CV RESUMIDO PROF. DOUTOR RUFINO SILVA

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PRESENT POSITION/TITLE

- MD, PhD
- Associate Professor of Ophthalmology, University of Coimbra
- Head of the Medical Retina Service, Department of Ophthalmology, University Hospital of Coimbra

DEPARTMENT, INSTITUTION

Faculty of Medicine, University of Coimbra

Department of Ophthalmology, University Hospital of Coimbra Coimbra, Portugal

EDUCATION/TRAINING

Institution and location	Degree	mm/yy	Field of study
University of Coimbra, Portugal	MD	06/1985	Medicine
University Hospital of Coimbra, Portugal	Internship	09/1987	Medicine
Scheie Eye Institute, Univ. of Pennsylvania, USA	Observership	07/1988	Ophthalmology
Wilmer Eye Institute, Baltimore, USA	Observership	07/1990	Retina
University Hospital of Coimbra, Portugal	Residency	12/1991	Ophthalmology
University of Coimbra, Portugal	Master degree	05/1994	Ophthalmology
Manhattan Eye and Ear Hospital, USA	Observership	07/1995	Retina
University Hospital of Coimbra, Portugal	Senior Specialist/ Consultant	08/2006	Ophthalmology
University of Coimbra, Portugal	PhD	11/2007	Ophthalmology
University of Coimbra, Portugal	Invited Professor	01/2010	Ophthalmology

PERSONAL STATEMENT

As an ophthalmologist with more than 20 years of expertise, I have been primarily committed to the study and treatment of retinal diseases. My main interest is on Agerelated Macular Degeneration (AMD), but I have also significant experience on the diagnosis and management of other retinal problems, such as retinal vein occlusion (RVO), pathologic myopia, among others. I daily combine clinical care with clinical research, teaching and leadership activities, which allows me to reach my goals of developing a strong scientific activity based on clinical practice. These activities take primarily place at the Faculty of Medicine of University of Coimbra and at the Department of Ophthalmology of the University Hospital of Coimbra. I also have a strong collaboration with the Association for Innovation and Biomedical Research on Light and Image (AIBILI), Coimbra, as a physician and a researcher.

My broad experience in research includes the participation in more than 60 clinical trials and projects, more than 30 of them as Principal Investigator. With the goal of contributing to the better understanding of retinal diseases, their prevention, risk factors and their innovative treatment, most of these studies were primarily focused on AMD. For example, I participated in several multicenter clinical trials with different therapies, such as verteporfin photodynamic therapy (PDT), anti-VEGF injections and treatment with corticosteroids.

My main areas of research include: early markers and risk factors of AMD progression, including imaging, genetics and metabolomics; epidemiology of AMD; characterization of food habits in the Portuguese population and correlation with AMD prevalence; and polypoidal choroidal neovascularization. In all these fields I have been particularly involved in developing investigator-driven clinical trials. As a clinicianscientist, my research is also focused on identifying the sequence of changes in the chorioretinal interface that lay the path for the development of choroidal neovascularization (CNV),



and the progression from early to late AMD. My goal is to identify the morphological features that define the earliest identifiable CNV lesion and to evaluate the sensitivity of quantitative imaging analysis compared to the conventional clinical exam.

POSITIONS AND HONORS

Current Professional Positions

- **Since 1992** Ophthalmologist; Department of Ophthalmology, University Hospital of Coimbra, Portugal
- **Since 1994** Investigator; AIBILI Association for Innovation and Biomedical Research on Light and Image, Coimbra, Portugal
- **Since 2006** Senior Consultant in Ophthalmology; University Hospital of Coimbra, Portugal
- Since 2007 Head of the Medical Retina Service; Department of Ophthalmology, Coimbra University Hospital, Portugal
- Since 2009 Professor of Ophthalmology; Faculty of Medicine, University of Coimbra, Portugal
- Since 2014 Coordinator for Clinical Research; Vision Science Unit, Faculty of Medicine, University of Coimbra, Portugal
- **Since 2014** Director of the Residency Program of Ophthalmology; University Hospital of Coimbra, Portugal

Medical and Scientific appointments

- 1996 1998 Head of the Retina and Vitreous Group; Portuguese Society of Ophthalmology (also on 2002 2004 and 2008 2010)
- 1998 2000 Member of the Writing Council; Journal of the Portuguese Society of Ophthalmology
- 2009 2012 Head of the Retina and Vitreous Group; Portuguese Society of Ophthalmology
- 2009 2012 Board Member; Board of Ophthalmology, Portuguese Medical Association
- 2010 2012 Member of the Directive Council; Portuguese Society of Ophthalmology

Professional Memberships

- AAO American Academy of Ophthalmology
- ARVO Association for Research in Vision and Ophthalmology
- Club Jules Gonin
- ESCRS European Society of Cataract and Refractive Surgery
- EURETINA European Society of Retinal Specialists [Scientific Committee (2008-2009); Research Committee (2009-2016)]
- EVER European Vision and Eye Research
- EVICR.net European Vision Institute Clinical Research Network [AMD Scientific Committee]
- E3 European Eye Epidemiology Network
- FAN Fluorescein Angiography Club
- GER Group of Retinal Specialists President
- SERV Spain Society of Retina and Vitreo
- SPO Portuguese Society of Ophthalmology, etc.

