



# Fabiana Mallone

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**Data di nascita:** 25 mag 89 | **Nazionalità:** Italiana | **Sesso** Femminile |

[fabiana.mallone@uniroma1.it](mailto:fabiana.mallone@uniroma1.it) | Viale del policlinico 155, 00186, Roma, Italia

## ● ESPERIENZA LAVORATIVA

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ATTUALE  
**SPECIALISTA IN OFTALMOLOGIA**

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1 FEB 20 – ATTUALE – Roma, Italia  
**ASSEGNISTA DI RICERCA PRESSO IL DIPARTIMENTO DI ORGANI DI SENSO, UNIVERSITÀ 'SAPIENZA' ROMA**

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VINCITRICE DEL BANDO DI SELEZIONE PER IL CONFERIMENTO DI UN ASSEGNO PER LA COLLABORAZIONE AD ATTIVITA' DI RICERCA CAT. A TIPOLOGIA I. Codice AR-A 2/2020 Id. 1/AP Prot. n. 584 del 26/10/20. Rep. n.29 Class.VII/1.

20 – 21  
**MEDICO FREQUENTATORE - UP MALATTIE OCULARI RARE, INFIAMMATORIE E DEGENERATIVE.** – AZIENDA OSPEDALIERA UNIVERSITARIA POLICLINICO UMBERTO I, ROMA

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20 – ATTUALE  
**COLLABORATORE SCIENTIFICO E DOCENTE PRESSO AIMS (ACCADEMIA ITALIANA PER LA FORMAZIONE DEI MEDICI ASPIRANTI SPECIALIZZANDI)**

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19  
**TIROCINIO DI ALTA SPECIALIZZAZIONE PRESSO IL DIPARTIMENTO DI CHIRURGIA VITREORETINICA DEL ROYAL EYE HOSPITAL DI MANCHESTER, UK.**

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15 – 19  
**SPECIALIZZANDA IN OFTALMOLOGIA – UNIVERSITARIA 'SAPIENZA', ROMA**

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FEB 18  
**MISSIONE UMANITARIA IN TOGO, AFRICA**

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15  
**ISCRIZIONE ALL'ALBO DEI MEDICI-CHIRURGI DELL'ORDINE PROVINCIALE DI ROMA DAL 19/03/2015 CON NUMERO: 61490**

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12 – 13  
**BORSA DI COLLABORAZIONE (150 ORE LAVORATIVE), DIPARTIMENTO DI IGIENE E SANITÀ PUBBLICA – UNIVERSITÀ 'SAPIENZA', ROMA**

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## ● ISTRUZIONE E FORMAZIONE

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**ESASO ECAMPUS - MASTERCLASS 1 PEARLS ON MEDICAL RETINA, MASTERCLASS 2 PEARLS ON ANTERIOR SEGMENT & GLAUCOMA, MASTERCLASS 3 LIVE SURGERY**

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GEN 20

**SPEAKER, ALCON VITREOUS CLUB – CORSO DI CHIRURGIA VITREORETINICA, MILANO.**

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19

**TIROCINIO DI ALTA SPECIALIZZAZIONE PRESSO IL DIPARTIMENTO DI CHIRURGIA VITREORETINICA DEL ROYAL EYE HOSPITAL DI MANCHESTER, UK.**

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SET 19

**PARTECIPAZIONE A V MEETING SCIENTIFICO ANNUALE BEECS (BRITISH EMERGENCY EYE CARE SOCIETY). CENTRE FOR LIFE, NEWCASTLE UPON TYNE**

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15 – 19

**DIPLOMA DI SPECIALIZZAZIONE IN OFTALMOLOGIA CONSEGUITO IN DATA 20/11/2019. TESI SPERIMENTALE: 'LE NEUROTROFINE NELLE MEMBRANE EPIRETINICHE: ERM IDIOPATICHE VS ERM SECONDARIE'. VOTAZIONE 70/70 CON LODE. – Università 'Sapienza', Roma**

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FEB 19

**SPEAKER, CONGRESSO: 'CASE REPORTS 2019: LA GESTIONE DEI CASI COMPLESSI 2019', RESPONSABILE PROF. T. ROSSI. FONDAZIONE SANTA LUCIA, ROME**

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APR 19 – NOV 19

**SOU - CORSO TEORICO E PRATICO DI ECO OFTALMOLOGIA ED OCT. FOGGIA/CHIETI/ROMA**

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NOV 18

**'SAREYE' CORSO DI CHIRURGIA OCULARE. ROMA.**

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SET 18

**VITREORETINAL ESASO SIMULATOR COURSE. LUGANO, SWITZERLAND.**

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LUG 18

**VITREORETINAL SURGERY ESASO MODULE. LUGANO, SWITZERLAND.**

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SET 18

**XIV CORSO SOU, CHIETI-PESCARA**

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MAR 15

**AMERICAN HEART ASSOCIATION BASIC LIFE SUPPORT - DEFIBRILLATION (BLS/D). CERTIFICAZIONE DI COMPETENZA IN RIANIMAZIONE CARDIOPOLMONARE.**

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NOV 14

**ESAME DI STATO PER L'ABILITAZIONE ALLA PROFESSIONE DI MEDICO CHIRURGO (DM 270) , SESSIONE DI NOVEMBRE 2014 – Azienda Ospedaliera Universitaria Policlinico Umberto I 'Sapienza', Roma**

