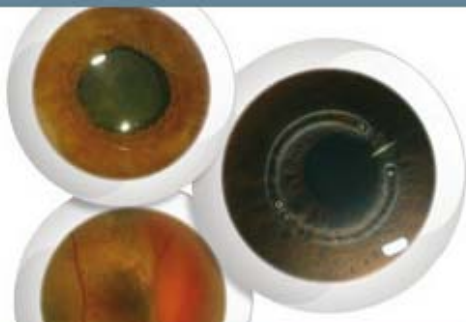


# Tècniques diagnòstiques en els tumors intraoculars. Factors pronòstics

Dra M<sup>a</sup> Antonia Saornil Alvarez  
Unidad de referencia del SNS (CSUR).  
Tumores Intraoculares del adulto.  
Hospital Clínico Universitario  
Universidad de Valladolid



CAT | CAST

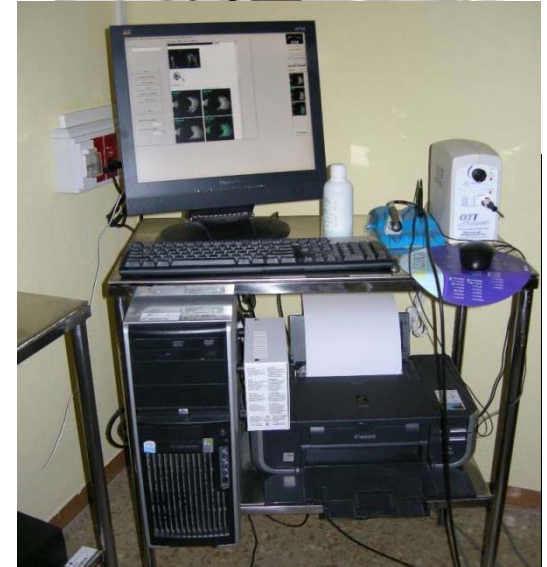
BARCELONA 24 | 25 | 26 NOVEMBRE 2011  
HOTEL BARCELÒ SANTS | BARCELONA

**42** CONGRÉS  
DE LA SOCIETAT CATALANA  
D'OFTALMOLOGIA

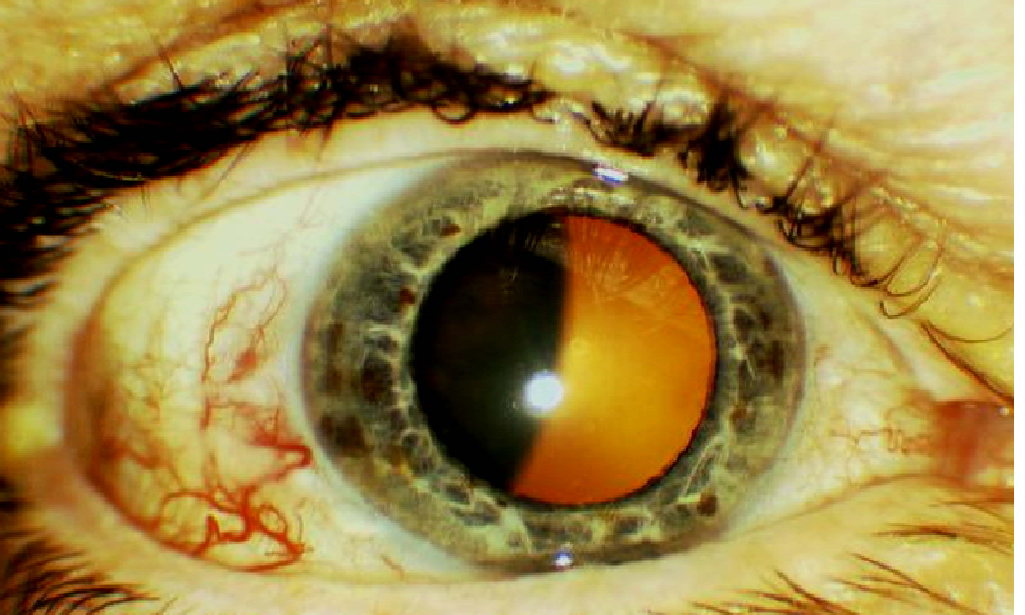
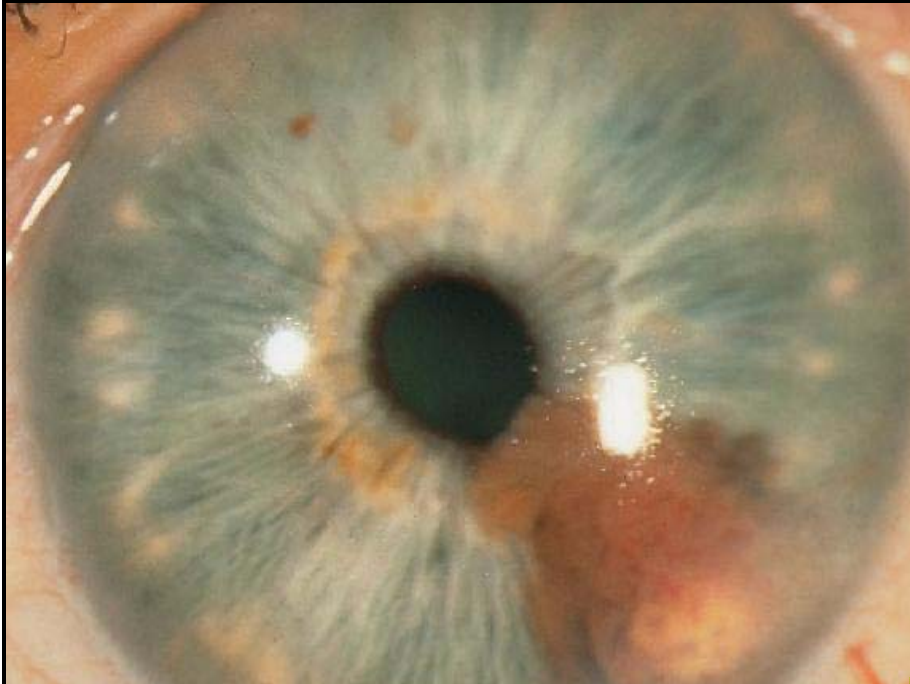
CIRURGIA REFRACTIVA  
Uveïtis  
Oncologia ocular

# TUMORES INTRAOCULARES: METODOS DE DIAGNÓSTICO

- BIOMICROSCOPIA DE POLO ANTERIOR
- TRANSILUMINACIÓN O DIAFANOSCOPIA
- OFTALMOSCOPIA/RETINOGRAFÍA
- ANGIOGRAFÍA
  - Fluoresceína
  - Verde indocianina
- AUTOFLUORESCENCIA
- OCT
- ECOGRAFIA

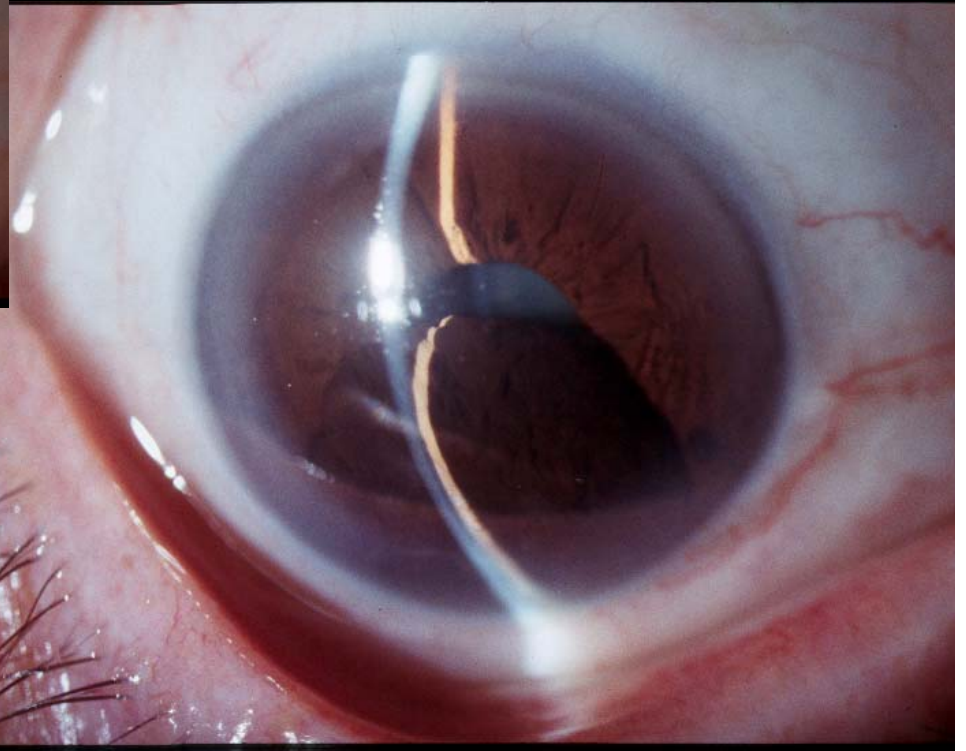
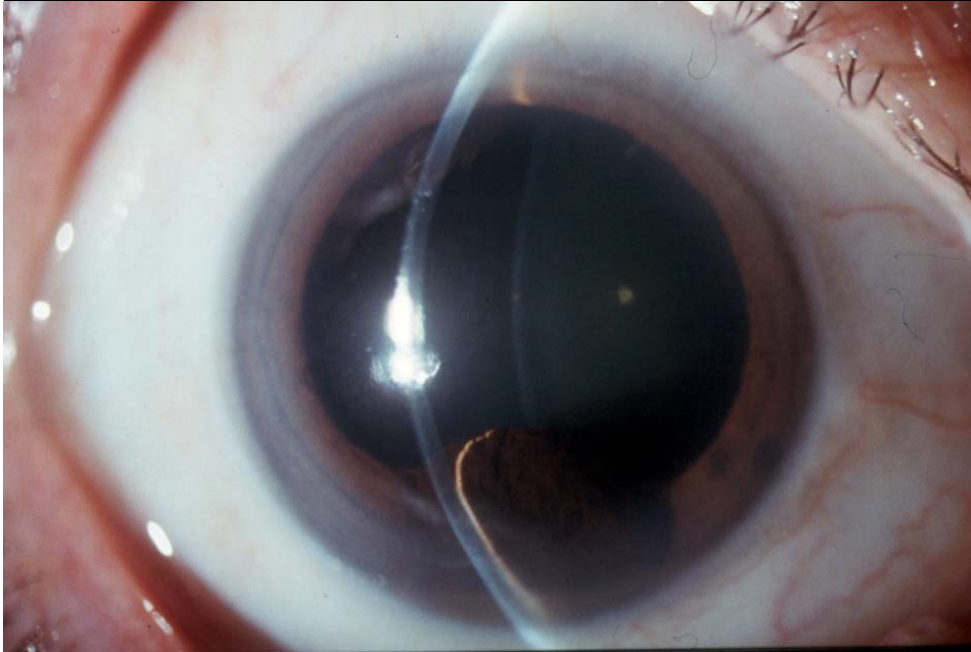


# TUMORES INTRAOCULARES: BPA



## TUMORES INTRAOCULARES: BPA

SEGUIMIENTO FOTOGRÁFICO =  
DOCUMENTACIÓN DE ACTIVIDAD



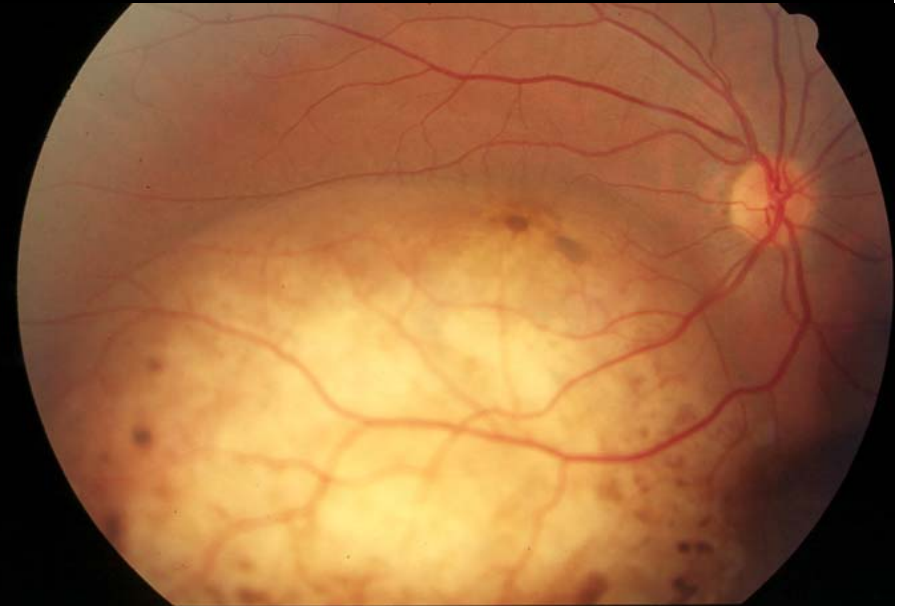
# TUMORES INTRAOCULARES: TRANSILUMINACIÓN

- EVALUA:
  - Tamaño
  - Extension
- TIPOS
  - Transpupilar
  - Transocular

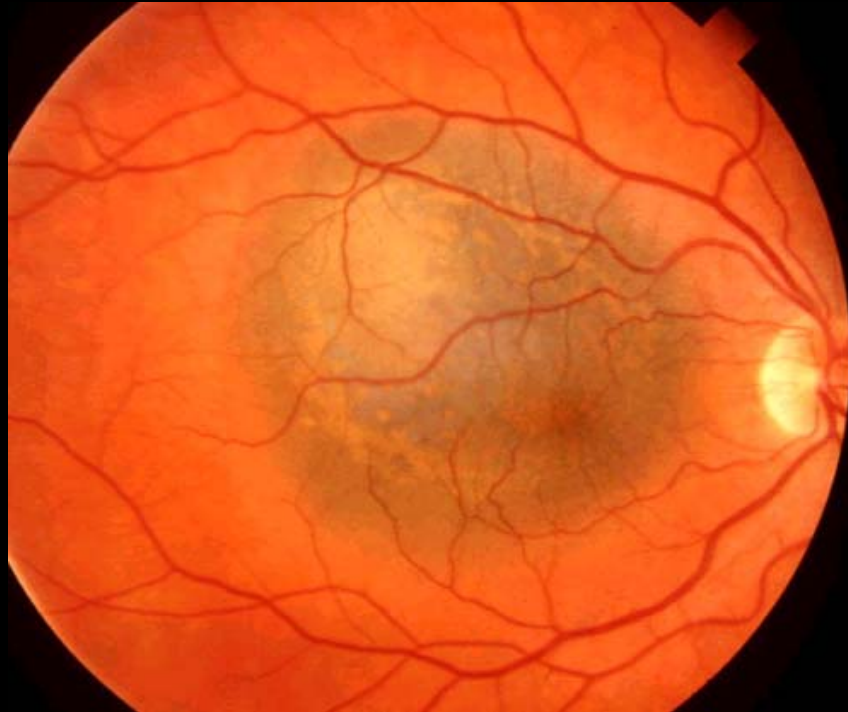


# TUMORES INTRAOCULARES: OFTALMOSCOPIA RETINOGRAFIA

- Afectación primaria
  - Coroides
  - EPR
  - Retina sensorial
- Extensión invasión
  - Espacio subretiniano
  - Retina
  - Vitreo
- Distancias, medidas margenes
  - NO, fovea, limbo
- Crecimiento o regresion



