



AZIENDA SANITARIA PROVINCIALE DI  
AGRIGENTO  
PRESIDIO OSPEDALIERO S.GIOVANNI DI DIO  
U.O.C. DI OCULISTICA  
DIRETTORE: DR. E. CRISCIMANNA



# La terapia anti-VEGF intravitreale e gli anticoagulanti

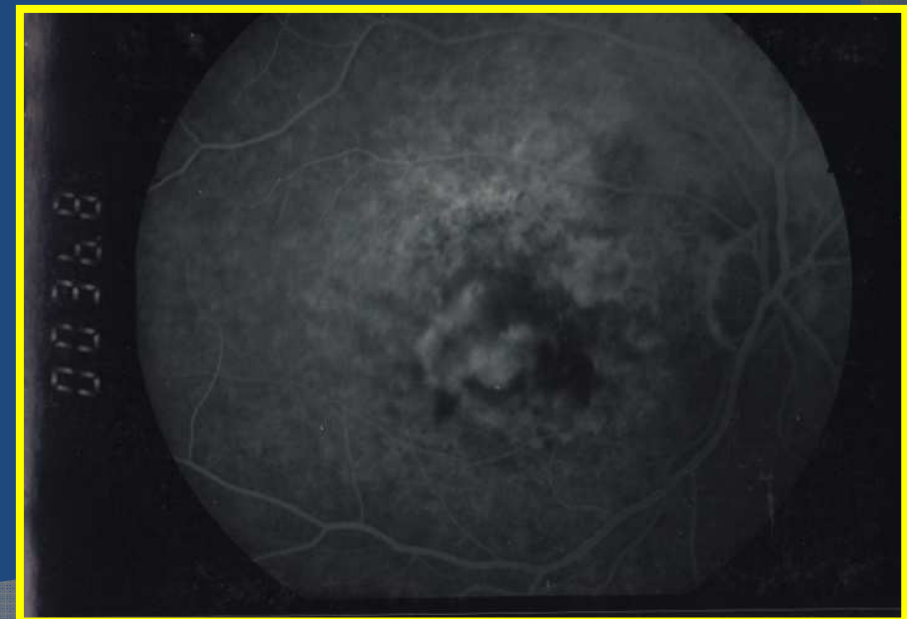
S. Cipolla  
L. Capostagno  
R. Falsone  
A. Ferrante  
G. Gallo Afflitto  
E. Criscimanna



# Caso clinico

- ◎ Donna
- ◎ 77 anni
- ◎ Ipertensione arteriosa, dislipidemia, fibrillazione atriale
- ◎ Coumadin (warfarin sodico)
- ◎ OD DMLE con MNV, nel 2007 intravitreale di bevacizumab
- ◎ OS DMLE secca
- ◎ Ottobre del 2010 OD riattivazione di MNV, 2 I.V. bevacizumab

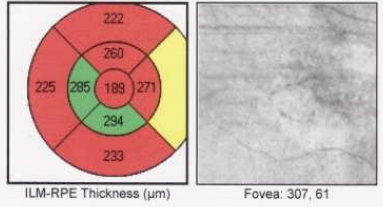
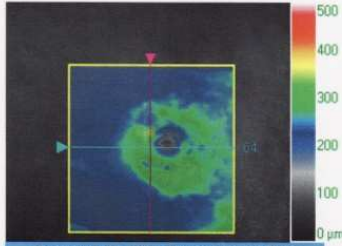
Dicembre 2010  
OD Vn 1/50 n.m.



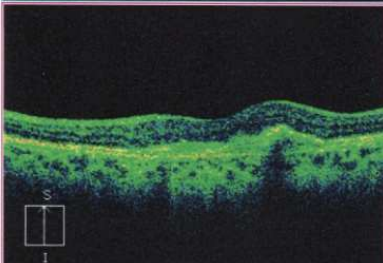
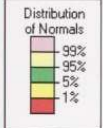
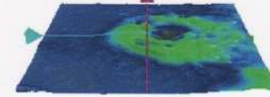
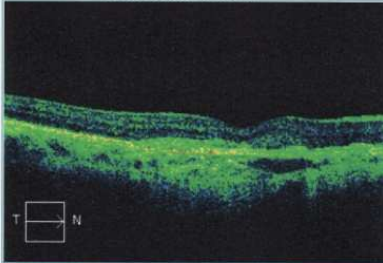
ID: CZMI1034457209      Exam Date: 16.12.2010      Osp. S. Giovanni Di Dio  
 DOB: 16.02.1933      Exam Time: 11:08  
 Gender: Female      Technician: Operator, Cirrus  
 Doctor:      Signal Strength: 6/10

