Title: Artificial Intelligence and imaging processing in Optical Coherence Tomography and digital images in Uveitis.

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ABSTRACT:

Computer vision, understanded as the area of science that trains computer to interpret digital images through both artificial intelligence (AI) and classical algorithms, has significantly advanced the analysis and interpretation of optical coherence tomography (OCT) in retina research. Its development to assist uveitis diagnosis and prognosis is still undergoing, but important efforts have been made in the field. The automatising of image processing in uveitis could be fundamental to establish objective and standardised outcomes for future clinical trials In addition, it could help to better understand the disease and its progression. The aim of this review is to summarise the recent advances of computer vision in imaging processing in uveitis, with a particular focus in optical coherence tomography images.

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1. INTRODUCTION

The concept of Artificial Intelligence (AI) has always fascinated researchers since the development of initial computers. The proper definition of AI has been part of many discussions.[1] Its origin dates from 1936, when a mathematician, Alan Turing, published his well-known article about “computable numbers”. This article mentioned for the first time the concept of “algorithm”, which establishes the basis of theorical computer science and computers themselves.[2, 3] Later on, in 1950, he wrote the article titled “Computing Machinery and Intelligence” that explains “The Turing Test” which supposedly could determine whether or not a machine is intelligent.[4]

Some years later, in 1956, John McCarthy, recognized as the father of AI, defined it as “the science and engineering of making intelligent machines”.[5] It is currently defined by the Oxford dictionary “as the theory and development of computer systems able to perform tasks normally requiring human intelligence, such as visual perception, speech recognition, decision-making, and translation between languages”.[6]

One of the applications of AI that is increasingly being explored in medicine is machine learning, in particular deep learning. Deep learning techniques permit algorithms, which are organized in multiple processing layers, to “learn” data to provide a particular outcome.[7] These techniques have revolutionized the field of image processing in ophthalmology.[8] Its use is widespread in the retina research with new applications being developed particularly in diabetic retinopathy, age related macular degeneration and optical coherence tomography (OCT) segmentation.[8-10] Although these techniques are still relegate to research domain, they potentially could aid to detect pathology without medical supervision or predict an outcome in a particular patient.

The use of AI techniques is not always necessary to develop algorithms of signal processing and classical algorithms could also be used. In that sense, we could use a

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broader term: “computer vision”, that can use either AI or classical algorithms to observe, analyse, process, and identify patterns from visual data with high speed and accuracy.[11] In other words, “computer vision” is the scientific area that deals with how computers can get high-level understanding from digital images and videos. The aim of this paper is to review the use of AI computer vision in the automatic image processing of uveitides. Those papers referring to the use of the software contained within any commercial device have not been included in this review.

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2. IMAGE PROCESSING IN ANTERIOR SEGMENT OCT.

The current gold-standard method for quantifying anterior chamber (AC) inflammation involves the subjective counting of cells and flare grading through the clinical examination with a slit lamp.[12] Different initiatives have tried to overcome that challenge trying to automatise the AC inflammation score by the OCT imaging processing.

In that sense, several efforts have demonstrated the correlation of the SUN (Standardization of Uveitis Nomenclature) working group AC cells score with the automatic grading using the Image J Particle Analysis algorithm (http://imagej.net/Particle_Analysis) in single b-scans of swept-source (SS) OCT,[13] or ImageIQ (Cleveland, OH, USA) combined with ImagePro Plus (Media Cybernetics, Rockville, MD, USA) platform in B-scans and 3D reconstructions in spectral-domain (SD) OCT,[14] or MATLAB (Mathworks, Natick, MA, USA) in high speed (HS) OCT.[15]

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Apart from clinical cells grading, Invernizzi et al. correlated the aqueous signal intensity using the in-built software of the SS-OCT device, with the laser flare photometry measurements. It showed a positive correlation in active uveitis patients, but no correlation was found in the case of inactive uveitis patients.[16] Lu et al. also added the smoothness of the posterior corneal surface to Invernizzi et al.'s analysis, for which they used an algorithm implemented in MATLAB to calculate the tangent angle of each point of the posterior surface of the cornea, disclosing that the maximum posterior corneal surface smoothness was the best indicator for the diagnosis of uveitis involving the anterior segment according to ROC curve analysis.[17]