# TUMORES INTRAOCULARES: OFTALMOSCOPIA RETINOGRAFIA



# TUMORES INTRAOCULARES: OFTALMOSCOPIA RETINOGRAFIA



ENERO 2003



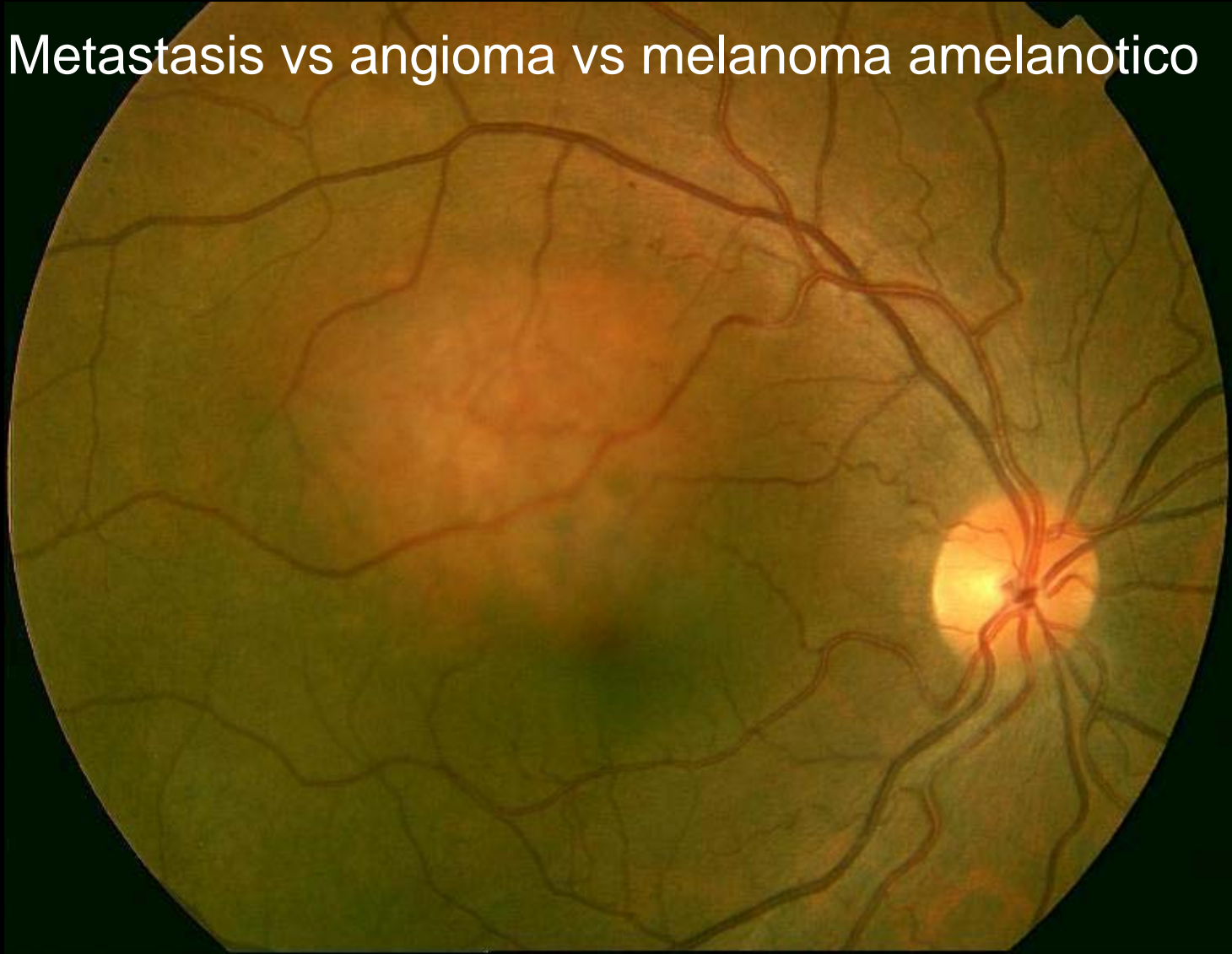
MAYO 2007



# TUMORES INTRAOCULARES: ANGIOGRAFIA

MASA SOLITARIA AMELANOTICA UNILATERAL:

Metastasis vs angioma vs melanoma amelanotico

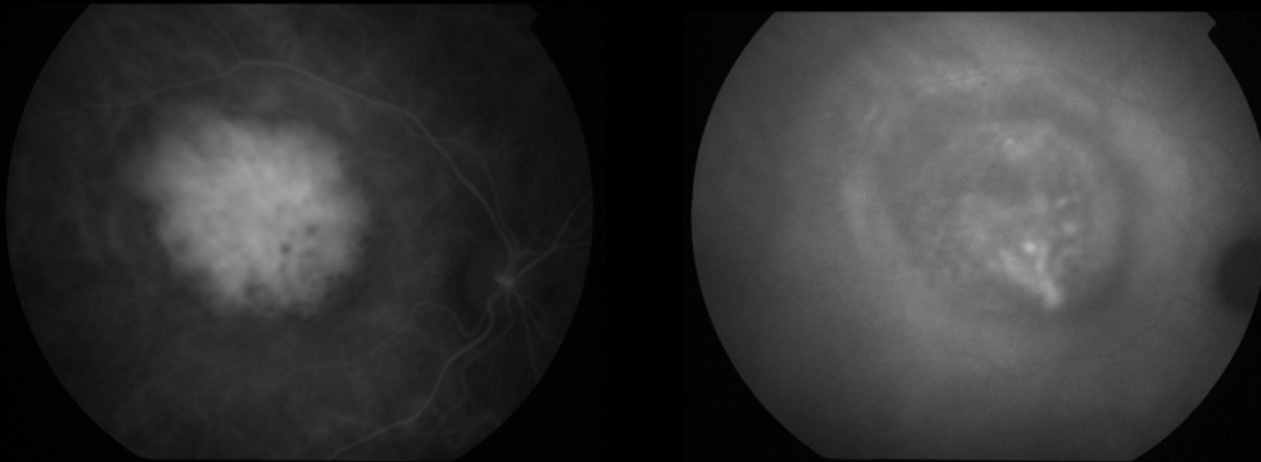


## ANGIOGRAFIA FLUORESCEINA



Hiperfluorescencia en fases iniciales que aumenta a lo largo de la prueba

## ANGIOGRAFIA INDOCIANINA VERDE



Hiperfluorescencia en fases iniciales que aumenta  
+ fenomeno de lavado en tiempos tardíos



ANGIOMA CIRCUNSCRITO DE COROIDES

This fundus photograph shows the posterior pole of the eye. The optic disc is visible on the right side, with a normal cup-to-disc ratio. The retinal vasculature is clearly visible, showing a normal branching pattern. A circumscribed choroidal angioma is present, appearing as a localized, reddish-orange lesion in the choroid, which is visible through the retina. The lesion is well-defined and does not appear to be associated with any retinal pathology. The overall appearance is that of a benign, circumscribed choroidal angioma.

# TUMORES INTRAOCULARES: ANGIOGRAFIA



**TUMORES INTRAOCULARES:  
AUTOFLUORESCENCIA/OCT**  
NEVUS Vs MELANOMA DE COROIDES  
**Características de melanoma pequeño**

To **F**ind **S**mall **C**horoidal **M**elanoma

**U**sing helpful **H**ints:

**T**= thickness > 2mm

**F**= subretinal fluid

**S**= symptoms

**C**= orange pigment

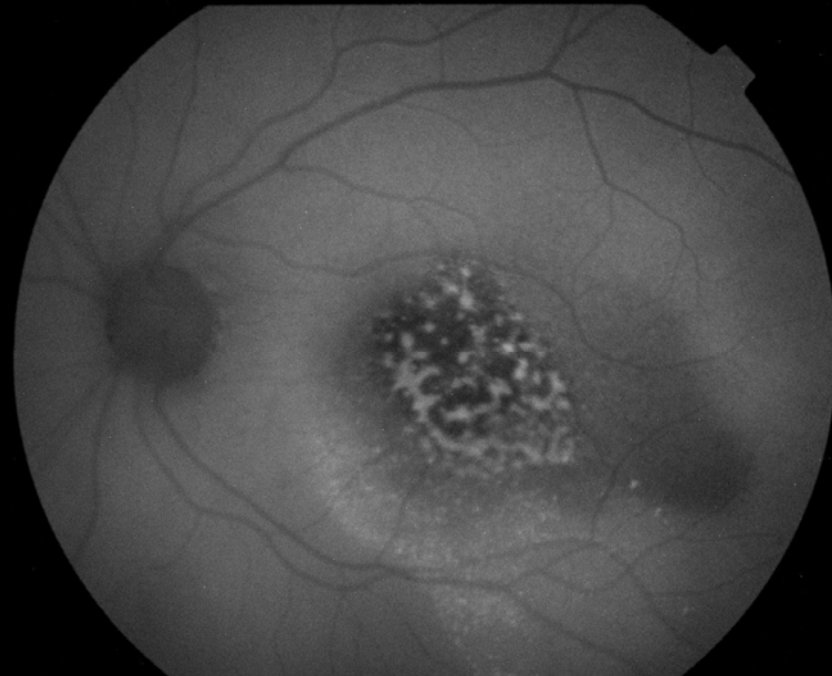
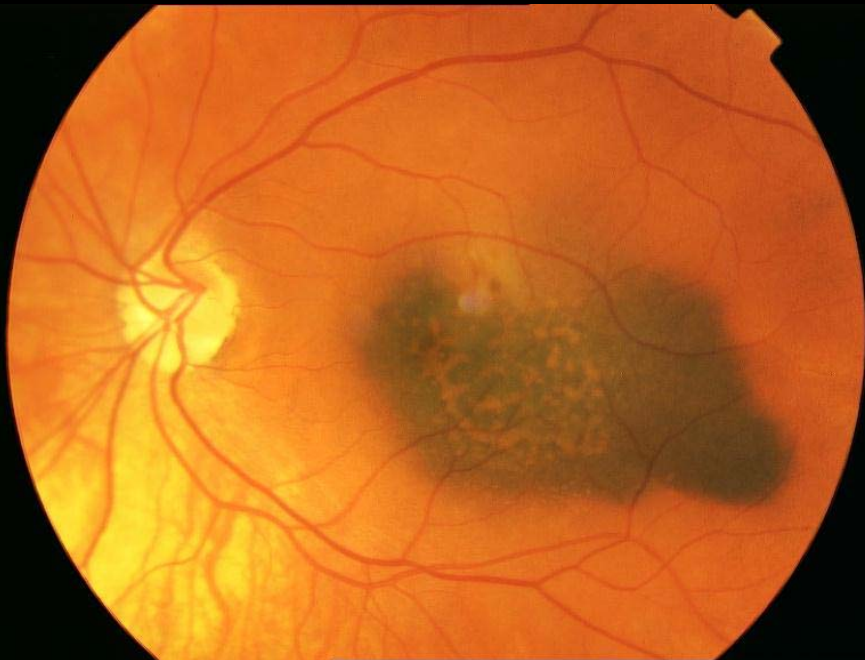
**M**= margin touch optic disk