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11 – 14

**PERCORSO DI ECCELLENZA. PARTECIPAZIONE A 120 ORE DI LEZIONI FRONTALI E 480 ORE SUDDIVISE TRA INTERNATO ELETTIVO E IL PROGETTO DI RICERCA 'GLI ANTICORPI MONOCLONALI IN AMBITO OFTALMOLOGICO: NUOVO APPROCCIO TERAPEUTICO' – Università 'Sapienza', Roma**

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08 – 14

**LAUREA IN MEDICINA E CHIRURGIA CONSEGUITA IL 24/07/2014. TESI SPERIMENTALE 'L'ASSOTTIGLIAMENTO DELLO SPESSORE COROIDEALE E DELLO STRATO DELLE FIBRE NERVOSE RETINICHE NELLA MALATTIA DI ALZHEIMER'. VOTAZIONE 110/110 CON LODE. – Università 'Sapienza' di Roma**

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DIC 12  
**BASIC LIFE SUPPORT (BLS) COURSE RESCUE DOCTOR DIPLOMA** – Croce Rossa Italiana

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FEB 08  
**'BOCCONI TALENT SCOUT PROGRAM'** – Università Bocconi , Milano

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07 – 08  
**'AWARDING OF EXCELLENCE'** – Liceo Scientifico Innocenzo XII , Anzio (Rm)

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03 – 08  
**DILPOMA DI MATURITÀ SCIENTIFICA. VOTAZIONE 100/100.** – Liceo Scientifico Innocenzo XII , Anzio (Rm)

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08  
**FIRST CERTIFICATE IN ENGLISH UNIVERSITY OF CAMBRIDGE (COUNCIL OF EUROPE LEVEL B2)**

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07  
**TRINITY COLLEGE LONDON EXAM, GRADE 10**

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07  
**EUROPEAN COMPUTER DRIVING LICENCE (ECDL)**

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06  
**UNIVERSITY COLLEGE OF DUBLIN (UCD)- UPPER ENGLISH COURSE.**

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## ● **PROGETTI**

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21  
**Co-Investigator del progetto: 'Valutazione della risposta immunitaria mucosale dopo vaccinazione per SARS-Cov2'. RM12117A5D9DB5E3.**

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Tutor Prof. Marta Sacchetti, 'Sapienza' University Umberto I Hospital, Rome

21  
**Principal Investigator del progetto di ricerca: 'Conjunctival expression of transient receptor potential (TRP) channels in inflammatory and degenerative ocular surface diseases'. AR12117A86AB1EEF.**

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Tutor Prof. Alessandro Lambiase, 'Sapienza' University Umberto I Hospital, Rome

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**Co-investigator del progetto: 'Caratterizzazione del pathway dell'IL-8 d e del suo recettore CXCR1 nella superficie oculare di pazienti affetti da glaucoma sottoposti a chirurgia filtrante: possibile biomarker predittivo dell'outcome chirurgico'.**

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Tutor Prof. Alice Bruscolini, 'Sapienza' University Umberto I Hospital, Rome

20  
**Co-investigator del progetto: 'Sicurezza ed efficacia di applicazioni topiche di collirio ottenuto con sistema HY-tissue PRP nel trattamento dell'occhio secco secondario a Graft versus Host Disease (GvHD)'.**

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Tutor Prof. Alessandro Lambiase, 'Sapienza' University Umberto I Hospital, Rome

19  
**Co-Investigator del progetto: 'Long-term outcomes of intravitreal injections for choroidal neovascularization in patients with pathologic myopia: analysis of prognostic factors.'**

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Tutor Prof. Magda Gharbiya, 'Sapienza' University Umberto I Hospital, Rome

18

**Principal Investigator del progetto di ricerca: 'Neurotrophins in Idiopathic Epiretinal (iERM) Membranes at the time of Membrane Peeling: molecular characterization of the two types of iERMs'. AR11816436687015.**

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Tutor Prof. Alessandro Lambiase, 'Sapienza' University Umberto I Hospital, Rome

18

**Co-Investigatore del progetto: 'Neurofibromatosis Type I: morpho-functional evaluation at chorioretinal level'.**

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Tutor Prof. Antonietta Moramarco, 'Sapienza' University Umberto I Hospital, Rome

17

**Co-Investigatore del progetto: 'Nerve growth factor pathway and glaucoma: seeking new horizons'. AR11715C81D36AA2.**

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**Tutor Prof. Alessandro Lambiase, 'Sapienza' University Umberto I Hospital, Rome**

19 – ATTUALE

**Reviewer per l'International Journal Ophthalmology (IJO), L'European Journal of Neurology (EJoN) e per Journal of Ophthalmology (joph).**

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## ● PUBBLICAZIONI

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**Mallone F, Sacchetti M, Lambiase A, Moramarco A. Molecular Insights and Emerging Strategies for Treatment of Metastatic Uveal Melanoma. Cancers (Basel). 2020 Sep 25;12(10):2761. doi: 10.3390/cancers12102761. PMID: 32992823; PMCID: PMC7600598.**

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2020

### **Abstract**

Uveal melanoma (UM) is the most common intraocular cancer. In recent decades, major advances have been achieved in the diagnosis and prognosis of UM allowing for tailored treatments. However, nearly 50% of patients still develop metastatic disease with survival rates of less than 1 year. There is currently no standard of adjuvant and metastatic treatment in UM, and available therapies are ineffective resulting from cutaneous melanoma protocols. Advances and novel treatment options including liver-directed therapies, immunotherapy, and targeted-therapy have been investigated in UM-dedicated clinical trials on single compounds or combinational therapies, with promising results. Therapies aimed at prolonging or targeting metastatic tumor dormancy provided encouraging results in other cancers, and need to be explored in UM. In this review, the latest progress in the diagnosis, prognosis, and treatment of UM in adjuvant and metastatic settings are discussed. In addition, novel insights into tumor genetics, biology and immunology, and the mechanisms underlying metastatic dormancy are discussed. As evident from the numerous studies discussed in this review, the increasing knowledge of this disease and the promising results from testing of novel individualized therapies could offer future perspectives for translating in clinical use.