Additionally, Kang et al. showed that there was a statistically significant difference in the eccentricity of the anterior chamber cells calculated by an automatic algorithm implemented in Python (Python Software Foundation) among the diagnosis of uveitis, post-surgical inflammation and vitreous haemorrhage, being higher in the latter.[18]

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Equally, Derda-Ozer et al. proposed that the iris pigment optical density measured at the pupillary margin of SD-OCT with ImageJ could be a marker of Fuchs' heterochromic uveitis,[19] while Zarei et al. suggested the iris "smoothness index", which was defined as the ratio between the length of a straight line to the actual length of the boundaries also using Image J in SS-OCT, as a diagnostic feature of iris atrophy in Fuchs' heterochromic uveitis.[20]

3. IMAGE PROCESING IN RETINA AND VITREOUS OCT

3.1 Quantification of vitreous inflammation

Similarly, to the anterior chamber inflammation, the current gold-standard for scoring vitreous inflammation compromise the clinical examination with an indirect ophthalmoscope to compare vitreous haze against a set of standards photographs, being the scale proposed by the National Eye Institute in 1985, the one adopted by the SUN working group.[21] A big effort has been done to try to validate more objective measurements of vitreous inflammation. An example of this effort is the vitreous haze

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scale proposed by the University of Miami, that included 9 steps, 3 more than the one proposed by the National Eye Institute.[22, 23]

Besides, all these "clinical" methods are also affected by the transparency of the lens and anterior segment of the eye, therefore they are not very reliable in those circumstances, and equally are not able to detect small changes in the vitreous inflammation. For overcoming these challenges, several authors have proposed to measure the vitreous intensity using macular OCT scans.

To correct for lens or anterior segment opacities it was proposed to calculate the relative intensity of the vitreous cavity with the intensity of the retinal pigment epithelium (RPE).[24] This study disclosed that the relative vitreous intensity was higher in uveitis eyes with clinical vitreous haze and also this parameter was positively correlated with visual acuity, AC cells clinical score, and AC flare.[24] Later on, the same group proposed to use ratio between vitreous intensity and the mean values below the vitreous (segmenting the inner limiting membrane to use it like the boundary between those two regions) to avoid artefacts in the ratio caused by hyper-reflective areas in the retina that will cause a shadowing in the RPE, but will not affect vitreous reflectivity.[25] This algorithm was initially validated by Montesano et al.[26] Although this study failed to find a difference in vitreous haze between patients with multiple sclerosis and healthy controls, it should be noted that this study did not include patients with active vitreous inflammation at the time of OCT assessment.[25] Initially the OCT image processing was semiautomated, but later on the same group presented a fully automated software named VITAN (from VITreous Analysis software).[27] This software in uveitis patients showed a moderate correlation with clinical vitreous haze scores.[27] Barbosa et al. replicated this approach using ImageJ and similarly obtained a moderate correlation with the clinical vitreous haze score.[28] Zarranz-Ventura et al. showed that the correlation of the OCT measurement with the

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clinical score remained significant when adjusting by factors like AC cells, AC flare, and phakic or vitrectomy status.[29] Terheyden et al. suggested that 3 OCT b-scans could be sufficient to obtain a reliable vitreous intensity automatic measurement, without needing to assess more b-scans.[30] However, all these techniques could have important limitations when used in real world settings as other conditions such as vitreous haemorrhages could be mistaken by inflammation.