**U**= Ultrasound hollowness

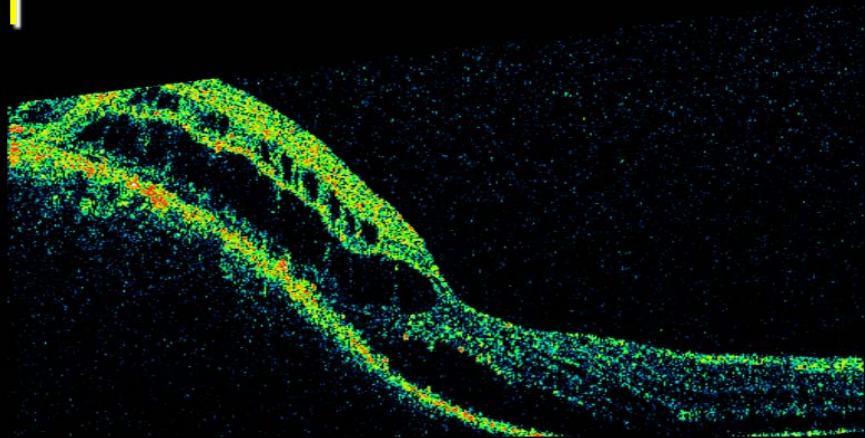
**H**= Halo absence



# AUTOFLUORESCENCIA

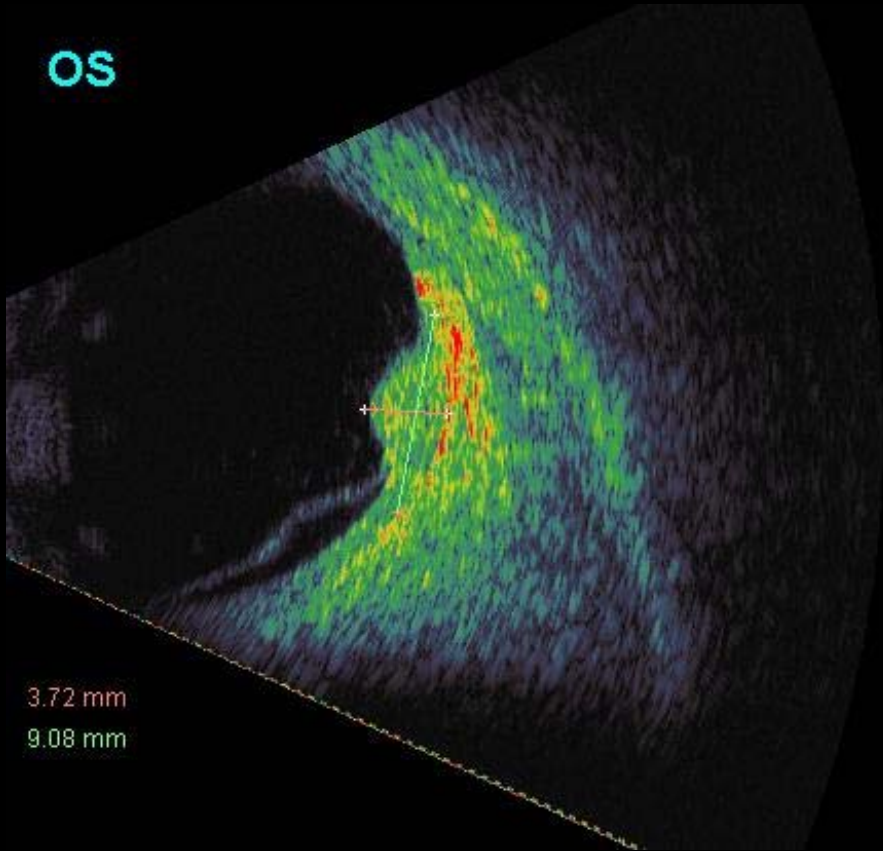


# OCT

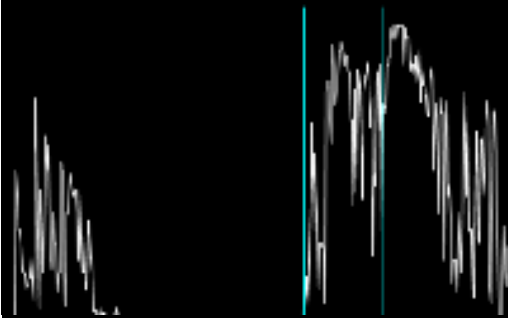


# TUMORES INTRAOCULARES: Ecografía

OS

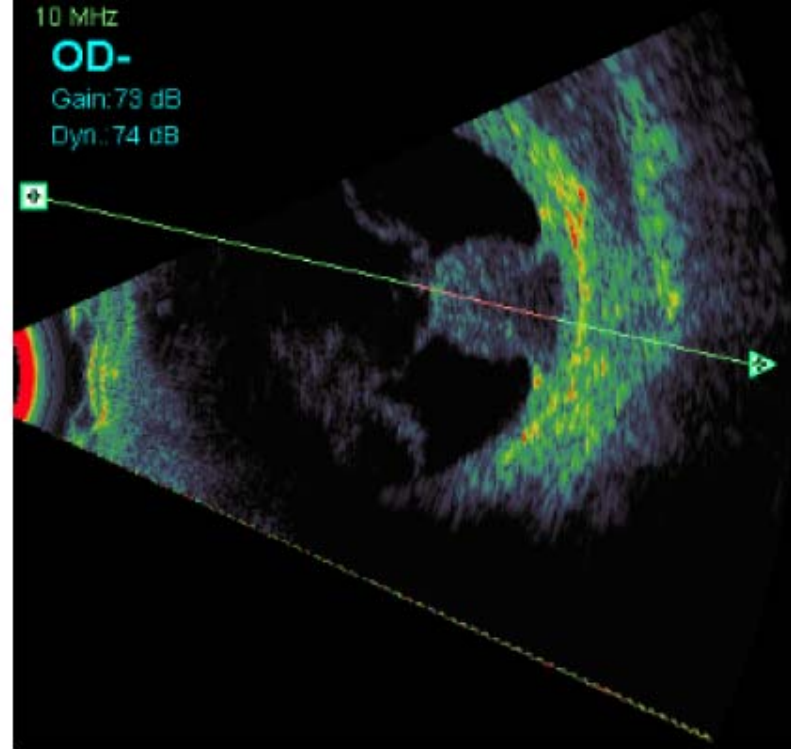


3.72 mm  
9.08 mm

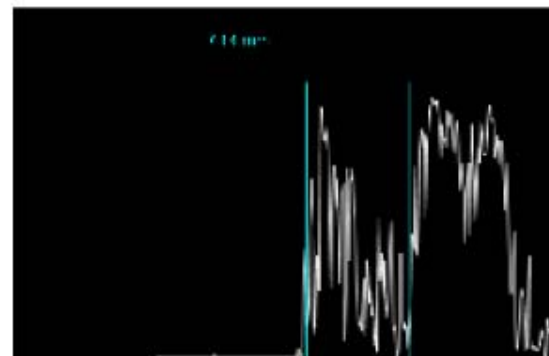


- Borde abrupto
- Hiperecogenicidad homogénea
- D de R exudativo

10 MHz  
OD-  
Gain: 73 dB  
Dyn: 74 dB



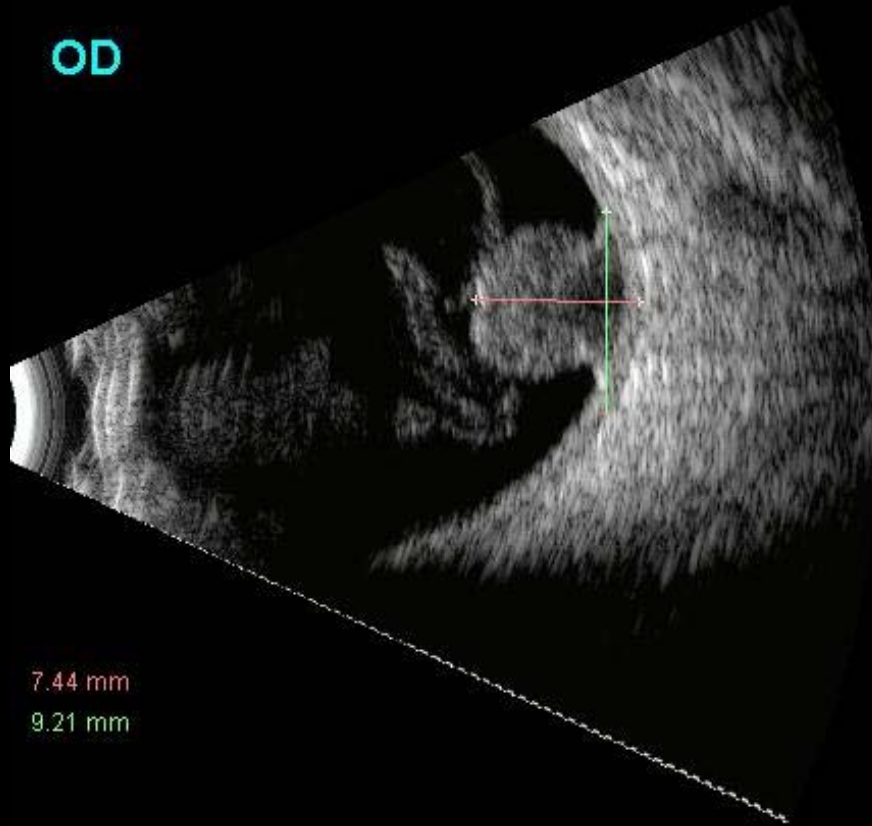
OD



- Champiñon
- Vacio ecogenico
- Kappa
- Exc coroidea

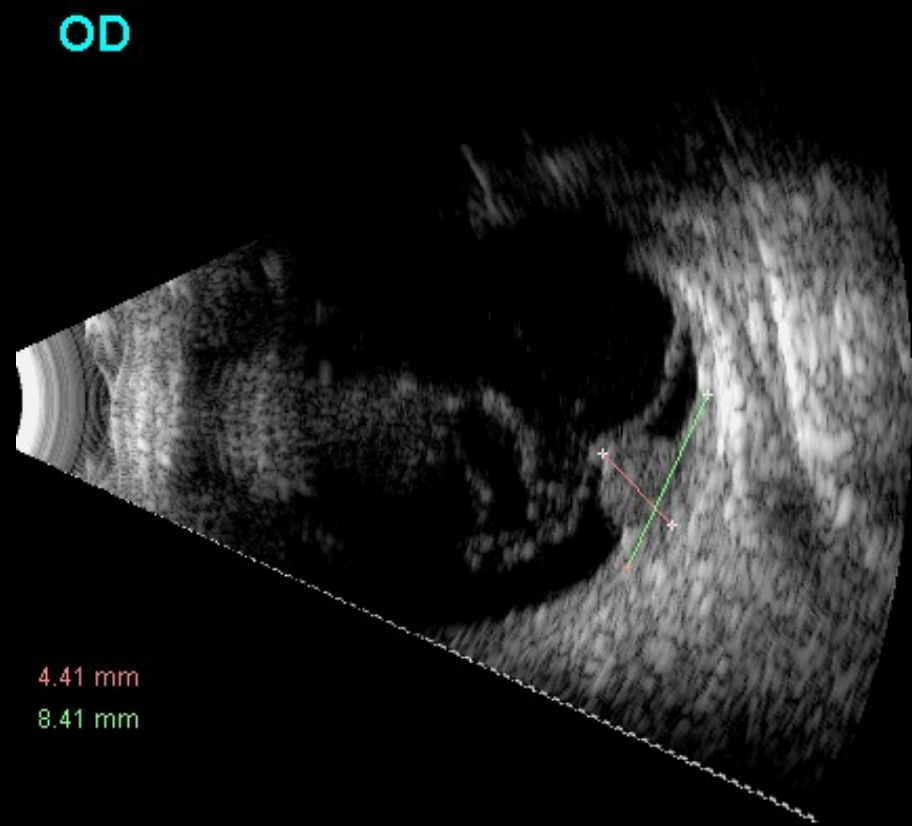
# TUMORES INTRAOCULARES: Ecografía

OD



**Prebraquiterapia sept 2007**

OD

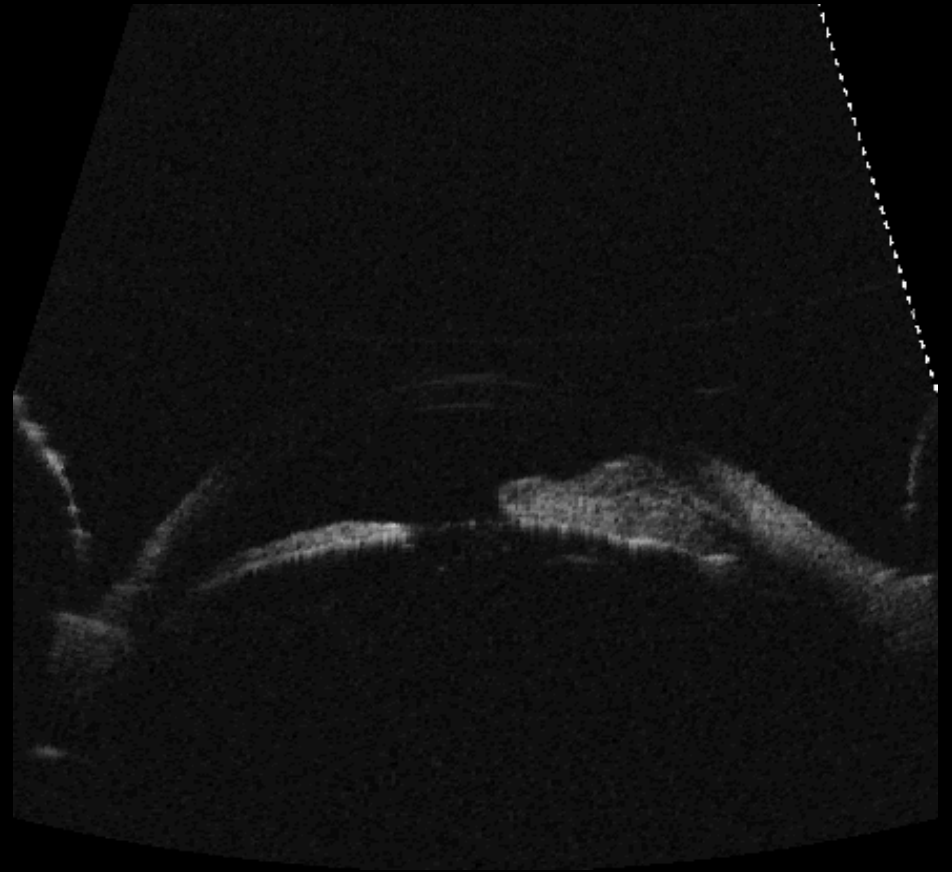
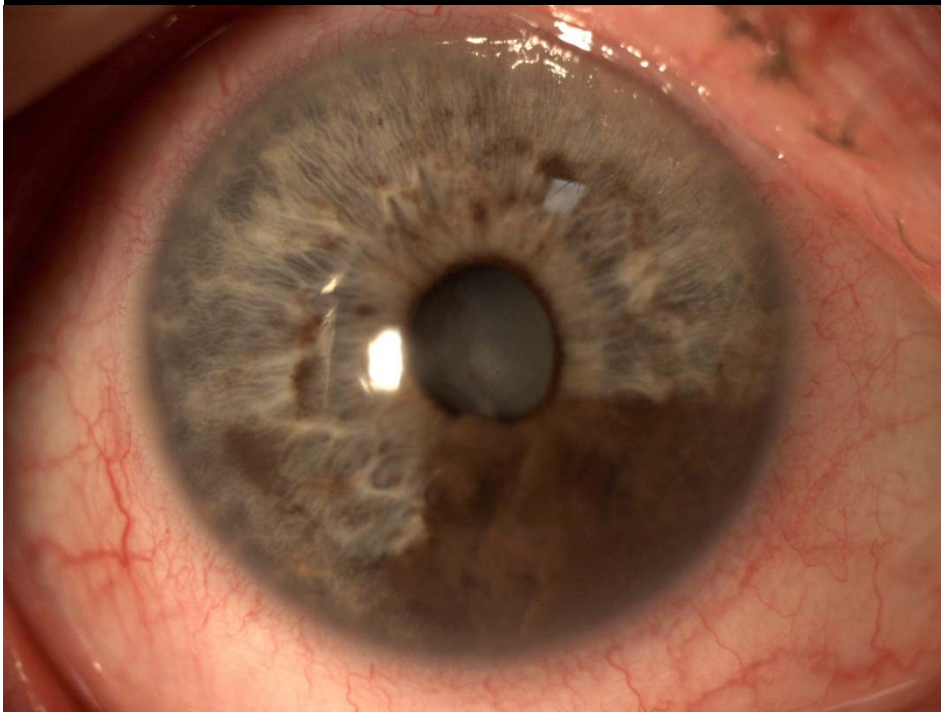