**Macula Thickness : Macular Cube 512x128**

OD  OS



Overlay: ILM - RPE Transparency: 50 %  
 High-definition mode



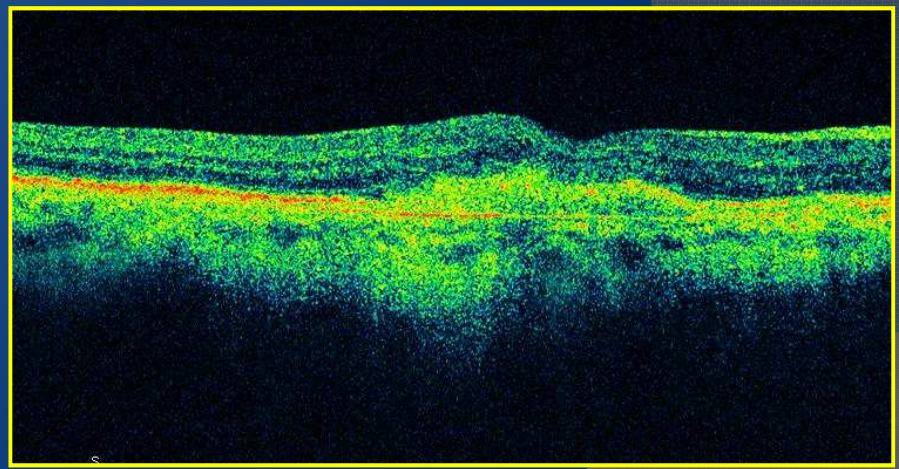
	Central Subfield Thickness (μm)	Cube Volume (mm <sup>3</sup> )	Cube Average Thickness (μm)
ILM - RPE	189	8,5	235

Comments

Doctor's Signature

SW Ver: 4.5.1.11  
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 Page 1 of 1

OD



# OS Vc 4/10



ID: CZMI1034457209 Exam Date: 16.12.2010 Osp. S. Giovanni Di Dio  
DOB: 16.02.1933 Exam Time: 11:10  
Gender: Female Technician: Operator, Cirrus  
Doctor: Signal Strength: 6/10

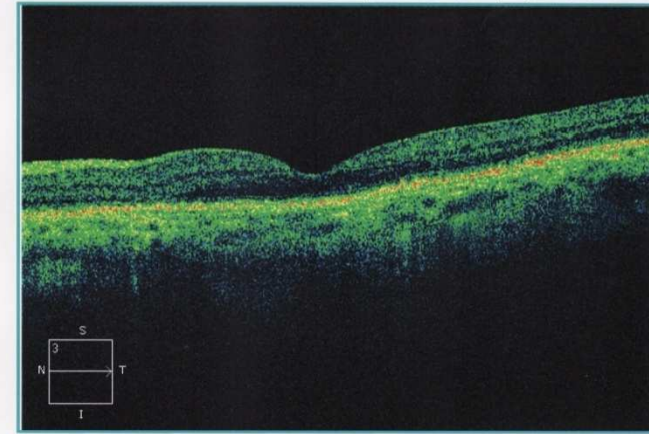
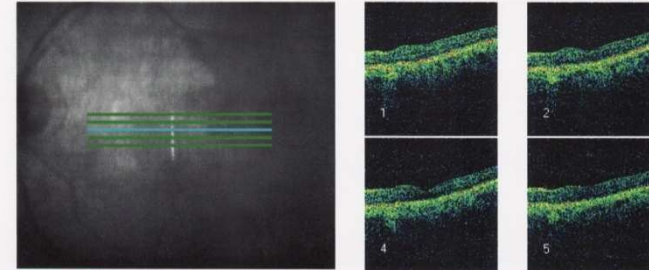
## High Definition Images: 5 Line Raster

OD  OS

Scan Angle: 0°

Spacing: 0,25 mm

Length: 6 mm



Comments

Doctor's Signature

SW Ver: 4.5.1.11  
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Page 1 of 1

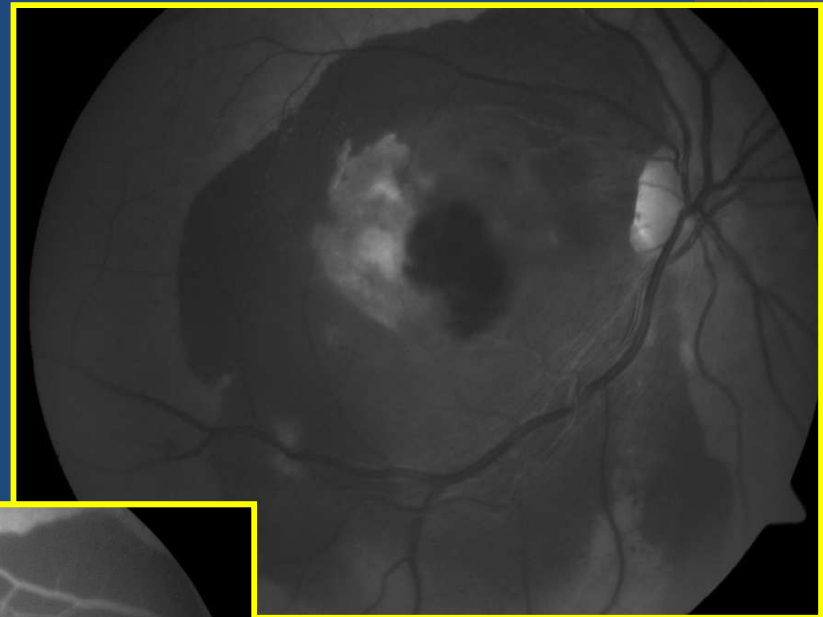
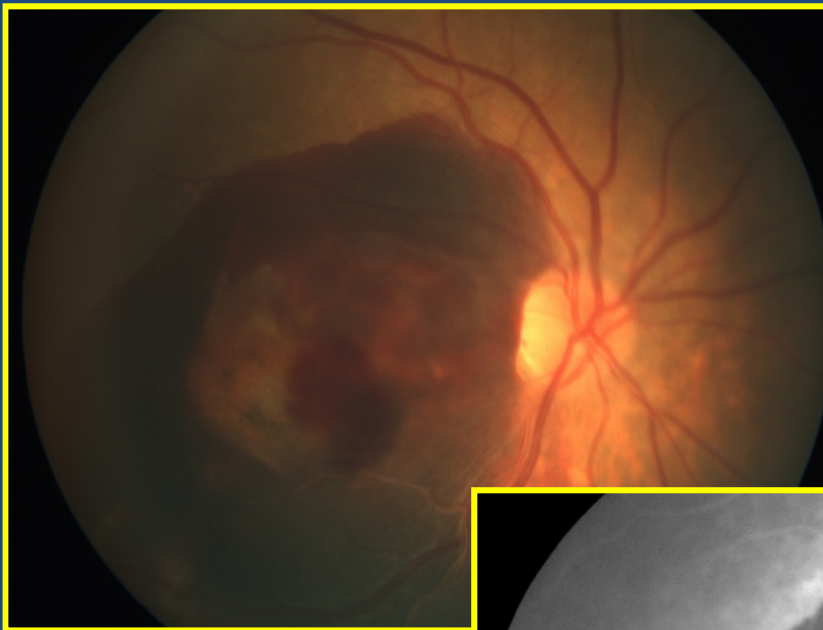
Gennaio 2011