**Keywords:** adjuvant therapy; combined therapy; immunotherapy; liver-directed-therapies; metastatic dormancy; metastatic therapy; metastatic uveal melanoma (mUM); prognostication; targeted-therapy; uveal melanoma (UM).

2020

## Abstract

The aim of this study is to investigate the potential neuroprotective effect of high-doses vitamins B1, B6 and B12 in patients with relapsing-remitting multiple sclerosis (RRMS) and persistent visual loss after acute optic neuritis (AON). Sixteen patients (20 eyes) diagnosed with RRMS and visual permanent disability following AON were enrolled for the present open, pilot study. Each patient was treated with oral high-doses 300 mg of vitamin B1, 450 mg of vitamin B6 and 1,500 mcg of vitamin B12, as add-on treatment to concomitant disease-modifying therapies (DMTs) for consecutive 90 days. Outcome measures were to determine changes from baseline to month three in visual acuity (VA) and visual field (VF) testing, with correlations with clinical parameters. Logistical regression was performed to evaluate predictors of final VA. A statistically significant improvement was registered in visual acuity ( $p = 0.002$ ) and foveal sensitivity threshold (FT) ( $p = 0.006$ ) at follow-up compared to baseline. A similar trend was demonstrated for mean deviation (MD) ( $p < 0.0001$ ), and pattern standard deviation (PSD) ( $p < 0.0001$ ). Age at the time of inclusion was positively correlated with latency time ( $\rho = 0.47$ ,  $p = 0.03$ ), while showing a negative correlation with visual acuity ( $\rho = -0.45$ ,  $p = 0.04$ ) and foveal sensitivity threshold ( $\rho = -0.6$ ,  $p = 0.005$ ) at follow up. A statistically significant correlation was demonstrated between foveal sensitivity threshold and visual acuity at baseline ( $\rho = 0.79$ ,  $p < 0.0001$ ). In a linear regression model, the main predictor of visual acuity at follow up was the foveal sensitivity threshold ( $B = 1.39$ ;  $p < 0.0001$ ). Supplemental high-dose vitamins B1, B6 and B12 resulted as effective therapy to improve visual function parameters in MS-related visual persistent disability.

**Keywords:** B Vitamins group; neuroprotection; visual function.

Mallone F, Marcelli M, Monsellato R, Franzone F, Gharbiya M, Lambiase A. Self-sealing posterior scleral perforation in airgun ocular trauma, surgical tip: a case report. *BMC Ophthalmol.* 2020 Apr 22;20(1):164. doi: 10.1186/s12886-020-01435-8. PMID: 32321467; PMCID: PMC7178978.

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2020

## Abstract

**Background:** Intraorbital metallic foreign bodies have varied clinical presentations. Here, we report the unusual case of intraoperative evidence of spontaneously healed posterior scleral perforation in a severe ballistic trauma without previous instrumental signs of penetrating wound and complete visual restoration after surgery.

**Case presentation:** The patient was hit by several lead hunting pellets in the chest, abdomen, limbs, face and orbit. Computed Tomography (CT) images revealed the presence of a pellet within the orbitary cavity, close to the optic nerve, with no signs of penetrating ocular wound. While performing vitrectomy for severe vitreous hemorrhage, a point of strong adherence between a old hemorrhage and retinal surface was identified and managed conservatively, as it was attributed to trauma related-impact area. So, lead foreign body took an unusual trajectory impacting the globe and finally lodging back in the deep orbitary cavity, in absence of significant ocular injury and with visual prognosis preservation.

**Conclusions:** Our findings provide further information on orbital injuries from airguns, a theme of growing popularity and concern. Intraoperative recognition of hardly removable old hemorrhagic clot as self-blockage site of posterior scleral penetrating trauma, allowed for surgical stabilization and minimal solicitation of the area to avoid inadvertent perforation.

**Keywords:** Airgun; Case report; Ocular trauma; Pellet; Vitreous hemorrhage.

Moramarco A, Mallone F, Pirraglia MP, Bruscolini A, Giustolisi R, La Cava M, Lambiase A. Clinical Features of Ocular Syphilis: a Retrospective Clinical Study in an Italian Referral Centre. *Semin Ophthalmol.* 2020 Jan 2;35(1): 50-55. doi: 10.1080/08820538.2020.1723651. Epub 2020 Feb 8. PMID: 32036734.