**Postbraquiterapia 2011**



# BIOMICROSCOPIA ULTRASÓNICA ANTERIOR

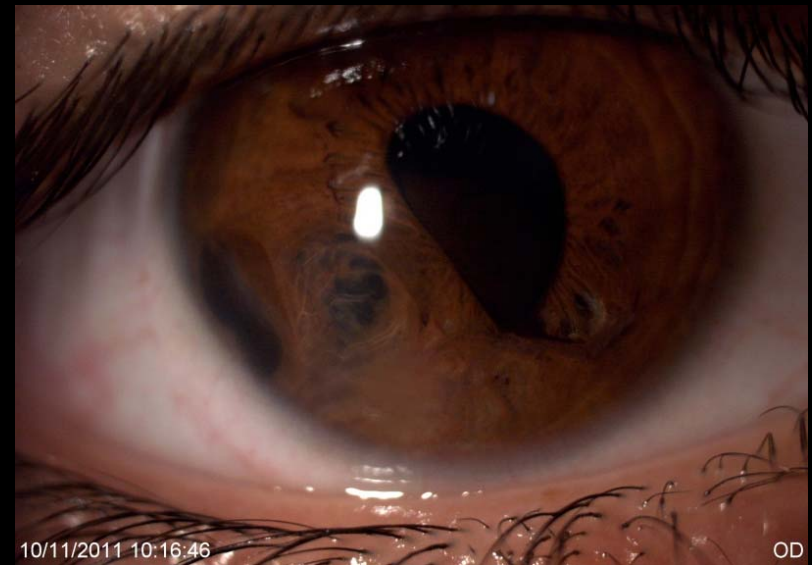
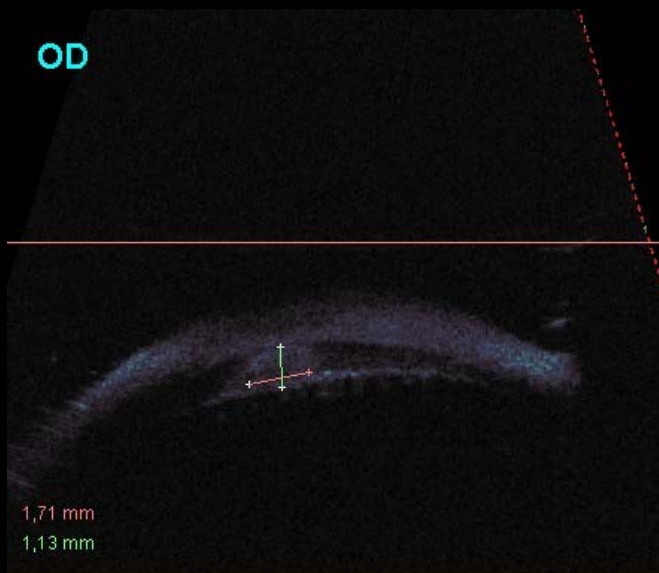
- Localización precisa
- Extension posterior
- Medidas
- Monitorizacion



# BIOMICROSCOPIA ULTRASÓNICA ANTERIOR



OD



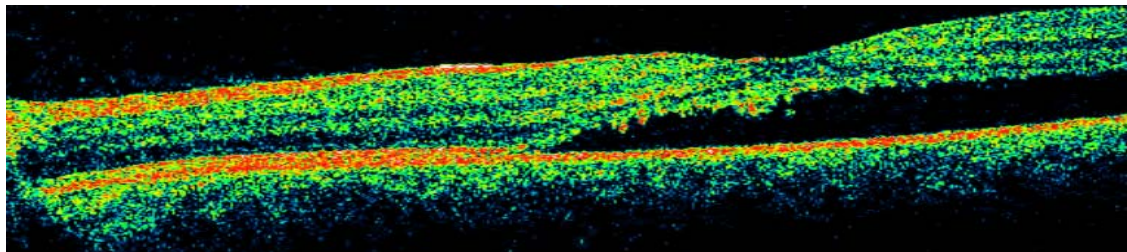
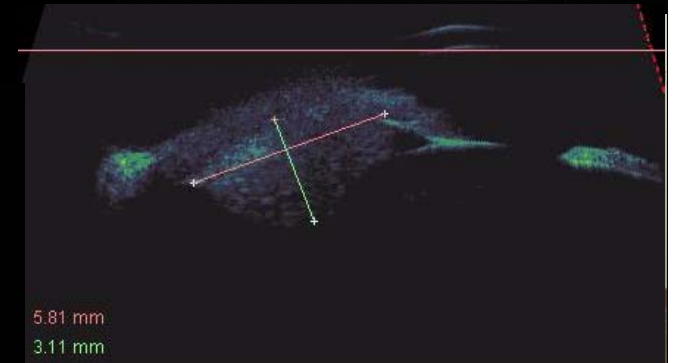
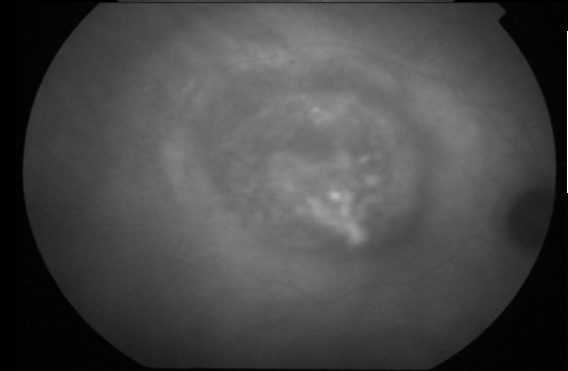
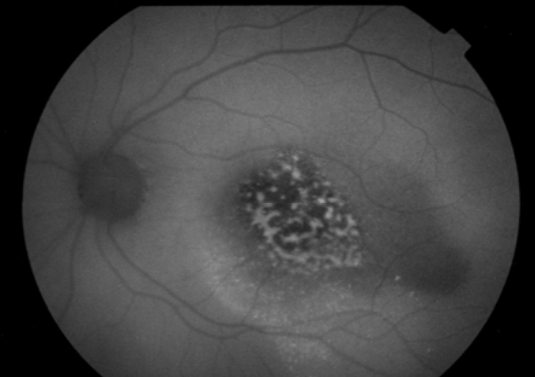
35 MHz

OD



# TUMORES INTRAOCULARES: METODOS DE DIAGNÓSTICO

- BIOMICROSCOPIA DE POLO ANTERIOR/  
OFTALMOSCOPIA/RETINOGRAFIA/  
TRANSILUMINACION
  - Registro gran calidad:morfologia
  - Evolución: crecimiento/regresion/medidas
- ANGIOGRAFIA:Fluoresceina/Verde Indocianina
  - DX Angiomas
  - Vascularizacion
- AUTOFLUORESCENCIA
  - Pigmento naranja/ EPR/FSR
- OCT
  - Deteccion precoz edema macular y FSR
- ECOGRAFIA OCULAR POSTERIOR/BMU
  - Diagnostico, medidas, crecimiento/regresion



# MELANOMA UVEAL : Supervivencia / Factores pronósticos

- Precisión Diagnóstica Clínica Expertos > 99%
- Enf sistémica al Dx 1-2%
- MORTALIDAD GLOBAL 15 > 40% independiente del tto

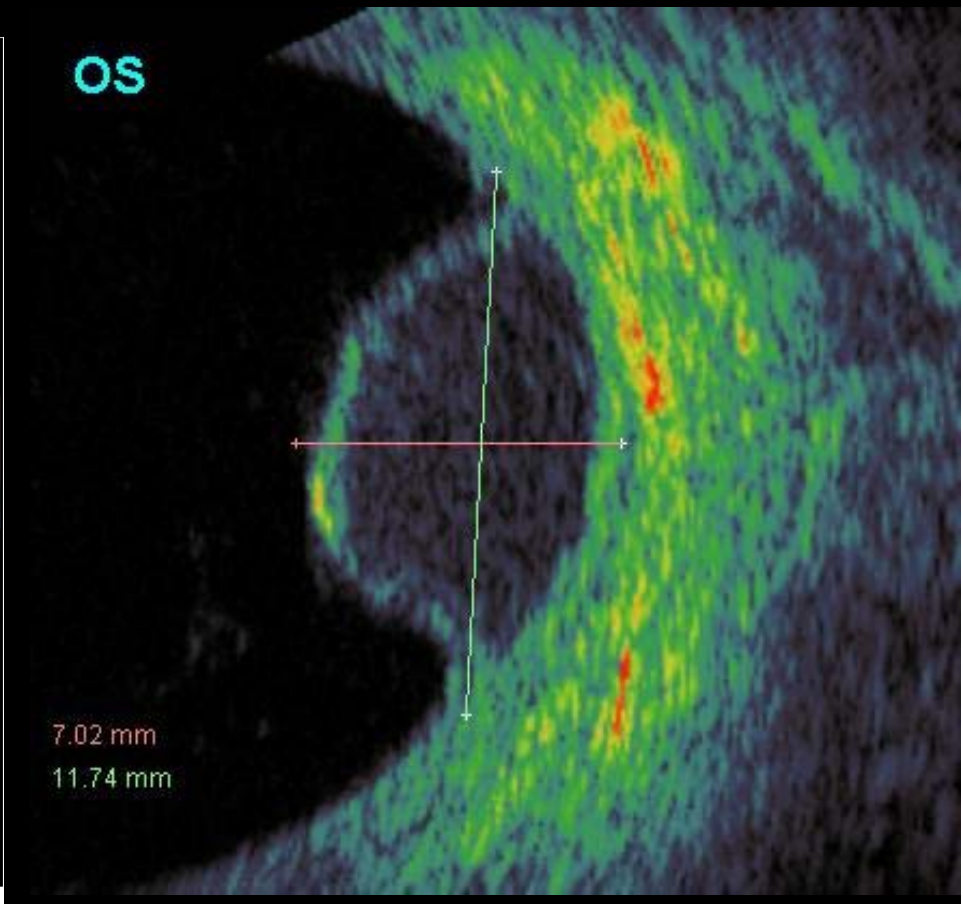
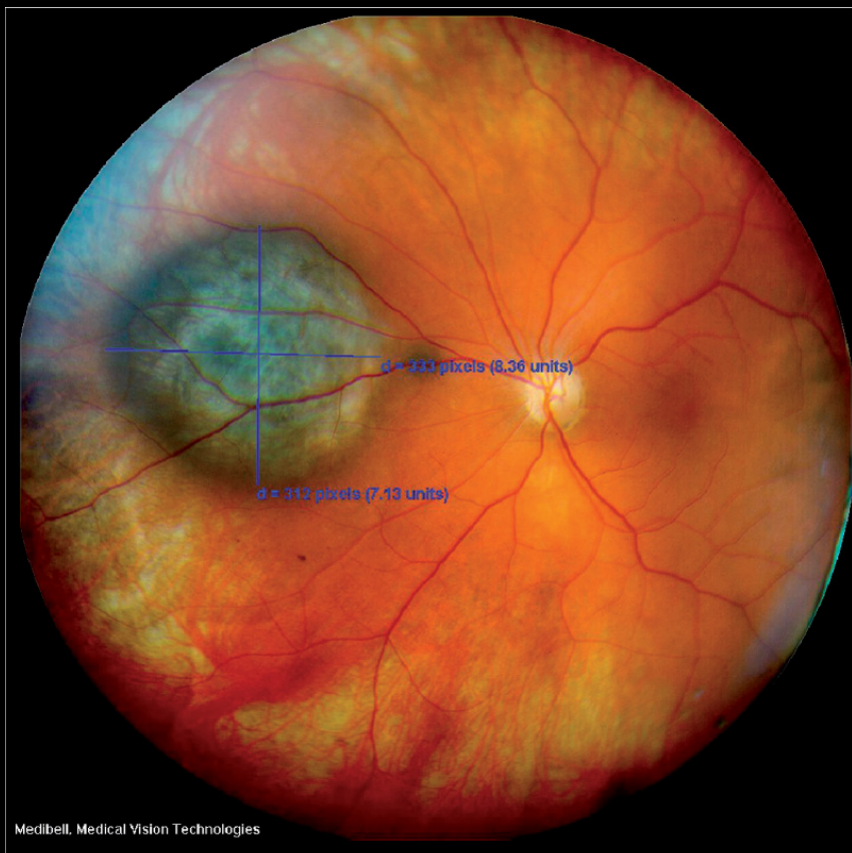
10 MHz  
METASTASIS SUBCLINICAS