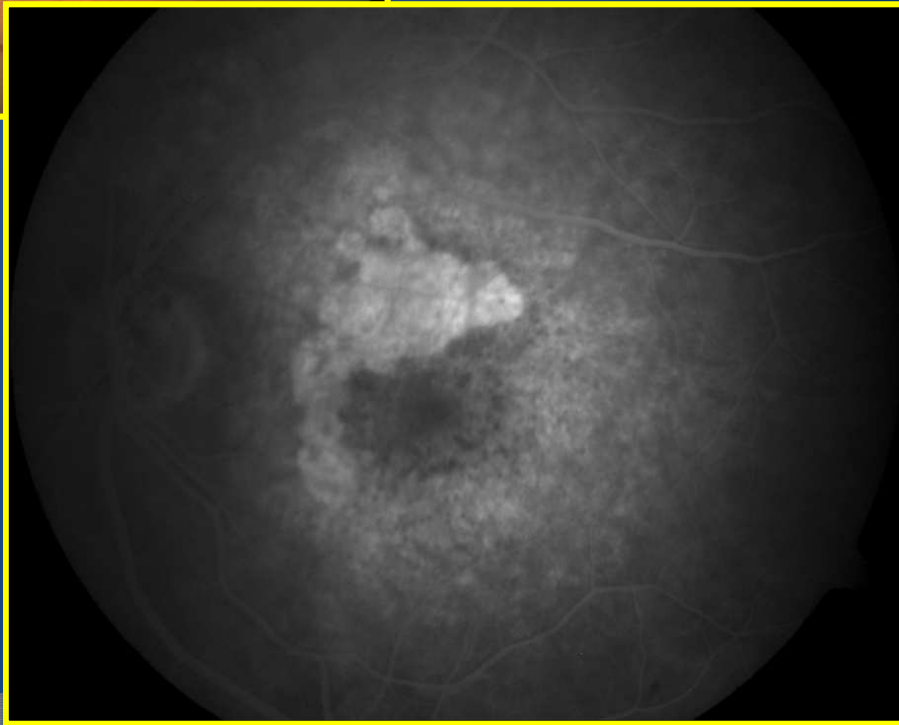
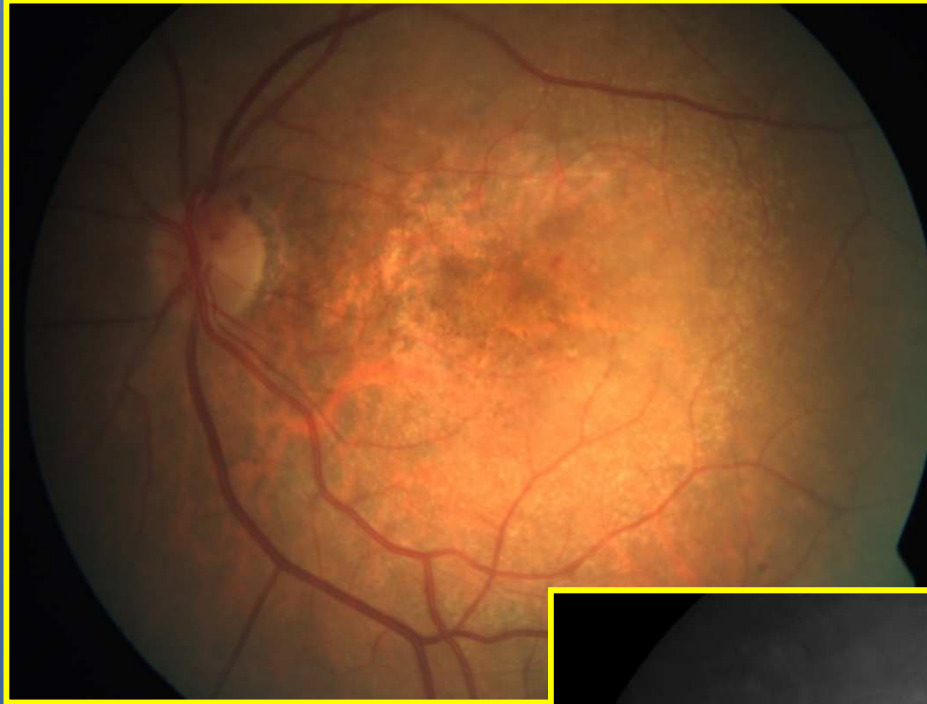
OD iniezione intravitreale di  
Ranibizumab

Sostituzione del coumadin con  
Calciparina 0.2 ml

A 20 giorni: Ulteriore calo del visus → 1/100

Scotoma centrale





OS



Retina. 2010 Oct;30(9):1386-9.