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2020

## Abstract

**Purpose:** To describe the clinical characteristics and visual prognosis of ocular involvement in syphilis. **Design:** A retrospective cohort study. **Methods:** We studied the charts of 24 patients who visited our Ophthalmological Centre in Rome, Italy. All patients with serological evidence of syphilitic infection were included. **Results:** Ocular involvement was the first manifestation of syphilitic disease in 96% and Human Immunodeficiency Virus (HIV) seropositivity was found in 29% of the cases. The most frequent ocular manifestation was posterior uveitis. Vitreous involvement was frequent. Patients with papillitis at onset showed better visual outcome with antisyphilitic treatment. Posterior uveitis at onset and HIV seropositivity were negative prognostic factors for visual outcome. HIV-positive patients showed more severe and frequent bilateral course of ocular involvement in syphilis. **Conclusions:** The ophthalmologist should suspect syphilis in patients with uveitis or optic neuropathy associated with high-risk sexual behaviour and/or HIV, or in patients with posterior placoid chorioretinitis, necrotising retinitis, or interstitial keratitis.

**Keywords:** HIV; infectious uveitis; posterior uveitis; syphilis.

2019

## Abstract

**Background:** Gorlin-Goltz syndrome, also known as nevoid basal cell carcinoma syndrome, is a rare genetic disorder that is transmitted in an autosomal dominant manner with complete penetrance and variable expressivity. It is caused in 85% of the cases with a known etiology by pathogenic variants in the PTCH1 gene, and is characterized by a wide range of developmental abnormalities and a predisposition to multiple neoplasms. The manifestations are multiple and systemic and consist of basal cell carcinomas in various regions, odontogenic keratocystic tumors and skeletal anomalies, to name the most frequent. Despite the scarce medical literature on the topic, ocular involvement in this syndrome is frequent and at the level of various ocular structures. Our study focuses on the visual apparatus and its annexes in subjects with this syndrome, in order to better understand how this syndrome affects the ocular system, and to evaluate with greater accuracy and precision the nature of these manifestations in this group of patients.

**Results:** Our study confirms the presence of the commonly cited ocular findings in the general literature regarding the syndrome [hypertelorism (45.5%), congenital cataract (18%), nystagmus (9%), colobomas (9%)] and highlights strabismus (63% of the patients), epiretinal membranes (36%) and myelinated optic nerve fiber layers (36%) as the most frequent ophthalmological findings in this group of patients.

**Conclusions:** The presence of characteristic and frequent ocular signs in the Gorlin-Goltz syndrome could help with the diagnostic process in subjects suspected of having the syndrome who do not yet have a diagnosis. The ophthalmologist has a role as part of a multidisciplinary team in managing these patients. The ophthalmological follow-up that these patients require, can allow, if necessary, a timely therapy that could improve the visual prognosis of such patients.

**Keywords:** Gorlin syndrome; Gorlin-Goltz syndrome; Myelinated optical nerve fiber layers; Nevoid basal cell carcinoma syndrome; Ocular anomalies; Odontogenic keratocyst.

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Bruscolini A, La Cava M, Mallone F, Marcelli M, Ralli M, Sagnelli P, Greco A, Lambiase A. Controversies in the management of neuromyelitis optica spectrum disorder. *Expert Rev Neurother.* 2019 Nov;19(11):1127-1133. doi: 10.1080/14737175.2019.1648210. Epub 2019 Aug 12. PMID: 31339052.

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2019

## Abstract

**Introduction:** Neuromyelitis optica spectrum disorders (NMOSD) are autoimmune diseases of the central nervous system mainly involving the optic nerves and spinal cord. Many advances have been made in understanding the immunopathology of NMOSD and related clinical classification, nevertheless, open issues in management and effective therapeutic approaches still remain. **Areas covered:** In this article, the authors reviewed and discussed the scientific evidence in pathogenesis and pharmacological therapy of NMOSD addressing the more recent advances in new biological treatment option and therapeutic strategy that may help to improve management of this condition. **Expert opinion:** Despite current immunopathogenic evidence, NMOSD management represents a challenge due to the poorly validated diagnostic, prognostic and therapeutic biomarkers. A tailored approach is mandatory to improve the management of the different disease clinical settings.

**Keywords:** Neuromyelitis optica spectrum disorders (NMOSD); aquaporin-4 immunoglobulin G (AQP4-IgG); diagnostic criteria; emerging treatment; immunopathogenesis; management; myelin oligodendrocyte glycoprotein immunoglobulin G (MOG-IgG); standard treatment.

2019

## Abstract

**Purpose:** The aim of this study was to provide a classification of the different retinal vascular arrangements in neurofibromatosis 1 (NF1), with appropriate qualitative and quantitative information.

**Methods:** This study was conducted on 334 consecutive patients with NF1 and 106 sex-matched and age-matched healthy control subjects. Each patient underwent a comprehensive ophthalmological examination inclusive of near-infrared reflectance retinography by using the spectral domain Optical coherence tomography (OCT), a complete dermatological examination and 1.5 T MRI scan of the brain to assess the presence of optic nerve gliomas. To evaluate the predictability and the diagnostic accuracy of our identified retinal microvascular arrangements, we calculated the diagnostic indicators for each pattern of pathology, with corresponding 95% CI. In addition, we evaluated the association between the microvascular arrangements and each National Institutes of Health diagnostic criteria.

**Results:** Microvascular abnormalities were detected in 105 of 334 NF1 patients (31.4%), the simple vascular tortuosity was recognised in 78 of 105 cases (74.3%) and whether the corkscrew pattern and the moyamoya-like type showed a frequency of 42.8% (45 of 105 cases) and 15.2% (16 of 105 cases), respectively. We found a statistically significant correlation between the presence of retinal microvascular abnormalities and the patient age ( $p=0.02$ ) and between the simple vascular tortuosity, the patient age and the presence of neurofibromas ( $p=0.002$  and  $p=0.05$ , respectively).