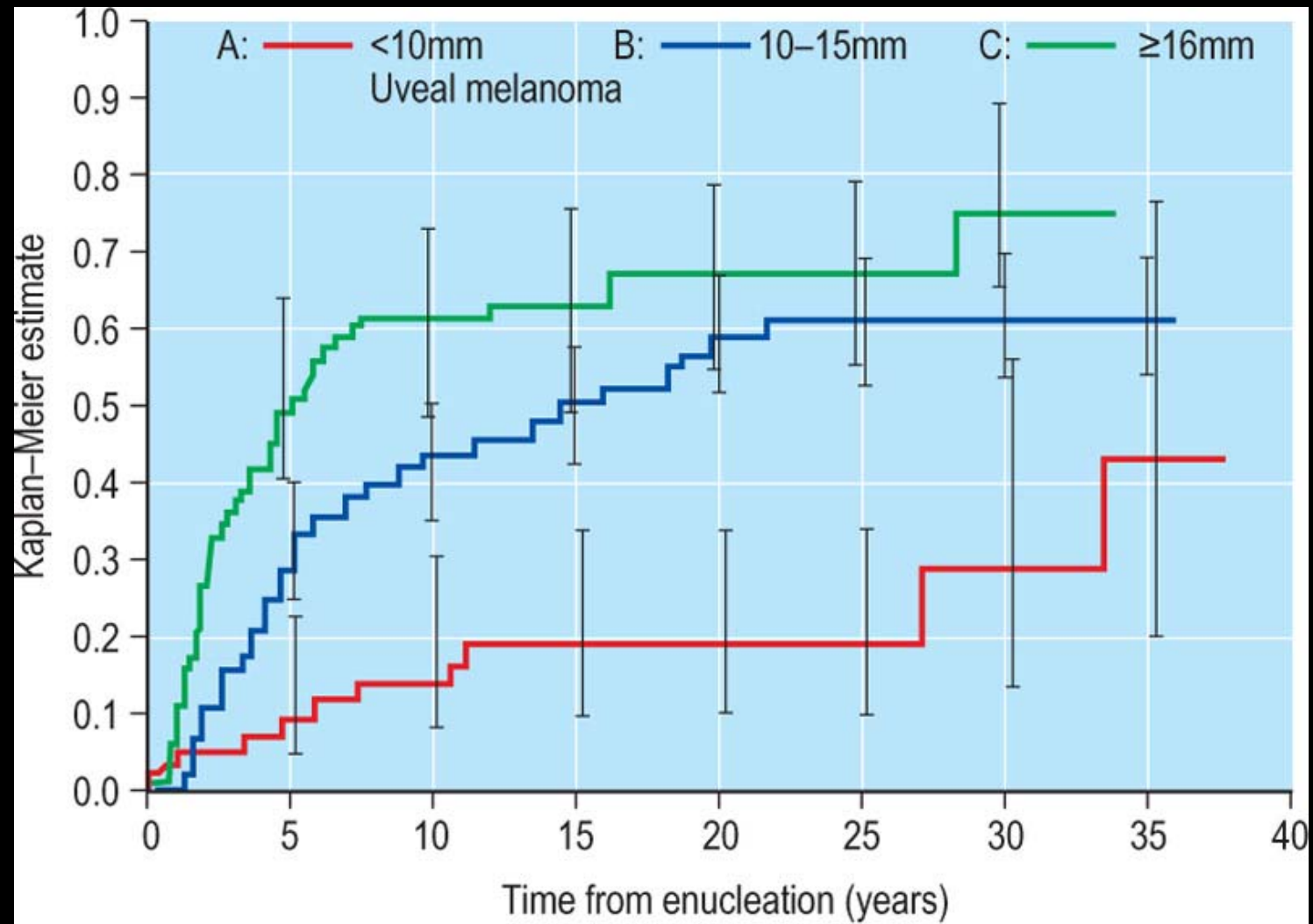
# ¿COMO IDENTIFICAR AL PACIENTE CON RIESGO DE METÁSTASIS?

- FACTORES PRONÓSTICOS
  - CLÍNICOS
  - HISTOPATOLÓGICOS
  - CITOGENÉTICOS
  - BIOLOGIA MOLECULAR

# Melanoma uveal: Factores Pronósticos clínicos

- LTD: mayor diametro tumoral
- Altura

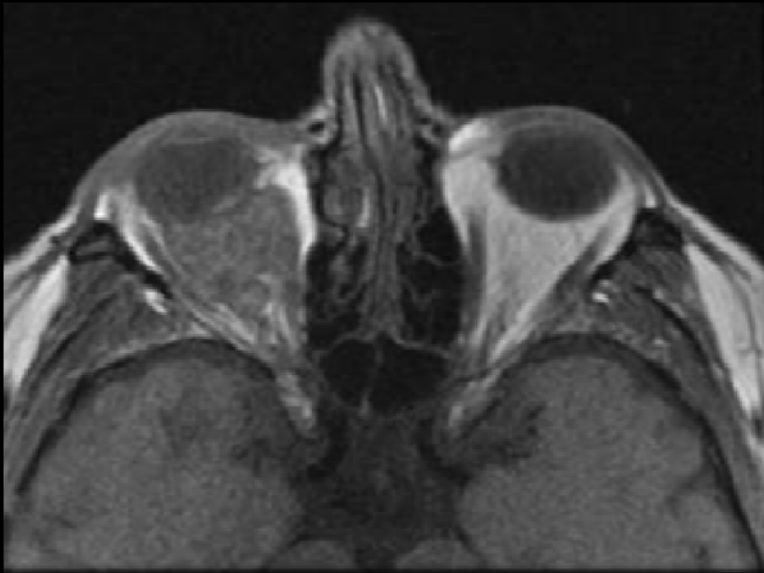
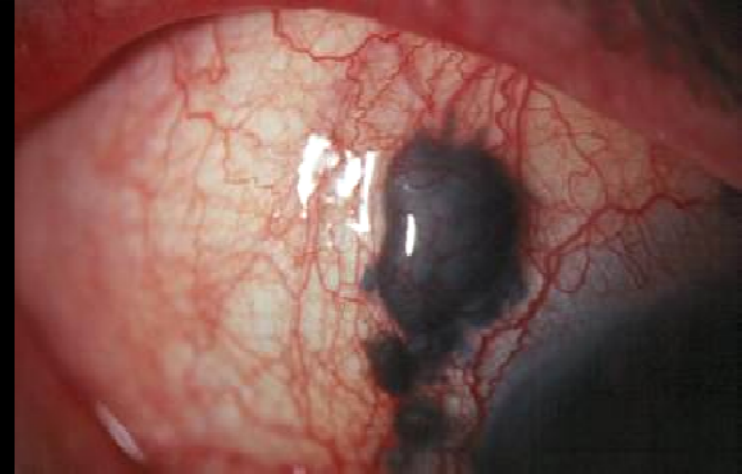
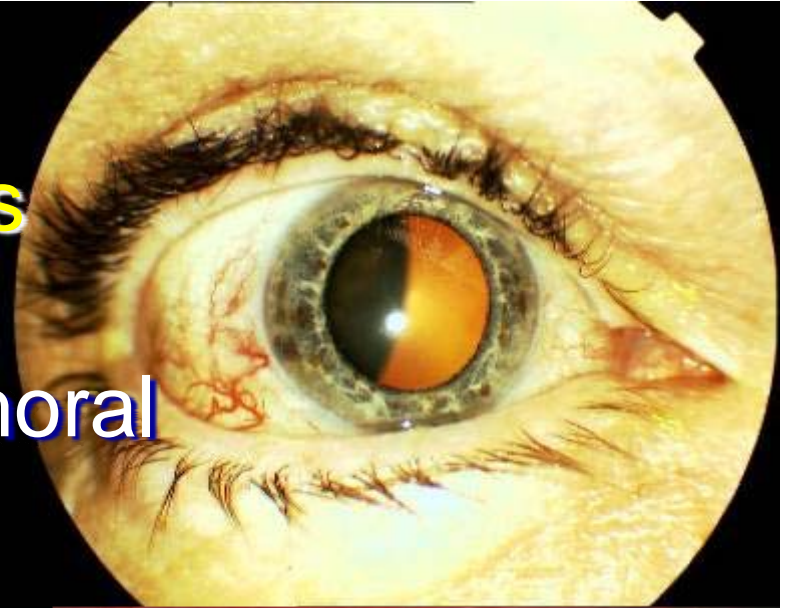




A:	44	39	34	28	21	14	6	2	0
B:	161	102	78	55	38	24	13	2	0
C:	69	30	18	12	8	7	3	0	0

# Melanoma uveal: Factores Pronósticos clínicos

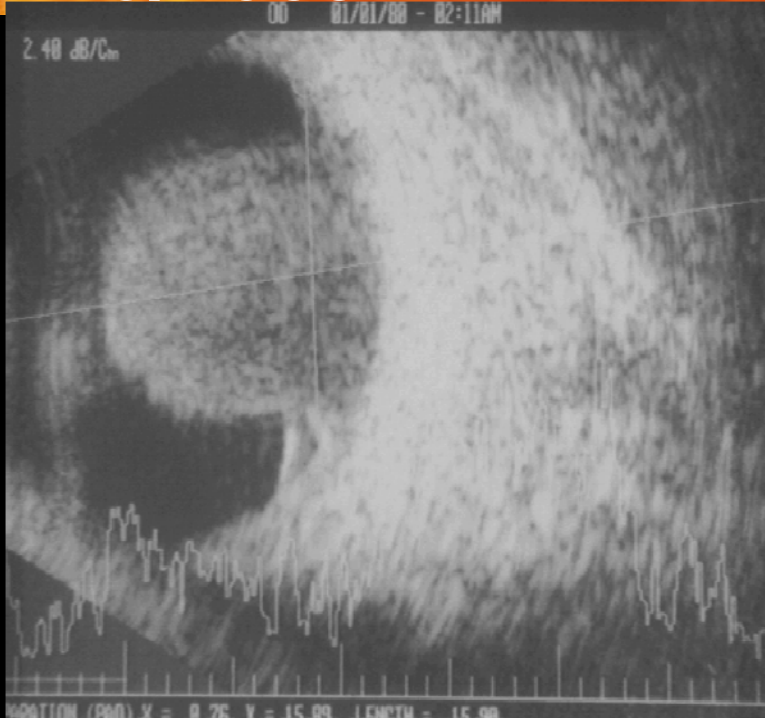
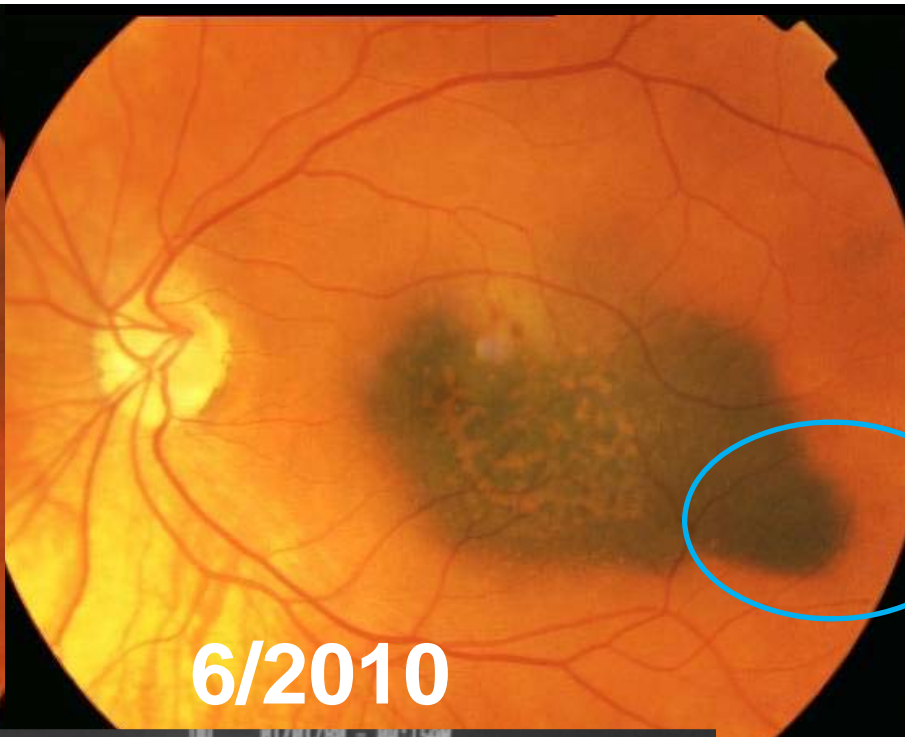
- LTD: mayor diametro tumoral
- Altura
- **Afectacion cuerpo ciliar**
- **Extension extraescleral**





# Melanoma uveal: Factores Pronósticos clínicos

- LTD: mayor diametro tumoral
- Altura
- Afectacion cuerpo ciliar
- Extension extraescleral
- Actividad/crecimiento
- Post-tratamientos conservadores
  - Recurrencias
  - Patron de regresion