## Incidence of hemorrhagic complications after intravitreal bevacizumab (avastin) or ranibizumab (lucentis) injections systemically anticoagulated patients.

Mason JO 3rd, Frederick PA, Neimkin MG, White MF Jr, Feist RM, Thomley ML, Albert MA Jr.

Retina Consultants of Alabama, Callahan Eye Foundation Hospital, Birmingham, Alabama 35233, USA.  
retinarounds@mac.com

### Abstract

**PURPOSE:** To assess the risk of hemorrhagic complications when performing intravitreal injections on systemically anticoagulated patients.

**METHODS:** A single-center retrospective case series of 520 consecutive patients (675 eyes) receiving 3,106 endothelial growth factor injections. Patients on the systemic anticoagulants Coumadin (warfarin sodium) or Plavix (clopidogrel bisulfate) were identified, as well as patients on aspirin. Demographic parameters were recorded relevant anticoagulant medications, preoperative/postoperative best-corrected visual acuities and intraocular previous ocular surgery, relative ocular diagnoses, and injection complications.

**RESULTS:** Of all patients, 104 were on Coumadin (134 eyes; 548 injections), 90 were on Plavix (123 eyes; 548 injections), 7 were on both Coumadin and Plavix (8 eyes; 33 injections), and 319 were not anticoagulated (402 injections). Also, 1,254 injections were on patients taking aspirin. There were no hemorrhagic complications (choroidal hemorrhage, vitreous hemorrhage, or increased submacular hemorrhage) noted in the Plavix ( $P = 1.0000$ ; 95% confidence interval = 0.0000-0.0088), Coumadin ( $P = 1.0000$ ; 95% confidence interval = 0.0000-0.0084) or aspirin ( $P = 1.0000$ ; 95% confidence interval = 0.0000-0.0037) groups.

**CONCLUSION:** The risk of hemorrhagic complications in systemically anticoagulated patients receiving intravitreal injections is extremely low. Because of the demonstrated thromboembolic risk of stopping anticoagulant therapy, we recommend that patients continue their current regimen without cessation.

Klin Monbl Augenheilkd. 2010 Apr;227(4):289-91. Epub 2010 Apr 20.

## Hemorrhagic complications after intravitreal injections of ranibizumab in patients under coumarin-type anticoagulation

Loukopoulos V, Meier C, Gerding H.

Abteilung für Retinologie, Klinik Pallas, Olten, Switzerland.

### Abstract

**BACKGROUND:** It was the aim of this retrospective study to evaluate the risk of extra- or intraocular hemorrhage associated with intravitreal injections of ranibizumab in patients receiving anticoagulation therapy with coumarin derivatives.

**PATIENTS AND METHODS:** 149 injections were performed in 50 patients who had preoperatively been instructed to continue their normal anticoagulation dose scheme. The coagulation status (Quick's time and/or INR) was checked the day before or on the day of injection. Clinical examinations including anterior and posterior segment biomicroscopy were performed in all patients within 24 hours before and 1 day, 1 week and 1 month after injection.

**RESULTS:** The average Quick value at the time of injection was 27 % +/- 15 % (median: 22 %, 95 % confidence interval: 24.6 - 29.3 %, range: 6 - 95 %), the average INR 2.32 +/- 0.79 (median: 2.2, 95 % confidence interval: 2.17 - 2.47, range: 0.8 - 4.9). Minor subconjunctival hemorrhages were observed in 26 of 149 injections (17.4 %). New intraocular hemorrhages or other coagulation-related complications associated to the injection therapy were not observed.

**CONCLUSIONS:** Our study suggests that there is a low risk of coagulation-related complications in patients undergoing intravitreal injections of ranibizumab even if the use of coumarin derivatives is continued within the normal therapeutic range.

## Submacular haemorrhage after intravitreal bevacizumab compared with intravitreal ranibizumab in large occult choroidal neovascularization.

Krishnan R, Goverdhan S, Lochhead J.

Ophthalmology Department, St Mary's Hospital, Newport, Isle of Wight, PO30 5TG, UK. radhikrishnan2004@yahoo.co.uk

### Abstract

**BACKGROUND:** Submacular haemorrhage may occur following intravitreal bevacizumab injection for large occult choroidal neovascularization (CNV) in age-related macular degeneration (AMD). We report the occurrence of submacular haemorrhage following intravitreal ranibizumab compared with intravitreal bevacizumab for large occult CNV in AMD.