**Conclusions:** We identified microvascular alterations in 31.4% of patients and a statistically significant association with patient age. Moreover, the most frequent type of microvascular alterations, the simple vascular tortuosity, resulted positively associated with age and with the presence of neurofibromas.

**Keywords:** NF1; NIR-OCT; microvascular abnormalities; moyamoya disease; ophthalmoscopy; retina.

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Moramarco A, Giustini S, Nofroni I, Mallone F, Miraglia E, Iacovino C, Calvieri S, Lambiase A. Near-infrared imaging: an in vivo, non-invasive diagnostic tool in neurofibromatosis type 1. *Graefes Arch Clin Exp Ophthalmol.* 2018 Feb;256(2):307-311. doi: 10.1007/s00417-017-3870-z. Epub 2017 Dec 30. PMID: 29290016.

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2018

## Abstract

**Purpose:** Only a few reports in the literature have investigated the presence of ocular abnormalities in neurofibromatosis type 1 (NF-1) patients. The aim of this study was to evaluate the prevalence of ocular abnormalities in a large population of NF1 patients, focusing on the choroidal changes.

**Methods:** This study was conducted on 160 consecutive patients with NF1 and 106 sex- and age-matched healthy subjects (control). Each patient underwent a complete ophthalmological examination inclusive of best-corrected visual acuity, intraocular pressure measurement, slit-lamp biomicroscopy, indirect fundus biomicroscopy, and near-infrared reflectance (NIR) retinography by using the spectral domain OCT. Moreover, all patients underwent complete dermatological exam and 1.5-Tesla MRI scan of the brain to assess the presence of optic nerve gliomas.

**Results:** Choroidal abnormalities were detected in 97% of patients, with a positive predictive value of 100% and a negative predictive value of 96.4%. Interestingly, a small number of patients (4/160; 2.5%) showed Lisch nodules without choroidal abnormalities, whereas a larger number of patients (22/160; 13.75%) presented choroidal lesions in absence of Lisch nodules. None of the patients showed the absence of both choroidal lesions and Lisch nodules. The number of choroidal lesions increased with age ( $r = 0.364$ ,  $p = 0.0001$ ) and with the severity of pathology ( $r = 0.23$ ,  $p = 0.003$ ). Any statistically significant correlation between choroidal lesions, visual acuity, and intraocular pressure was observed.

**Conclusions:** NIR imaging represents an in vivo, non-invasive, sensitive and reproducible exam to detect choroidal nodules in NF-1 patients, suggesting that choroidal changes may represent an additional diagnostic criteria for NF1.

**Keywords:** Choroid; Lisch nodules; NIR-Oct; Neurofibromatosis type 1; Ophthalmoscopy.

Gharbiya M, Giustolisi R, Marchiori J, Bruscolini A, Mallone F, Fameli V, Nebbioso M, Abdolrahimzadeh S. Comparison of Short-Term Choroidal Thickness and Retinal Morphological Changes after Intravitreal Anti-VEGF Therapy with Ranibizumab or Aflibercept in Treatment-Naive Eyes. *Curr Eye Res.* 2018 Mar;43(3):391-396. doi: 10.1080/02713683.2017.1405045. Epub 2017 Nov 22. PMID: 29166140.

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2018

## Abstract

**Purpose:** To evaluate choroidal thickness (CT) and retinal morphological changes in eyes with neovascular age-related macular degeneration (nAMD) following ranibizumab or aflibercept intravitreal treatment.

**Materials and methods:** This was a prospective, observational, comparative study where 76 eyes of 76 consecutive patients with treatment-naive nAMD were consecutively enrolled and randomized to ranibizumab 0.5 mg or aflibercept 2 mg injections. Spectral-domain optical coherence tomography images of the choroid were obtained by enhanced depth imaging modality. CT measurements were made of the subfoveal choroid, and at 500  $\mu$ m from the center of the fovea in the superior, inferior, temporal, and nasal quadrants. Central subfield retinal thickness, intraretinal fluid, subretinal fluid, and pigment epithelium detachment were evaluated. Patients were followed up for 3 months.

**Results:** Compared with baseline, CT decreased over time in both the ranibizumab and aflibercept group ( $P = 0.04$  and  $0.001$ , respectively). At each location, the decrease in CT was significantly more prominent in aflibercept with respect to ranibizumab-treated eyes ( $P < 0.05$ ). Among the different choroidal neovascularization subtypes, type 3 lesions showed the greatest CT decrease after anti-vascular endothelial growth factor injections ( $P = 0.003$ ). Choroidal thinning was significantly greater in type 3 lesions treated with aflibercept compared with ranibizumab ( $F = 13.6$ ,  $P = 0.002$ ). Post-treatment incidence of dry macula was higher in aflibercept- versus ranibizumab-treated eyes (50% vs. 76%,  $P = 0.03$ ).

**Conclusions:** CT reduction is greater in aflibercept-treated eyes, and type 3 lesions show the greatest thickness decrease. The post-treatment frequency of dry macula, evaluated by qualitative parameters, is higher in aflibercept-treated eyes, but is not correlated with CT change.

**Keywords:** Age-related macular degeneration; aflibercept; anti-VEGF; choroidal thickness; dry macula; optical coherence tomography; ranibizumab.