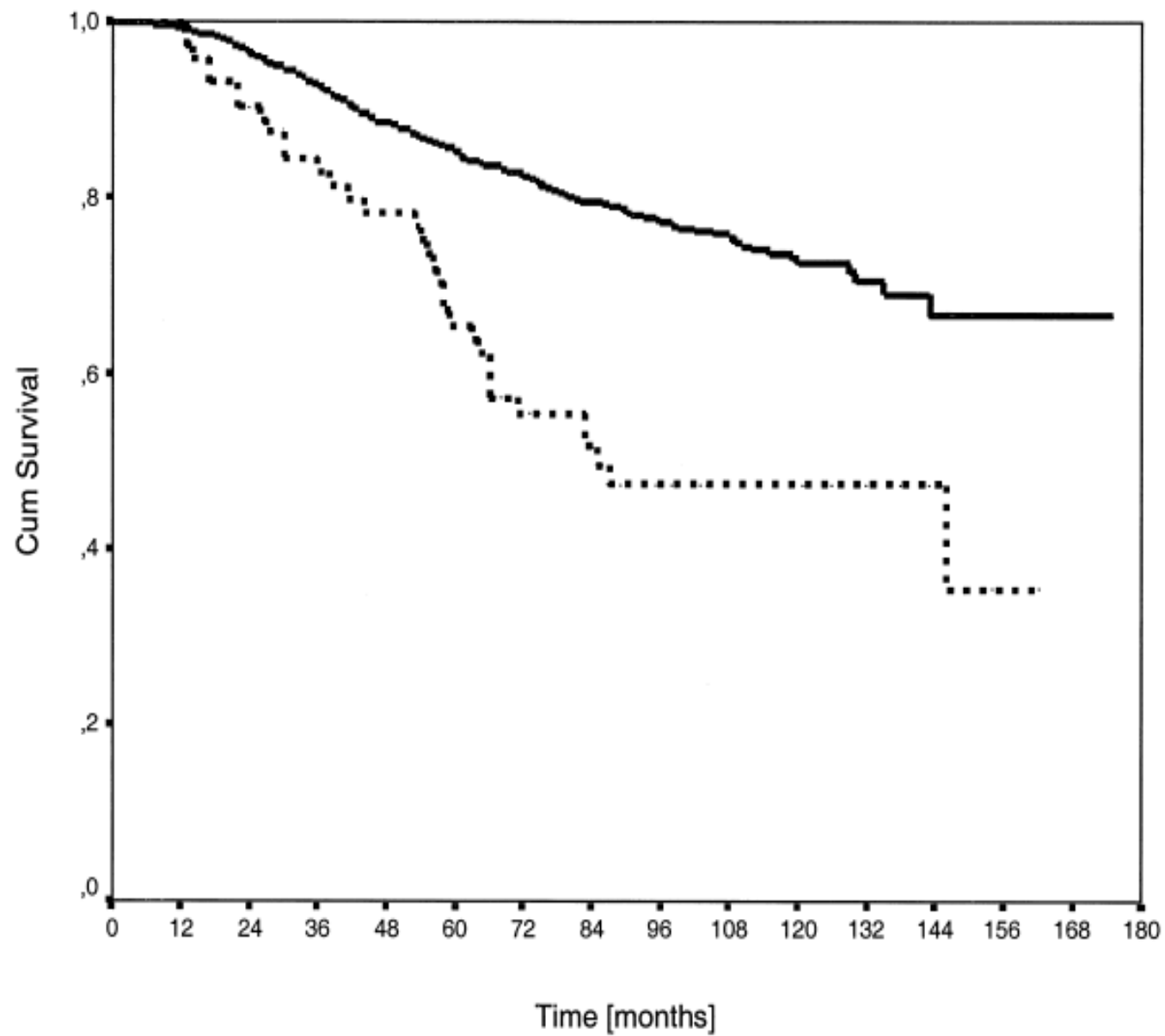
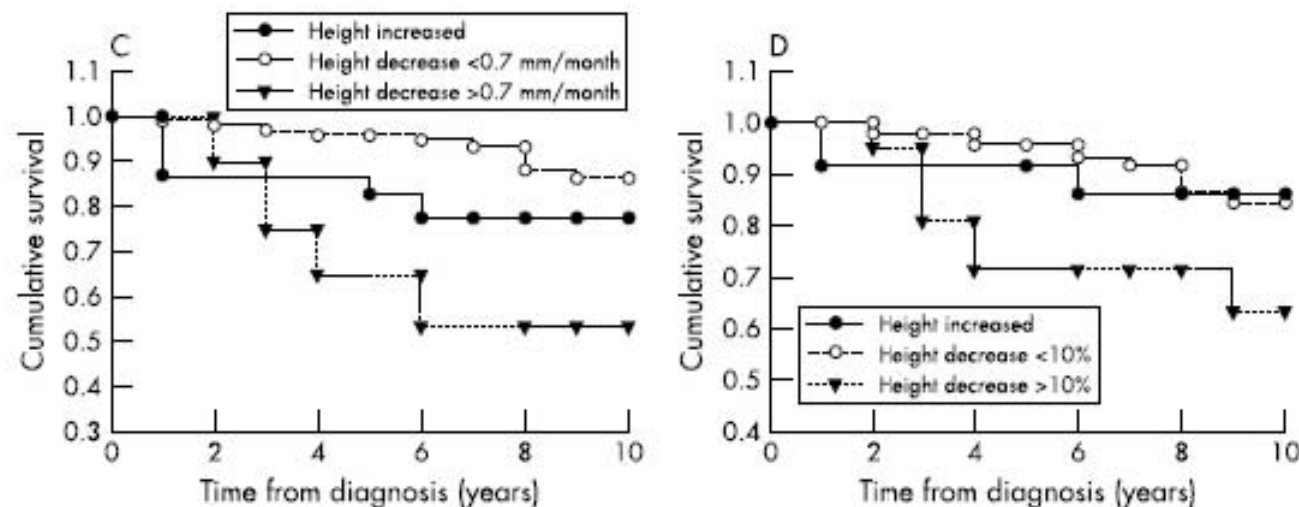


Fig. 5. Survival in function of local tumor control. Solid line = tumors controlled locally, dashed line = recurrent tumors.

# Post-brachytherapy initial tumour regression rate correlates with metastatic spread in posterior uveal melanoma

I Kaiserman, I Anteby, I Chowers, E Z Blumenthal, I Kliers, J Pe'er

*Br J Ophthalmol* 2004;88:892-895. doi: 10.1136/bjo.2003.036285

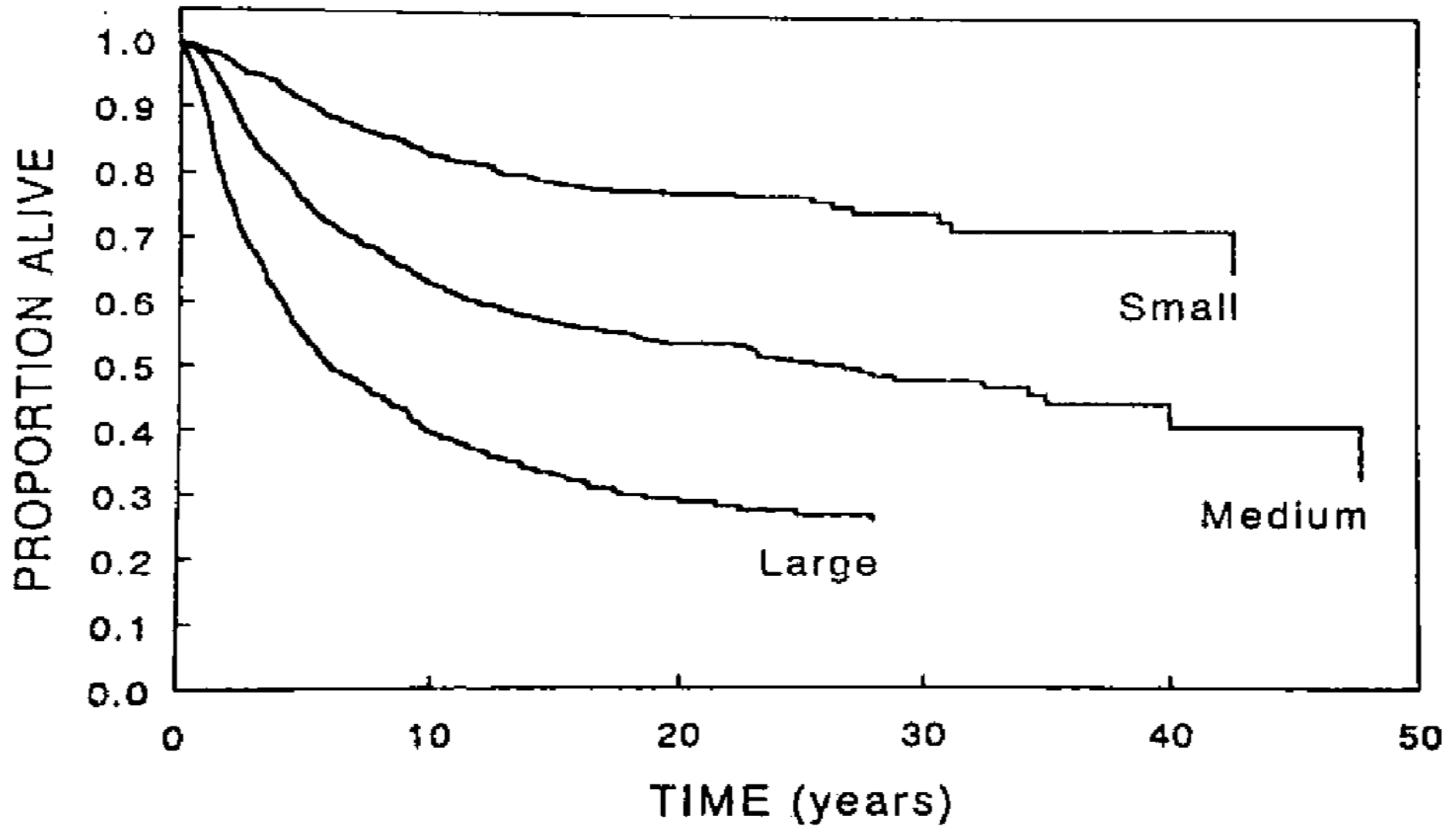


**Figure 2** The Kaplan-Meier survival plot stratified by pre-brachytherapy tumour height (A), reflectivity (B), and initial post-brachytherapy rate of height decrease both in mm (C) and in percentage of the initial height (D). (A)  $p=0.04$ , (B)  $p=0.8$ , (C)  $p=0.02$ , (D)  $p=0.04$ .

# Melanoma uveal: Factores Pronósticos Histopatológicos

- Localización:
  - Cuerpo ciliar
- Tamaño: LTD (AFIP)
  - Pequeño < 10 mm
  - Mediano 11-15 mm
  - Grande > 15 mm



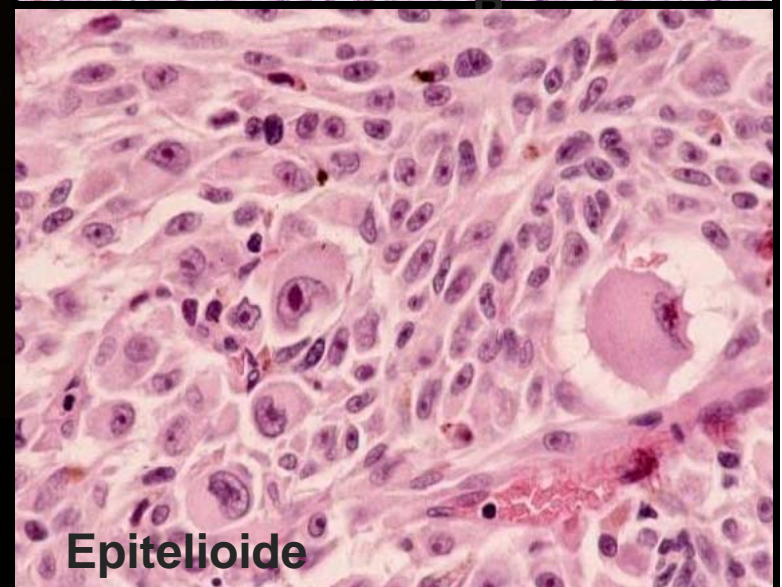
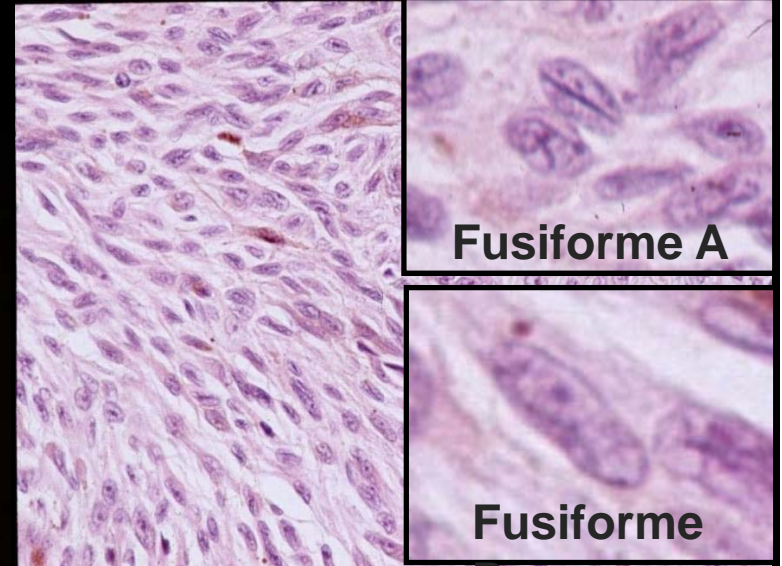
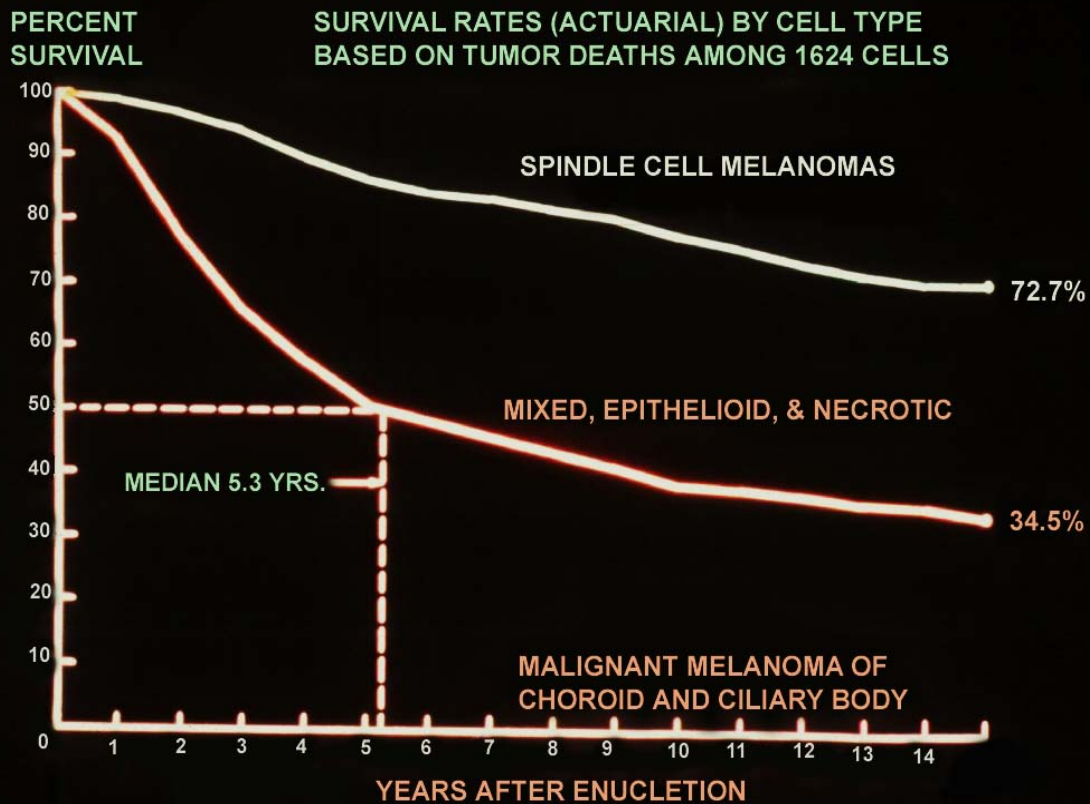