**METHODS:** Retrospective, comparative evaluation of two interventional case series. Evaluation of consecutive patients with occult CNV  $>$  or  $=$  15 mm<sup>2</sup> treated with intravitreal bevacizumab (n = 14) and intravitreal ranibizumab (n = 22) over a 2-year period within a single institution. Postoperative submacular haemorrhage, Early Treatment Diabetic Retinopathy Study-derived visual acuity, preoperative blood pressure and anticoagulant use were noted. The two groups were compared using Fisher's exact test.

**RESULTS:** The mean surface area of occult CNV at presentation was 20.9  $\pm$  5.4 mm<sup>2</sup> in the bevacizumab group and 24.0  $\pm$  11.0 mm<sup>2</sup> in the ranibizumab group. Fresh submacular haemorrhage was seen in 4 out of 14 patients following bevacizumab compared with 0 out of 22 patients following ranibizumab (P = 0.017, odds ratio = 19.29). Mean preoperative blood pressures were very similar between the groups. 28.6% of patients in the bevacizumab group were on oral anticoagulants compared with 31.8% in the ranibizumab group. None of the patients who developed postoperative haemorrhage were on anticoagulants.

**CONCLUSIONS:** Acute submacular haemorrhages appear to be a significant adverse event following intravitreal bevacizumab in occult CNV  $>$  or  $=$  15 mm<sup>2</sup>. Intravitreal ranibizumab appears to have a significantly lower incidence of postoperative submacular haemorrhage in occult CNV  $>$  or  $=$  15 mm<sup>2</sup>. Larger studies are required to identify the most appropriate agent for the treatment of large occult CNV.

# Profilo coagulativo

17.1.2011: INR 2,1 (iniezione intravitreale)

08.02.2011: INR 2,7 (calo del visus)