Other experience

- Editorial Board Member: Case Reports in Ophthalmology; European Journal of Ophthalmology; Ophthalmologica; Ophthalmic Research.
- Reviewer In International Journals: Acta Ophthalmologica; British Journal of Ophthalmology; Graefes Archives of Ophthalmology; Ophthalmology; Progress in Retinal and Eye Research; Retina; etc.



RESEARCH

Participation in more than 60 clinical trials and projects, more than 30 of them as Principal Investigator.

Summary/Example of recent research support

INVESTIGATOR-DRIVEN CLINICAL TRIALS

Title and role within study	Sponsor/Source	Period
Epidemiological study of the prevalence of Age- Related Macular Degeneration in Portugal Protocol CC-01-2009 (NCT01298674); Coordinating Investigator	AIBILI/Novartis	2009-2015
Life style and food habits questionnaire in the Portuguese population aged 55 or more. Protocol 4c-2012-04 (NCT01715870); Coordinating Investigator	AIBILI/Novartis	2012-2014
LOBS – Longitudinal Observational early Biomarkers Study. A multicenter study. Principal Investigator	Queens Univ., Belfast	2014-2015
Age-related macula degeneration: can metabolomic profile distinguish progressors? (FCT: HMSP-ICJ/0006/2013); Investigator	Portuguese F. Science & Techn./ Harvard Medical School	2014-2016
ATLANTIC – A Randomized, Double-masked, Sham-controlled Phase 4 Study of the Efficacy, Safety, and Tolerability of Intravitreal Aflibercept Monotherapy Compared to Aflibercept With Adjunctive Photodynamic Therapy in patients with Polypoidal Choroidal Vasculopathy. Protocol ECR-AMD-2015-09 (NCT02495181); Coordinating Investigator	AIBILI/Bayer e	2015 - Ongoing
Genotypic and Phenotypic characterization of retinal angiomatous proliferation (RAP) lesions. Protocol CEC/006/2015; Principal Investigator	AIBILI	2015 - Ongoing
Five-year incidence of Age-related Macular Degeneration in the central region of Portugal. Protocol 4C-2016-09 (NCT02748824); Coordinating Investigator	AIBILI/Novartis	2016-2017

INDUSTRY-SPONSORED CLINICAL TRIALS

Title and role within study	Sponsor/Source	Period
Phase 1-2: Safety, tolerability and efficacy Study of ESBA1008 Versus Lucentis® in the treatment of exudative AMD. Protocol C-10-083 (NCT01304693); Principal Investigator	Alcon	2011-2013
FOVISTA – A phase 3 randomized, double-masked, controlled trial to establish the safety and efficacy of intravitreous FOVISTA TM administered in combination with either Avastin® or Eylea® compared to Avastin® or Eylea® Monotherapy in subjects with subfoveal neovascular AMD. Protocol OPH1004B (NCT01940887); Principal Investigator	Ophthotech	2014 -2017



SALT – A 12-month, Phase IV, Randomized, Open Label, Multicenter Study to Compare Efficacy of 0.5 mg Ranibizumab PRN vs 2 mg Aflibercept Bimonthly Intravitreal Injections on RT Stability Till Month 6 of Treatment and Explore Functional Outcomes up to Month 12 in Patients With Neovascular AMD. Protocol CRFB002ADE23 (NCT01958918); Principal Investigator	Novartis	2014 -2017
TREND – A 12-month, Phase IIIb, Randomized, Visual Acuity Assessor-masked, Multicenter Study Assessing the Efficacy and Safety of Ranibizumab 0.5mg in Treat and Extend Regimen vs Monthly Regimen, in Patients with Neovascular AMD. Protocol CRFB002A2411 (NCT01948830); Principal Investigator	Novartis	2014-2015
HARRIER – A Two-Year, Randomized, Double-Masked, Multicenter, 2-Arm Study Comparing the Efficacy and Safety of RTH258 6 mg vs Aflibercept in Subjects with Neovascular AMD. Protocol RTH258-Coo2 (NCT02434328); Principal Investigator	Alcon	2015 - Ongoing
OCTAVE – A 24-month, Phase IIIb, Randomized, Double-masked, Multicenter Study Assessing the Efficacy and Safety of Two Treatment Regimens of o.5 mg Ranibizumab Intravitreal Injections Guided by Functional and/or Anatomical Criteria, in Patients With Neovascular AMD. Protocol CRFB002A2405 (NCT01780935); Principal Investigator	Novartis	2013-2015
MINERVA – A 12-month, randomized, double-masked, sham-controlled, multicenter study to evaluate the efficacy and safety of 0.5 mg ranibizumab intravitreal injections in patients with visual impairment due to VEGF driven choroidal neovascularization. Protocol CRFB002G2301 (NCT01840410); Principal Investigator	Novartis	2013-2015
SPECTRI – A phase III, multicenter, randomized, double-masked, sham-controlled study to assess the efficacy and safety of lampalizumab administered intravitreally to patients with GA secondary to AMD. Protocol GX29185 (NCT02247531); Principal Investigator	Roche	2015 - Ongoing
AZURE – An Open-label, Randomized, Active-controlled, Parallelgroup, Phase-3b Study of the Efficacy, Safety and Tolerability of 2mg Aflibercept Intravitreal Injections Using Two Different Treatment Regimens to Subjects With Neovascular AMD. Protocol BAY86-5321/16598 (NCT02540954);	Bayer	2015 - Ongoing