Trebbastoni A, Marcelli M, Mallone F, D'Antonio F, Imbriano L, Campanelli A, de Lena C, Gharbiya M. Attenuation of Choroidal Thickness in Patients With Alzheimer Disease: Evidence From an Italian Prospective Study. *Alzheimer Dis Assoc Disord.* 2017 Apr-Jun;31(2):128-134. doi: 10.1097/WAD.000000000000176. PMID: 27875364.

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2017

## Abstract

**Introduction:** To compare the 12-month choroidal thickness (CT) change between Alzheimer disease (AD) patients and normal subjects.

**Methods:** In this prospective, observational study, 39 patients with a diagnosis of mild to moderate AD and 39 age-matched control subjects were included. All the subjects underwent neuropsychological (Mini Mental State Examination, Alzheimer disease Assessment Scale-Cognitive Subscale, and the Clinical Dementia Rating Scale) and ophthalmological evaluation, including spectral domain optical coherence tomography, at baseline and after 12 months. CT was measured manually using the caliper tool of the optical coherence tomography device.

**Results:** After 12 months, AD patients had a greater reduction of CT than controls ( $P \leq 0.05$ , adjusted for baseline CT, age, sex, axial length, and smoking).

**Discussion:** CT in patients with AD showed a rate of thinning greater than what could be expected during the natural course of aging.

Moramarco A, Lambiase A, Mallone F, Miraglia E, Giustini S. A characteristic type of retinal microvascular abnormalities in a patient with Neurofibromatosis type 1. *Clin Ter.* 2019 Jan-Feb;170(1):e4-e9. doi: 10.7417/CT.2019.2101. PMID: 30789191.

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2019

## Abstract

This study aims to describe a typical retinal microvascular abnormality in patients with neurofibromatosis type 1 (NF-1). A 64-year-old man with diagnosis of NF-1 was evaluated by complete ophthalmological examination, including fluorescein angiography and spectral Domain OCT in Near-Infrared (NIR-OCT) modality. Slit lamp exam showed the presence of more than 10 Lisch nodules for each eye. Ophthalmic examinations and NIR-OCT scans showed the presence of retinal tortuous vessels ending in a 'puff of smoke' arrangement. The clinical significance as diagnostic and prognostic factor of this novel type of retinal microvascular abnormality in NF-1 should be further investigated.

**Keywords:** Microvascular abnormalities; Moya-Moya disease; NIR-OCT; Neurofibromatosis; Retina.



2021

## Abstract

**Background:** Retinitis Pigmentosa (RP) is the most frequent retinal hereditary disease and every kind of transmission pattern has been described. The genetic etiology of RP is extremely heterogeneous and in the last few years the large application of Next Generation Sequencing (NGS) approaches improved the diagnostic yield, elucidating previously unexplained RP causes and new genotype-phenotype correlations. The objective of this study was to reevaluate a previously reported family affected by Coats'-type RP without genetic diagnosis and to describe the new genetic findings.

**Case presentation:** Cohort, prospective, and single-center observational family case. Three individuals of a family, consisting of a mother and four sons, with a Coats phenotype were reevaluated after 25 years of clinical follow-up using visual acuity tests, ophthalmoscopy, Goldmann visual field, electroretinography (ERG), and spectral domain-optical coherence tomography (SD-OCT). Specifically, a RP NGS panel was performed on one member of the family and segregation analysis was required for the other affected and unaffected members. NGS analysis disclosed a RPGR (Retinitis Pigmentosa GTPase Regulator) gene truncating variant segregating with the phenotype in all the three affected members. RPGR mutations are reported as causative of an X-linked RP.

**Conclusions:** This is the first reported family with a Coats'-type RP associated to a RPGR mutation and segregating as a dominant X-linked disease, confirming the hypothesis of the genetic origin of this condition and expanding the phenotypic spectrum of diseases caused by RPGR gene mutations. The Authors suggest RPGR gene screening mutations in patients presenting this phenotype.

**Keywords:** Case report; Coats vasculopathy; Coats'-type retinitis pigmentosa; Hereditary disease; RPGR- XLRP- Coats'-like retinitis.

Moramarco A, Mallone F, Sacchetti M, Lucchino L, Miraglia E, Roberti V, Lambiase A, Giustini S. Hyperpigmented spots at fundus examination: a new ocular sign in Neurofibromatosis Type I. *Orphanet J Rare Dis.* 2021 Mar 23;16(1):147. doi: 10.1186/s13023-021-01773-w. PMID: 33757576; PMCID: PMC7986306.

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## Abstract

**Background:** Neurofibromatosis Type I (NF1), also termed von Recklinghausen disease, is a rare genetic disorder that is transmitted by autosomal dominant inheritance, with complete penetrance and variable expressivity. It is caused by mutation in the NF1 gene on chromosome 17 encoding for neurofibromin, a protein with oncosuppressive activity, and it is 50% sporadic or inherited. The disease is characterized by a broad spectrum of clinical manifestations, mainly involving the nervous system, the eye and skin, and a predisposition to develop multiple benign and malignant neoplasms. Ocular diagnostic hallmarks of NF1 include optic gliomas, iris Lisch nodules, orbital and eyelid neurofibromas, eyelid café-au-lait spots. Choroidal nodules and microvascular abnormalities have recently been identified as additional NF1-related ocular manifestations. The present study was designed to describe the features and clinical significance of a new sign related to the visual apparatus in NF-1, represented by hyperpigmented spots (HSs) of the fundus oculi.