INR: rapporto internazionale normalizzato

3.3.2011

## II iniezione intravitreale di Ranibizumab

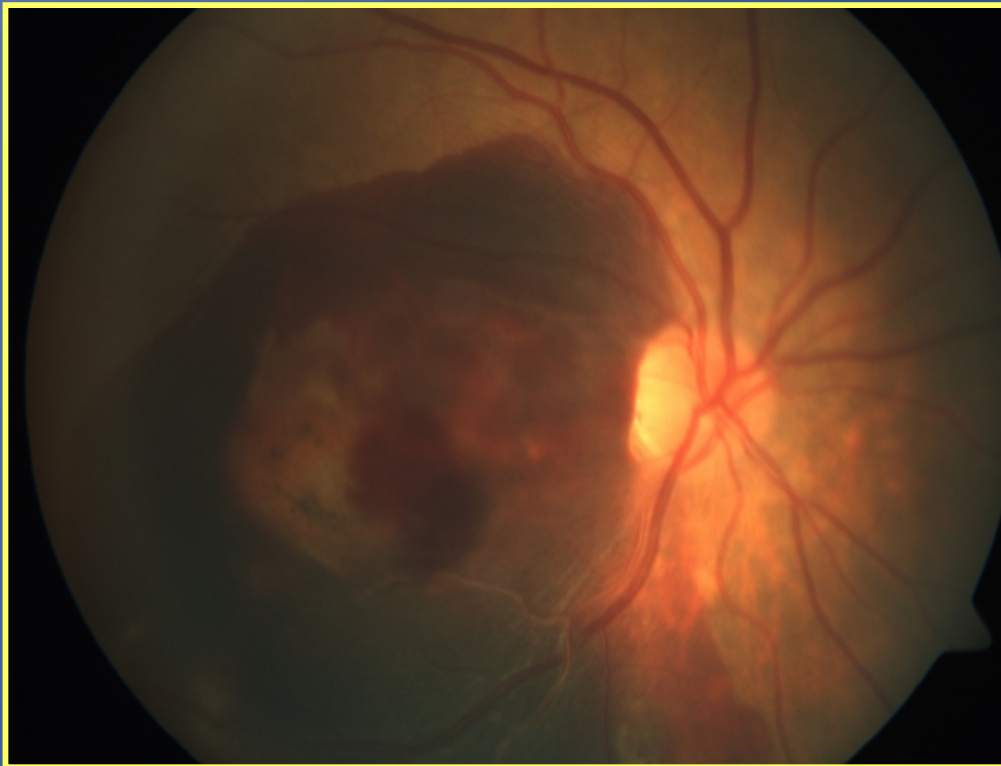
del 01/03/2011

### *TESTS COAGULATIVI*

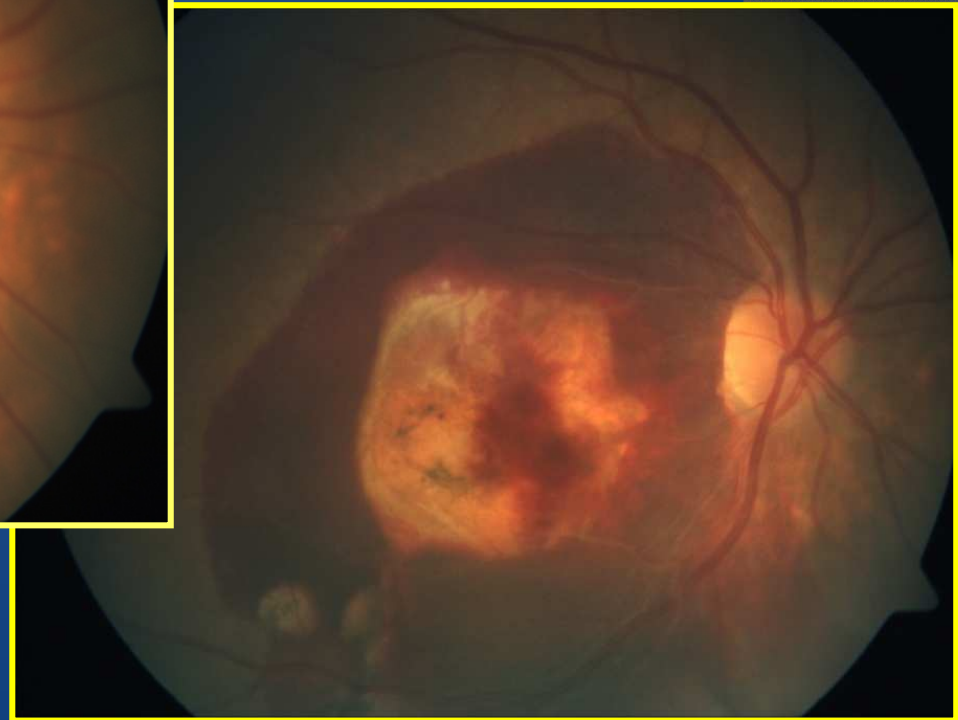
Tempo di protrombina	<b>19.4</b>	sec
Attività protrombinica	<b>58.46</b>	%
+ I. N. R.	<b>1.73</b>	