McLean IW, AFIP : 4410 casos

*Ian W McLean. Prognostic Features of uveal Malignant Melanoma*

*Ophthalmology Clinics of North America 1995;8:143*

# Melanoma uveal: Factores Pronósticos Histopatológicos



## Melanoma uveal: Factores Pronósticos Histopatológicos

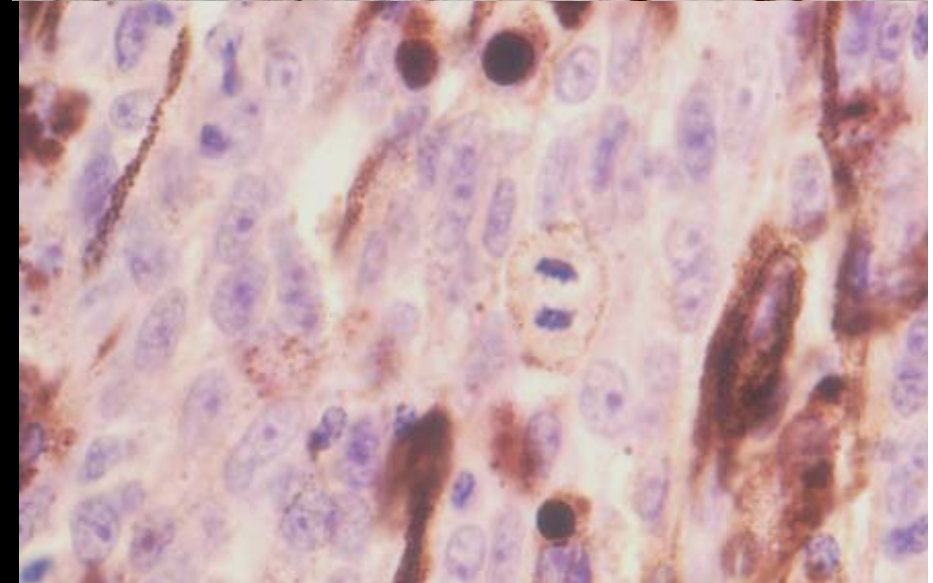
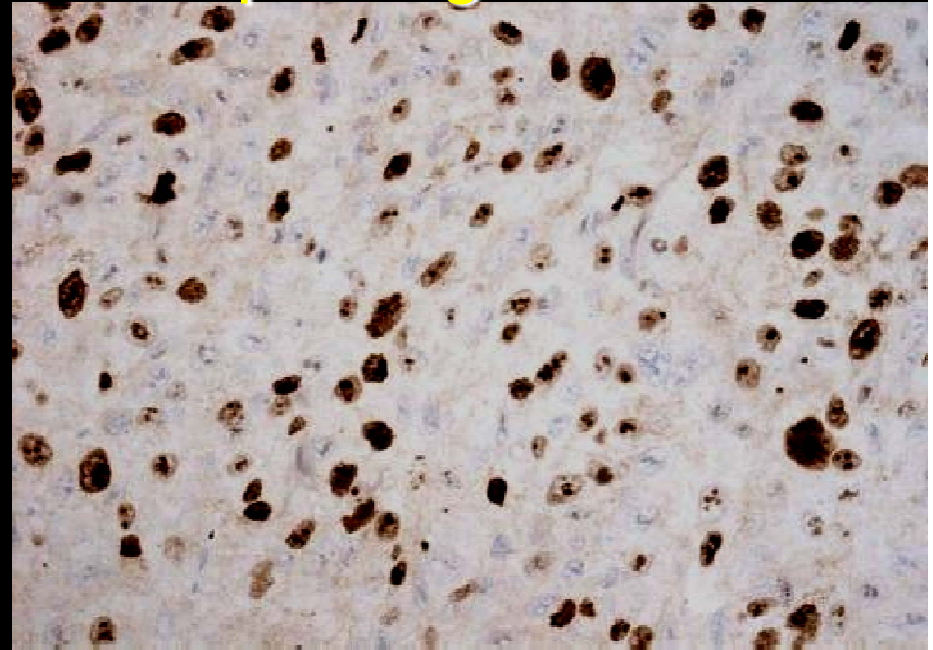
- Localización
- Tamaño: LTD
- Tipo celular
- Extension Extraocular:
  - LINEA DE TRANSECCION Q





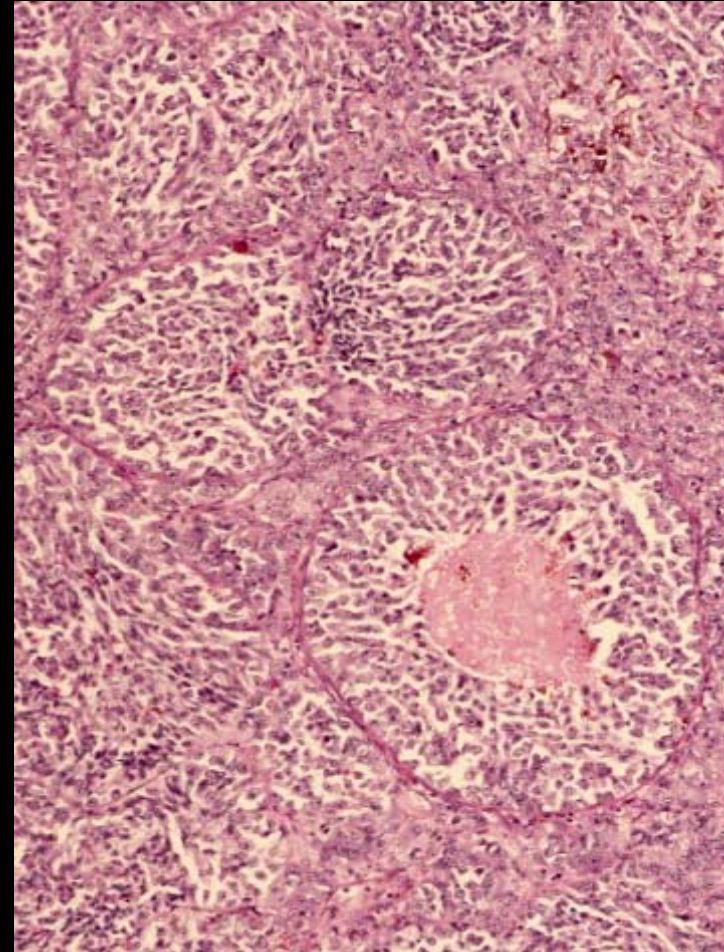
# Melanoma uveal: Factores Pronósticos Histopatológicos

- Localización
- Tamaño: LTD
- Extensión Extraocular
- Proliferación
  - N° mitosis por 40 CGA (x40)
  - Inmunohistoquímica
    - Ki 67/Mib-1
    - PCNA/PC-10



## Melanoma uveal: Factores Pronósticos Histopatológicos

- Localización ciliar
- Tamaño: LTD
- Tipo celular
- Extension Extraocular
- Proliferación
- Patrones vasculares
  - Loops/network



# Melanoma uveal: Factores Pronósticos Citogenéticos

- Anomalías Cromosómicas (FISH)
  - Monosomy 3, polisomy 8

DERS

Ophthalmol Clin N Am 18 (2005) 85–97

## Uveal Melanoma: Genetic Aspects

Arun D. Singh, MD<sup>a,\*</sup>, Bertil Damato, MD, PhD, FRCOphth<sup>b</sup>,  
Peter Howard, MSc, CIBiol<sup>c</sup>, J. William Harbour, MD<sup>d</sup>

### UVEAL MELANOMA: GENETIC ASPECTS

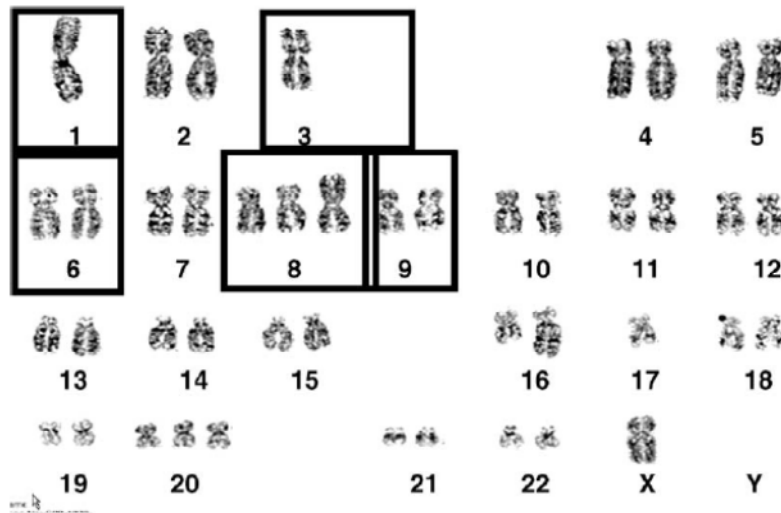
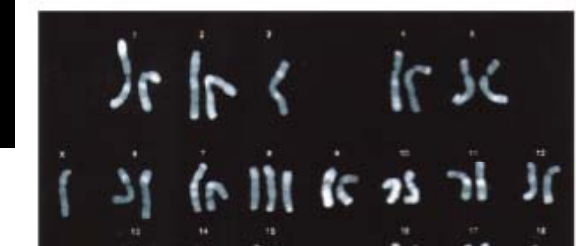


Fig. 1. Karyotype of a uveal melanoma. The boxes indicate the chromosomes most commonly found to be abnormal. The karyotype shows loss of chromosomes 3 and 1. There is also trisomy 8, with one chromosome showing an isochromosome 8q. This result indicates a poor prognosis for survival.



Vol. 8, 554–559, February 2002

Clinical Cancer Research

89

### Detection of Genetic Prognostic Markers in Uveal Melanoma Biopsies Using Fluorescence *in Situ* Hybridization

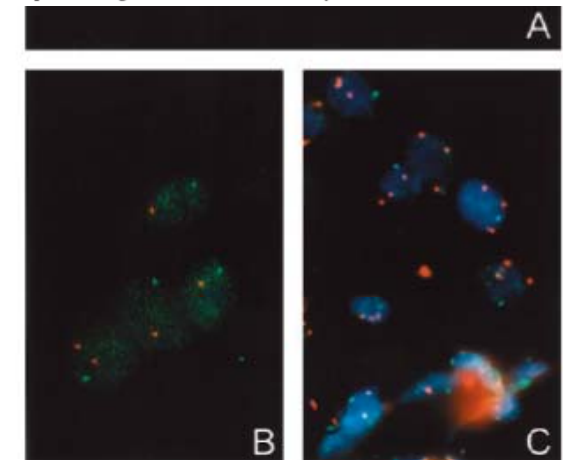


Fig. 2. A, karyotype of patient EOM-121: 47 XY,del(1)(p31p36),-3,der(4)t(1;4)(q12;q21),+8,+21. B, nuclei isolated from short-term culture of the tumor specimen hybridized with chromosome 3q24 (green) and 1p36 (red) probes. C, nuclei isolated from FNABs hybridized with probes for centromere 3 (green) and centromere 8 (red).