PUBLICATIONS

Principal Investigator

Author and co-author of more than 140 articles, chapters and books.

10 Selected Peer-reviewed Publications

1. Silva R, Berta A, Larsen M, Macfadden W, Feller C, Monés J; TREND Study Group. Treat-and-Extend versus Monthly Regimen in Neovascular Age-Related Macular Degeneration: Results with Ranibizumab from the TREND Study. Ophthalmology. 2018 Jan;125(1):57-65. doi: 10.1016/j.ophtha.2017.07.014.

- 2. Colijn JM, Buitendijk GHS, Prokofyeva E, Alves D, Cachulo ML, Khawaja AP, Cougnard-Gregoire A, Merle BMJ, Korb C, Erke MG, Bron A, Anastasopoulos E, Meester-Smoor MA, Segato T, Piermarocchi S, de Jong PTVM, Vingerling JR; EYE-RISK consortium, Topouzis F, Creuzot-Garcher C, Bertelsen G, Pfeiffer N, Fletcher AE, Foster PJ, Silva R, Korobelnik JF, Delcourt C, Klaver CCW; European Eye Epidemiology (E3) consortium. Prevalence of Age-Related Macular Degeneration in Europe: The Past and the Future. Ophthalmology. 2017 Dec;124(12):1753-1763. doi: 10.1016/j. ophtha.2017.05.035.
- 3. Laíns I, Kelly RB, Miller JB, Silva R, Vavvas D, Kim IK, Murta JN, Lasky-Su J, Miller JW, Husain D. Human Plasma Metabolomics Study across All Stages of Age-Related Macular Degeneration Identifies Potential Lipid Biomarkers. Ophthalmology. 2017 Aug 31. pii: S0161-6420(17)31093-X. doi: 10.1016/j.ophtha.2017.08.008. [Epub ahead of print]
- 4. Holz FG, Dugel PU, Weissgerber G, Hamilton R, Silva R, Bandello F, Larsen M, Weichselberger A, Wenzel A, Schmidt A, Escher D, Sararols L, Souied E. Single-Chain Antibody Fragment VEGF Inhibitor RTH258 for Neovascular Age-Related Macular Degeneration: A Randomized Controlled Study. Ophthalmology. 2016 May;123(5):1080-9. doi: 10.1016/j.ophtha.2015.12.030.
- 5. Hogg RE, Silva R, Staurenghi G, Murphy G, Santos AR, Rosina C, Chakravarthy U. Clinical characteristics of reticular pseudodrusen in the fellow eye of patients with unilateral neovascular age-related macular degeneration. Ophthalmology. 2014 Sep;121(9):1748-55. doi: 10.1016/j.ophtha.2014.03.015.
- 6. Silva R, Axer Siegel R, Elden B, Guimer R, Kirchof B, Papp A, Seres A, Gekkieva M, Nieveg A, Pilz S, for the Secure Study Group. The SECURE study: long-term safety of ranibizumab 0.5 mg in neovascular age-related macular degeneration. Ophthalmology. 2013 Jan;120(1):130-9. doi: 10.1016/j.ophtha.2012.07.026.
- 7. Silva R, Ruiz-Moreno JM, Gomez-Ulla F, Montero JA, Gregório T, Luz Cachulo M, Pires I, Cunha-Vaz JG, Murta JN. Photodynamic therapy for chronic central serous chorioretinopathy: a 4-year followup study. Retina. 2013 Feb;33(2):309-15. doi: 10.1097/IAE.0b013e3182670fbe.
- 8. Silva R. Myopic maculopathy: a review. Ophthalmologica. 2012;228(4):197-213. doi: 10.1159/000339893.
- 9. Silva R, Ruiz-Moreno JM, Nascimento JC, Carneiro A, Rosa PC, Barbosa A, Carvalheira F, Faria de Abreu JR, Cunha-Vaz JG. Short-term efficacy and safety of intravitreal ranibizumab for myopic choroidal neovascularization. Retina. 2008 Oct;28(8):1117-23.
- 10. Silva R, Figueira J, Cachulo ML, Duarte L, Faria de Abreu JR, Cunha-Vaz JG. Polypoidal choroidal vasculopathy and photodynamic therapy with verteporfin. Graefes Arch Clin Exp Ophthalmol. 2005;243(10):973-9.

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