A 10 giorni  
riduzione dello scotoma

Vn 1/50

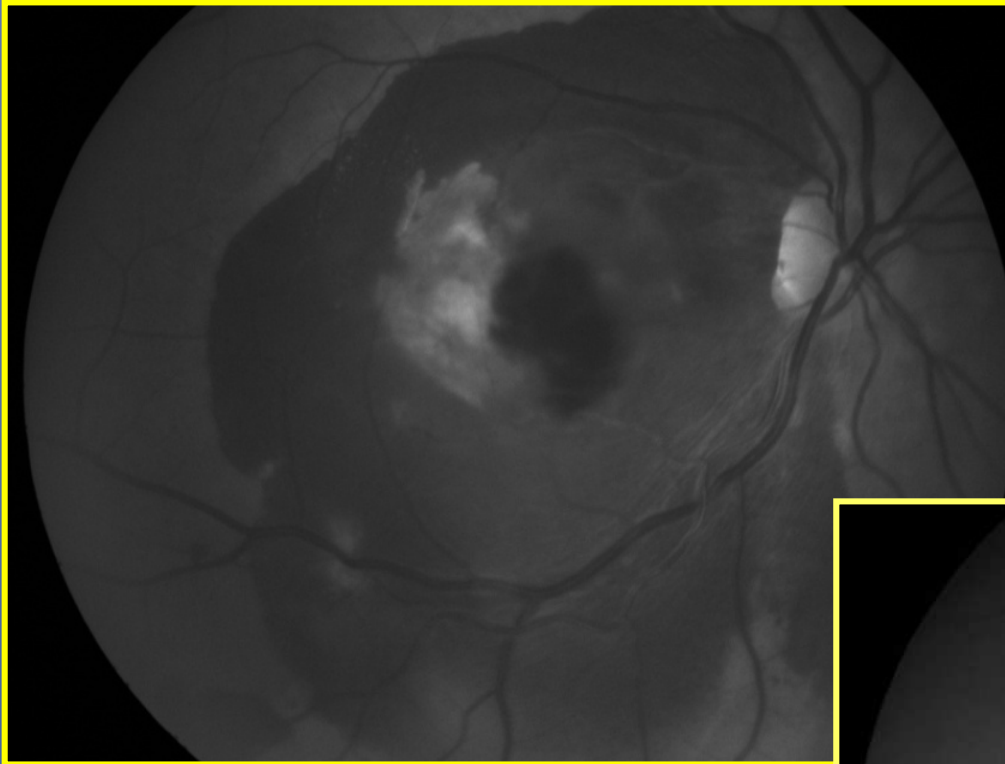


pre

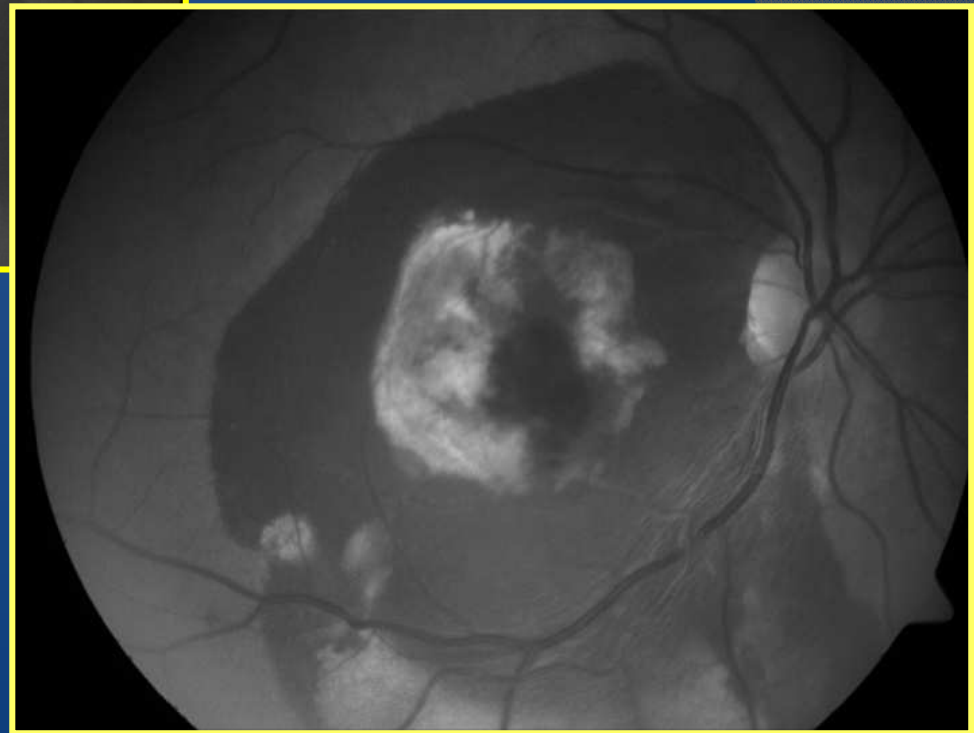


post

**A 10 GIORNI**

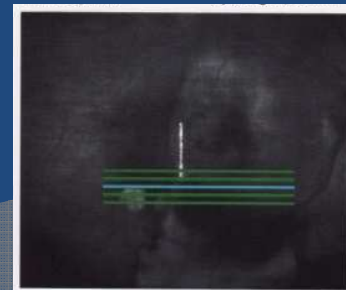
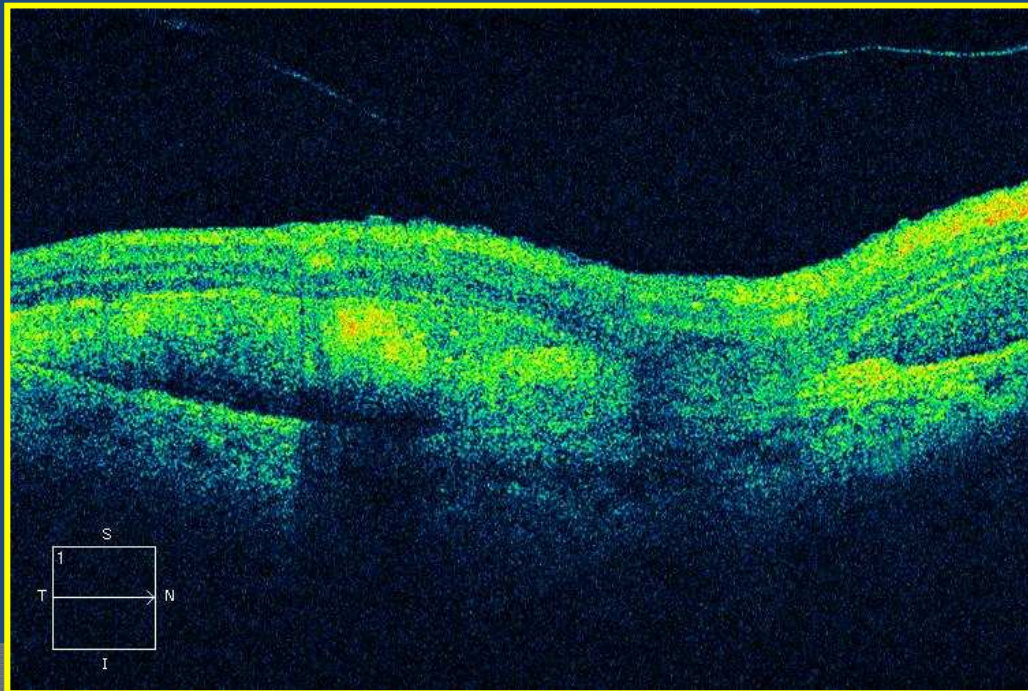
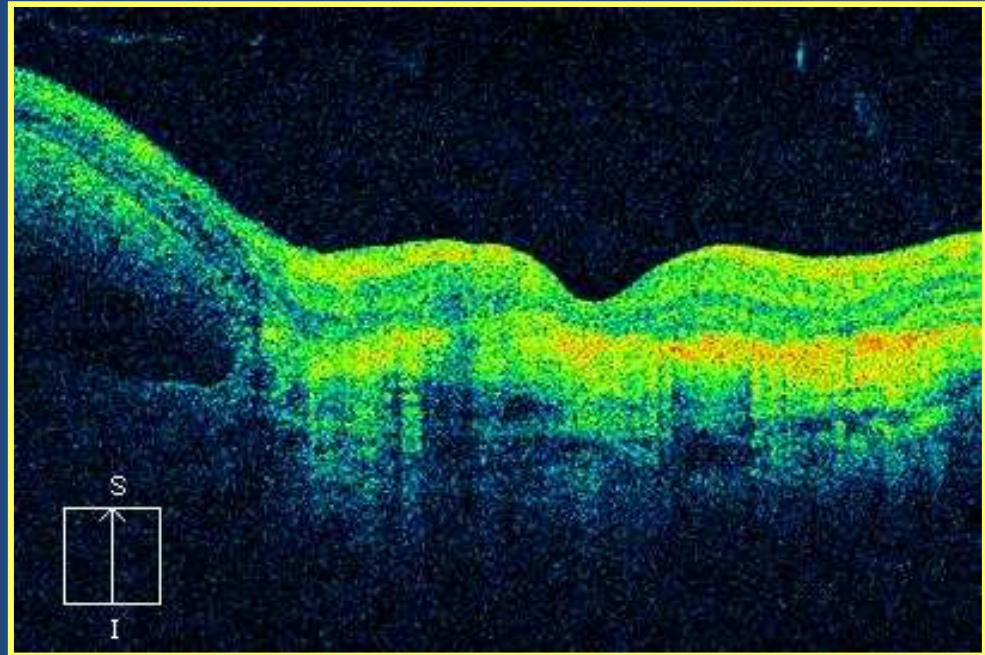