**Results:** HSs were detected in 60 (24.1%) out of 249 patients with NF1, with a positive predictive value of 100% and a negative predictive value of 44.2%. None of the healthy subjects (150 subjects) showed the presence of HSs. HSs were visible under indirect ophthalmoscopy, ultra-wide field (UWF) pseudocolor imaging and red-only laser image, near-infrared reflectance (NIR)-OCT, but they were not appreciable on UWF green reflectance. The location and features of pigmentary lesions matched with the already studied NF1-related choroidal nodules. No significant difference was found between the group of patients (n = 60) with ocular HSs and the group of patients (n = 189) without ocular pigmented spots in terms of age, gender or severity grading of the disease. A statistically significant association was demonstrated between the presence of HSs and neurofibromas (p = 0.047), and between the presence of HSs and NF1-related retinal microvascular abnormalities (p = 0.017).

**Conclusions:** We described a new ocular sign represented by HSs of the fundus in NF1. The presence of HSs was not a negative prognostic factor of the disease. Following multimodal imaging, we demonstrated that HSs and choroidal nodules were consistent with the same type of lesion, and simple indirect ophthalmoscopy allowed for screening of HSs in NF1.

**Keywords:** Choroidal nodules; Enhanced depth imaging OCT (EDI-OCT); Hyperpigmented spots (HSs); Indirect ophthalmoscopy; Near-infrared reflectance (NIR) imaging OCT (NIR-OCT); Neurofibromatosis Type I (NF1); Rare diseases; Ultra-wide field (UWF).

2020

Abstract

Schwannomatosis is a syndrome characterized by presence of schwannomas in the absence of bilateral vestibular schwannomas and meningiomas. Schwannomas interest frequently peripheral nerves (90%) and spinal nerves (75%). Schwannomatosis are generally sporadic; in 15 - 25% are familiar. The genes involved are SMARCB1 (40-50% of familial) and LZTR1. The reported phenotype continues to expand and evolve. We report the case of a patient with Schwannomatosis and Lisch nodules, typical manifestation of NF1.

Keywords: Lisch Nodules; Schwannomatosis; Schwannomas

Mallone F, Sacchetti M, Bruscolini A, Scuderi L, Marengo M and Lambiase A. Neurotrophic Factors in Glaucoma and Innovative Delivery Systems. *Appl. Sci.* 2020, 10(24), 9015; <https://doi.org/10.3390/app10249015>

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2020

**Abstract**

Glaucoma is a neurodegenerative disease and a worldwide leading cause of irreversible vision loss. In the last decades, high efforts have been made to develop novel treatments effective in inducing protection and/or recovery of neural function in glaucoma, including neurotrophic factors (NTFs). These approaches have shown encouraging data in preclinical setting; however, the challenge of sustained, targeted delivery to the retina and optic nerve still prevents the clinical translation. In this paper, the authors review and discuss the most recent advances for the use of NTFs treatment in glaucoma, including intraocular delivery. Novel strategies in drug and gene delivery technology for NTFs are proving effective in promoting long-term retinal ganglion cells (RGCs) survival and related functional improvements. Results of experimental and clinical studies evaluating the efficacy and safety of biodegradable slow-release NTF-loaded microparticle devices, encapsulated NTF-secreting cells implants, mimetic ligands for NTF receptors, and viral and non-viral NTF gene vehicles are discussed. NTFs are able to prevent and even reverse apoptotic ganglion cell death. Nevertheless, neuroprotection in glaucoma remains an open issue due to the unmet need of sustained delivery to the posterior segment of the eye. The recent advances in intraocular delivery systems pave the way for possible future use of NTFs in clinical practice for the treatment of glaucoma.

**Keywords:** [glaucoma](#); [neurotrophic factors \(NTFs\)](#); [neurotrophins \(NTs\)](#); [neuroprotection](#); [drug delivery systems](#); [microspheres](#); [gene therapy](#); [polymers](#); [nanoparticles](#); [implants](#)

D'Aguanno S, Mallone F, Marengo M, Del Bufalo D, Moramarco A. Hypoxia-dependent drivers of melanoma progression. *J Exp Clin Cancer Res.* 2021 May 8;40(1):159. doi: 10.1186/s13046-021-01926-6. PMID: 33964953; PMCID: PMC8106186.

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2021

**Abstract**

Hypoxia, a condition of low oxygen availability, is a hallmark of tumour microenvironment and promotes cancer progression and resistance to therapy. Many studies reported the essential role of hypoxia in regulating invasiveness, angiogenesis, vasculogenic mimicry and response to therapy in melanoma. Melanoma is an aggressive cancer originating from melanocytes located in the skin (cutaneous melanoma), in the uveal tract of the eye (uveal melanoma) or in mucosal membranes (mucosal melanoma). These three subtypes of melanoma represent distinct neoplasms in terms of biology, epidemiology, aetiology, molecular profile and clinical features. In this review, the latest progress in hypoxia-regulated pathways involved in the development and progression of all melanoma subtypes were discussed. We also summarized current knowledge on preclinical studies with drugs targeting Hypoxia-Inducible Factor-1, angiogenesis or vasculogenic mimicry. Finally, we described available evidence on clinical studies investigating the use of Hypoxia-Inducible Factor-1 inhibitors or antiangiogenic drugs, alone or in combination with other strategies, in metastatic and adjuvant settings of cutaneous, uveal and mucosal melanoma. Hypoxia-Inducible Factor-independent pathways have been also reported to regulate melanoma progression, but this issue is beyond the scope of this review. As evident from the numerous studies discussed in this review, the increasing knowledge of hypoxia-regulated pathways in melanoma progression and the promising results obtained from novel antiangiogenic therapies, could offer new perspectives in clinical practice in order to improve survival outcomes of melanoma patients.