# BIOLOGIA MOLECULAR: Perfil expresion global de genes

- Chip Microarray: analisis simultaneo de miles de genes
- Perfiles de genes asociados a melanomas con mayor valor pronostico que características histopatologicas y citogeneticas
  - Clase I: bajo grado
  - Clase II: alto grado, correlacion con monosomia 3

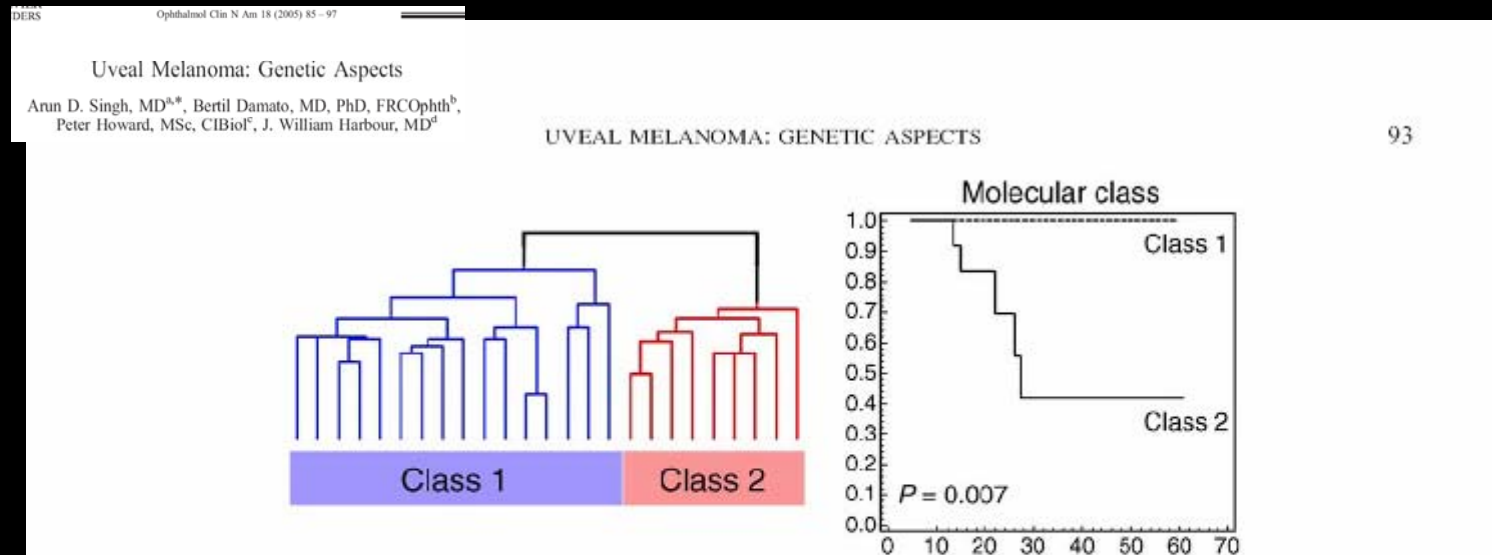
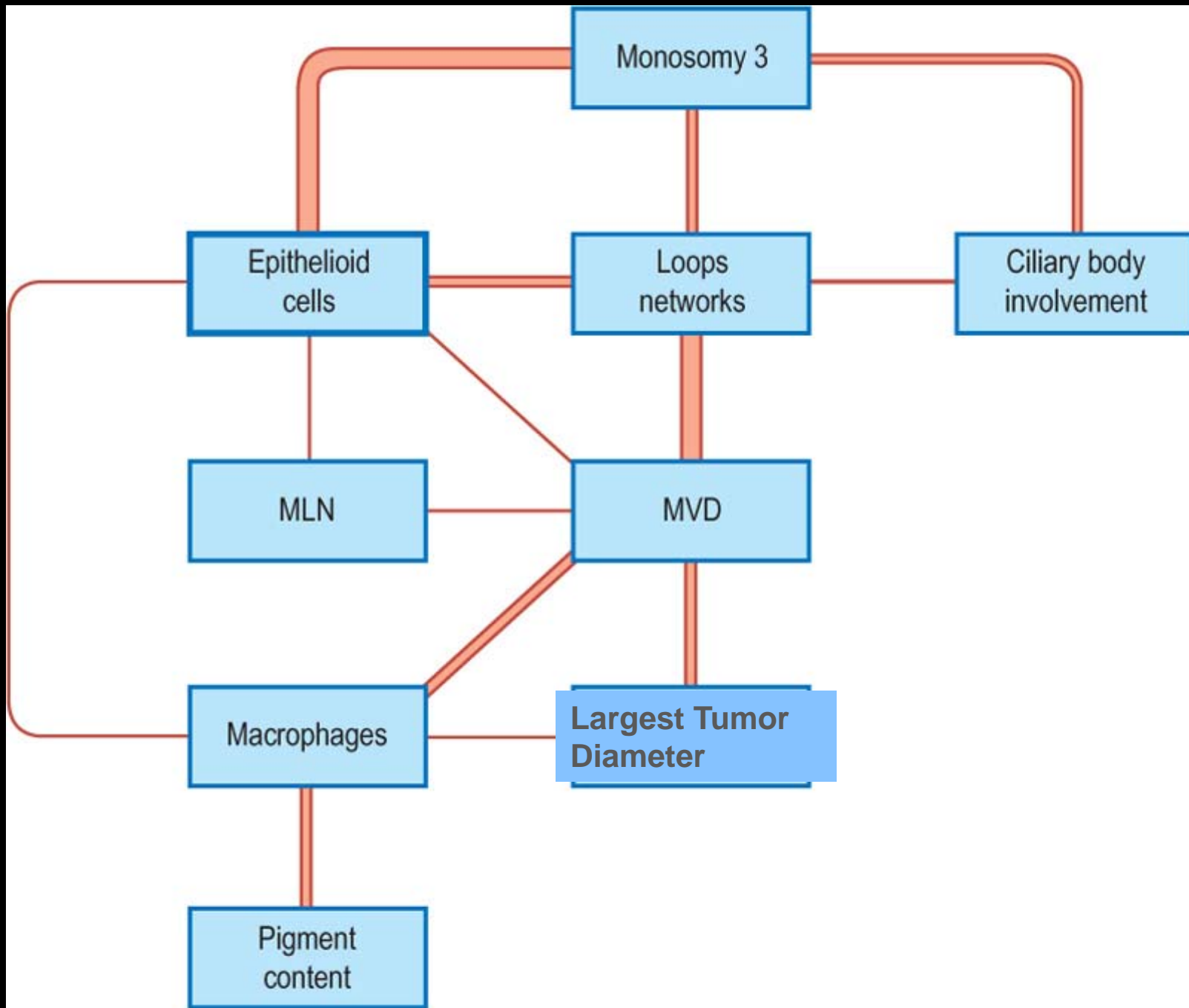


Fig. 4. Left panel, unsupervised hierarchical cluster analysis of gene expression microarray data from 25 primary uveal melanomas showing the natural segregation of tumors into two groups, class 1 and class 2. Right panel, Kaplan-Meier survival analysis showing no deaths among class 1 patients and five metastatic deaths among class 2 patients. This difference in survival was highly significant.



# ¿COMO IDENTIFICAR AL PACIENTE CON RIESGO DE METASTASIS?

- FACTORES PRONOSTICOS
  - CLINICOS
  - HISTOLOGICOS
  - CITOGENETICA : Monosomia 3/Trisomia 8
  - BIOLOGIA MOLECULAR: Clase I y II
- ¿Cual son los factores que influyen en el tiempo de desarrollo de la enfermedad sistémica?

# Circulating uveal melanoma cells: should we test for them?

*Can J Ophthalmol* 2008;43:155–8  
doi:10.3129/i08-011

*Bruno F. Fernandes, MD, PhD;  
Rubens N. Belfort, MD; Sebastian Di Cesare, MSc;  
Miguel N. Burnier Jr., MD, PhD, FRCSC  
McGill University Health Center &  
Henry C. Witelson Ocular Pathology Laboratory  
Montréal, Qué.*

J Clin Oncol. 2011 Oct 24. [Epub ahead of print]

## **Uveal Melanoma and BRCA1/BRCA2 Genes: A Relationship That Needs Further Investigation.**

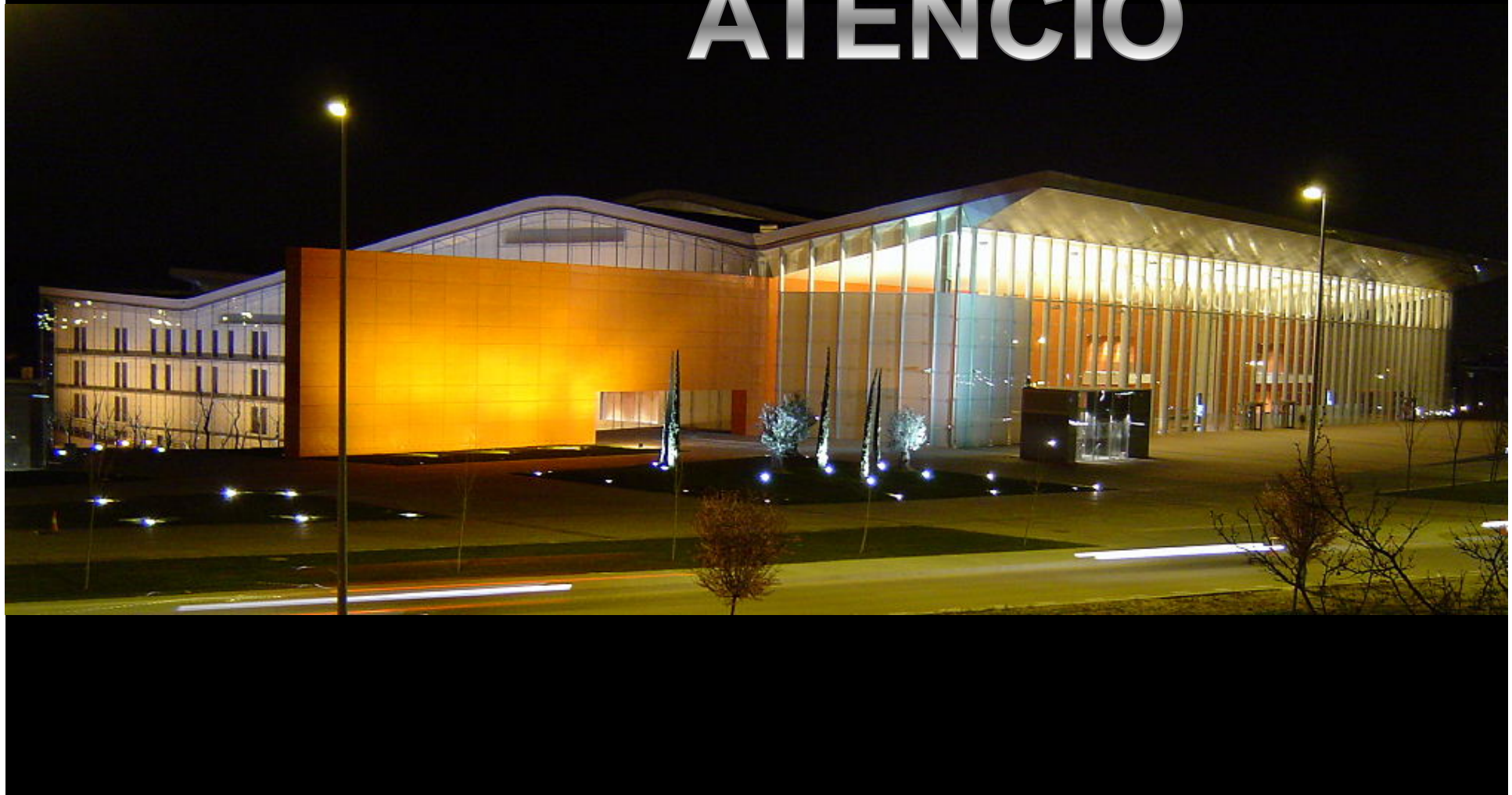
Cruz C, Teule A, Caminal JM, Blanco I, Piulats JM.

Institut Català d'Oncologia, L'Hospitalet de Llobregat, Barcelona, Spain.



# MOLTES GRÀCIES PER LA SEVA ATENCIÓ

AUDITORIO  
DE VALLADOLID



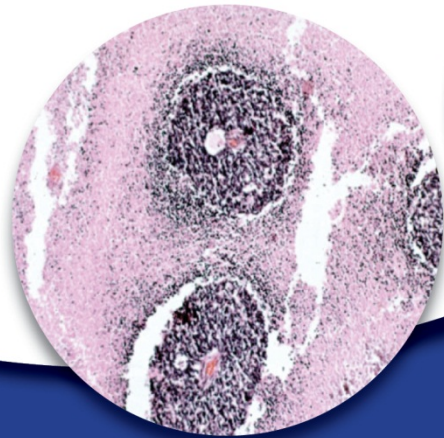
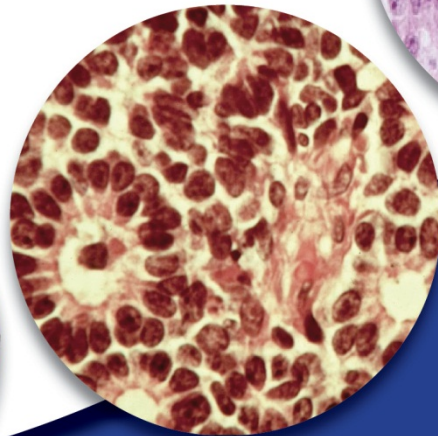
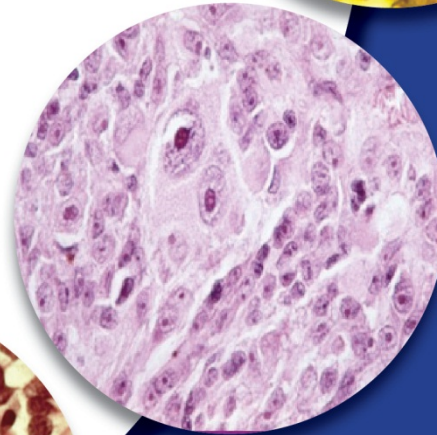
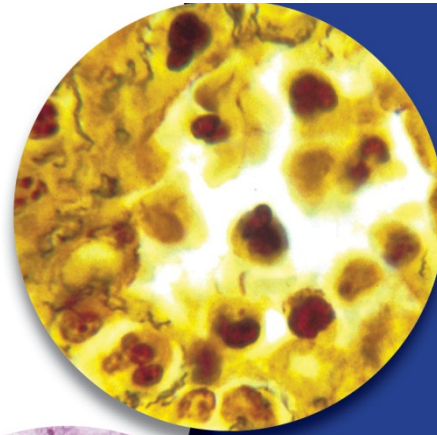


# BIOPSY

Valladolid - Spain

May, 18-19

2012



**Burnier  
International  
Ophthalmic  
Pathology  
Society**

More info: [dimeydiras@dimeydiras.com](mailto:dimeydiras@dimeydiras.com)