**Pre**



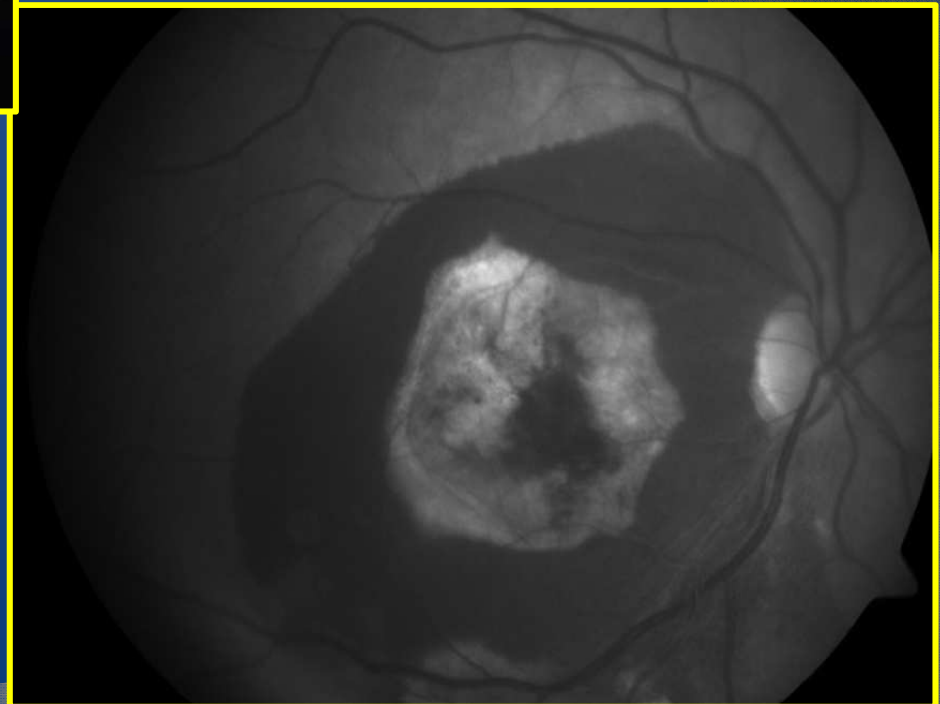
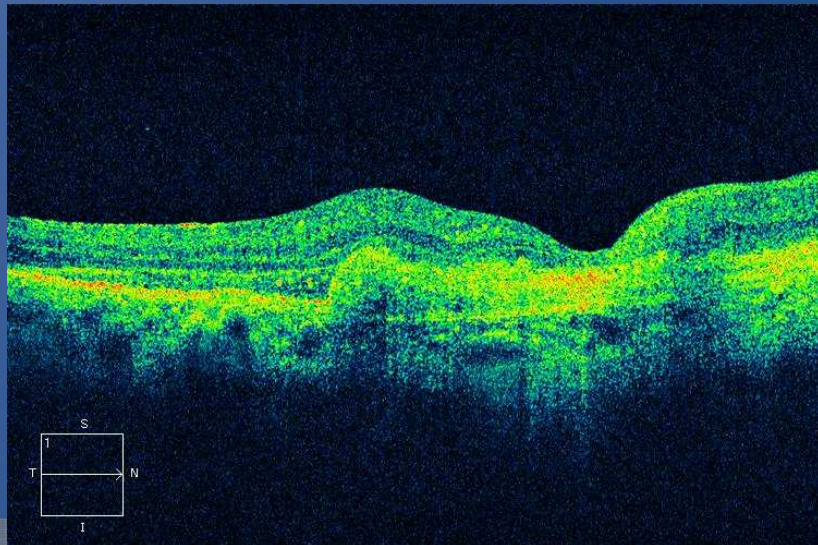
**Post**

A 10 giorni





**A 30 GIORNI**  
**VN 1/20 nm**



6.4.2011

# III intravitreale di Ranibizumab

del 05/04/2011

## *TESTS COAGULATIVI*

Tempo di protrombina	24.2	sec
Attività protrombinica	39.72	%
+ I. N. R.	2.2	

# TAKE HOME MESSAGE

- Rare complicanze post-operatorie emorragiche (dopo iniezione intravitreale) in pazienti che assumono terapia anticoagulante/antiaggregante
- Tra queste: emorragie sottoretiniche e/o coroideali
- Visto l'elevato rischio tromboembolico, la terapia anticoagulante/antiaggregante non deve essere sospesa prima di una iniezione intravitreale
- Monitoraggio del profilo coagulativo (INR)

# TAKE HOME MESSAGE

Le emorragie sottoretiniche si verificano in placche neovascolari ampie (occulte) indipendentemente dalla assunzione della terapia anticoagulante ?

*GRAZIE*