**Keywords:** Angiogenesis; Cutaneous melanoma (CM); HIF-1; Hypoxia; Mucosal melanoma (MM); Uveal melanoma (UM); Vasculogenic mimicry.

2021

## Abstract

Tumors of the ocular surface encompass a wide spectrum of conditions involving the conjunctiva and cornea, ranging from benign lesions to life-threatening malignancies. These tumors are rare; however, they are commonly seen in the ophthalmological clinical practice as a group.

The diagnosis of ocular surface tumors is mostly based on clinical evaluation of the conjunctiva and cornea and subsequent histologic confirmation. Recently, non-invasive diagnostic approaches including anterior segment high-resolution OCT (HROCT), showed promising results for their use as adjuvant for histology in case of suspicious lesions. The present review focused on the main malignant ocular surface tumors, including ocular surface squamous neoplasia (OSSN), melanocytic epithelial tumors, and conjunctival lymphoma, with the aim of discussing the epidemiological, clinical, and histopathological features, as well as to provide insights into classification and staging. In addition, the latest advances in the treatment of ocular surface tumors were reviewed, including the use of topical chemotherapy, which is gaining increasing acceptance over surgical tumor removal as it prevents surgery-related side effects and tumor recurrences.

**Keywords:** Ocular surface squamous neoplasia (OSSN); conjunctival melanoma; conjunctival lymphoma; anterior segment high-resolution OCT (HR-OCT); topical chemotherapy.

**F.Mallone, M.Sacchetti, A.Lambiase. Clinical approach to depositions and degenerations of the conjunctiva, cornea and sclera. Atlas of SOU textbook of Ophthalmology.**

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Chapter for Atlas of SOU textbook of Ophthalmology , SOU Program Committee

2021

## Abstract

Depositions and degenerations of the cornea, conjunctiva and sclera include a wide spectrum of conditions ranging from benign lesions to sight-threatening diseases. Most of these lesions are rare and poorly recognized; however, they are commonly seen in the ophthalmological clinical practice as a whole. The diagnosis of depositions and degenerations of the cornea, conjunctiva and sclera is mostly based on clinical evaluation. This chapter highlights clinical presentation of some of the most common corneal, conjunctival and scleral depositions and degenerations, as well as to provide insights into epidemiology, classification and staging. In addition, the latest advances in the treatment of these conditions were discussed. Prompt diagnosis and treatment are mandatory for preventing serious and irreversible ocular complications.

**Key-words:** Neurotrophic Keratitis (NK), Mooren's ulcer, Terrien's marginal degeneration (TMD), Peripheral [ulcerative keratitis \(PUK\)](#), Dellen, Corneal arcus, Salzmann nodular degeneration (SND), Crocodile shagreen degeneration, Calcific band keratopathy, Cornea verticillata, Cystinosis, Amyloidosis, Spheroidal degeneration, Linear iron deposits, Kayser-Fleischer ring, Pterygium, Pinguecula, Conjunctival concretions, Scleral hyaline plaque and scleromalacia.

**F.Mallone. VIII Edizione Manuali AIMS, Autore Manuale di Oftalmologia.**

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2021

2021

**Abstract:** The current standard treatment of myopic choroidal neovascularisation (mCNV) is intravitreal injection of VEGF antagonists. This study was proposed to assess efficacy and safety of intravitreal bevacizumab (IVB) for the treatment of mCNV over 10-year follow-up. Thirty eyes of 30 patients with treatment-naïve mCNV who underwent IVB and were followed-up for a minimum of ten years were recruited for the present retrospective cohort study. All participants were treated with three monthly IVB at baseline, and then evaluated and treated under pro-re nata (PRN) schedule. Outcome measures were to determine BCVA changes over years and identify the predictive factors of both final visual outcome and need for retreatment. Analysis of the main involved prognostic factors with correlations among variables is reported. Visual acuity remained stable at 10-year follow-up ( $p=0.001$ ) with the greatest improvement at 2 years ( $p<0.0001$ ) in all CNV locations. Baseline BCVA correlated positively with final BCVA ( $\beta=0.88$ ,  $p<0.0001$ ,  $R^2: 0.75$ ). No predictive factors for the need of additional injections were identified. Retinal and choroidal thickness significantly reduced over time, but without correlation with the number of injections. CNV max height and area significantly decreased at 10 years ( $p<0.0001$  and  $p=0.003$ , respectively), with complete regression of mCNV lesion in 40% of subjects. Intravitreal bevacizumab resulted as long-term effective and safe therapy for mCNV with sustained results at 10 years.

**Key-words:** ocular pharmacology; bevacizumab (IVB), pathologic myopia (PM), myopic choroidal neovascularization (mCNV), ophthalmology; drug delivery systems; long-term results

## ● **COMPETENZE LINGUISTICHE**

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**Lingua madre:** ITALIANO

**Altre lingue:**

	COMPRESIONE		ESPRESSIONE ORALE		SCRITTURA
	Ascolto	Lettura	Produzione orale	Interazione orale	
<b>INGLESE</b>	C1	C1	C1	C1	C1

Livelli: A1 e A2: Livello elementare B1 e B2: Livello intermedio C1 e C2: Livello avanzato

## ● **COMPETENZE DIGITALI**

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European Computer Driving Licence (ECDL)