3.2 Quantification of choroidal inflammation

The choroidal thickness has been proposed as an important inflammatory biomarker in some forms of uveitis.[31-34] However, the majority of articles referring to choroidal thickness in uveitis use manual segmentation to calculate the thickness.[35-37] Apart from choroidal thickness, an effort has been made to measure the flow attenuation and the vascularity at the level of the choroid. Agrawal et al. proposed the Choroidal Vascularity index (CVI) as an important biomarker in uveitis, described as the ratio of vascular area to the total choroidal area in enhanced deep imaging (EDI)-OCT, for that they manually segmented the choroid with a custom software and after processed it with ImageJ.[38] The CVI has been used as a marker of uveitis activity in different inflammatory choroidal diseases.[39-41]

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4. IMAGE PROCESSING IN OCT-ANGIOGRAPHY

OCT-angiography (OCTA) has been helpful in establishing the pathophysiology of some uveitis entities, such as acute posterior multiple placoid pigment epitheliopathy (APMPPE) or multiple evanescent white dots syndrome (MEWDS) among others.[42-51] Although the current software of the OCTA devices allows the quantification of some parameters, these tools are designed to characterise medical retina pathology and there is still an unmet need in image processing for uveitis entities.

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Wintergerst et al. using ImageJ (and Fiji its expanded version) calculated the vessel density, the skeleton density, vessel diameter and fractal dimension, while the choriocapillaris slabs were analysed for mean signal intensity and kurtosis of signal intensity distribution. This study showed that all the vascular retinal parameter were lower in patients with intermediate uveitis, regardless the presence of macular oedema, while the choriocapillaris showed a greater heterogeneity of perfusion in intermediate uveitis patients.[52] Equally, Kim et al. showed that the vessel density, the skeleton density and fractal dimension of the parafoveal capillaries were lower in the whole uveitic population in comparison with normal subjects.[53]

Regarding choroidal inflammation, Pakzad-Vaezi et al. designed a semiautomated method in MATLAB to segment and measure choriocapillaris flow deficit in serpiginous choroiditis.[54] In addition, McKay et al. proposed an algorithm to automatically identify and measure choroidal inflammatory lesions, with an excellent agreement with experienced human graders.[55] Chu et al. used a similar algorithm to automatically detect the number of choriocapillaris flow deficit/attenuation, and mean size and density of those lesions and showed that patients with posterior involvement uveitis have significant larger areas of flow deficit/attenuation that other uveitis patients without posterior involvement or healthy subjects.[56]

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5. IMAGE PROCESSING IN NON-OCT IMAGES

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Apart from OCT, other imaging modalities play an important role in uveitis and therefore AI and computer vision has also been applied to process these imaging modalities.

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Several authors have proposed algorithms to quantify fluorescein angiography in uveitic patients. However, the majority of authors manually segmented the leakage and ischemic areas.[57, 58] In that sense, Venkat et al. proposed an algorithm previously used in diabetic retinopathy to automatically quantify vascular leakage in ultra-wide-field fluorescein angiography in non-infectious posterior uveitis.[59]

Also, Passaglia et al. proposed the image processing of colour fundus photos to automatically calculate the vitreous haze and compare it with the clinical grading of those pictures.[60] Similarly, Parra et al. developed an AI system to screen for ocular toxoplasmosis in fundus pictures.[61]

6. ARTIFICIAL INTELLIGENCE IN TABULAR DATA SETS

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AI has also been used in uveitis to process clinical data not directly obtained from images. One of the examples is the program named Uvemaster. Uvemaster is a mobile phone application that uses clinical data to obtain the most probable diagnosis.[62]

Recently, the SUN working group used AI to define the criteria of 25 of the most common clinical uveitis diagnoses.[63] The first step was to collect cases of each uveitic entity, the final database included a total of 5766 cases, with about 100-200 cases per entity.[64] Those cases that obtained a 75% or greater consensus among the expert group to belong to a specific entity were selected for training the machine learning tool. The research team combined a training set of multiple approaches on a subset of the cases with a validation set of the performance of the criteria determined on a second subset of the cases. Overall, the AI system categorized over 90% within uveitic class.[65, 66] The final criteria of the 25 uveitic entity were later published. These 25 entities were: spondyloarthritis/HLA-B27-associated anterior uveitis,[67] juvenile idiopathic arthritis-associated chronic anterior uveitis,[68] Fuchs uveitis syndrome,[69] varicella zoster virus anterior uveitis,[70] herpes simplex anterior uveitis,[71] cytomegalovirus anterior uveitis,[72] pars planitis,[73] multiple sclerosis-associated intermediate uveitis,[74] intermediate uveitis non-pars planitis type,[75] Behçet disease uveitis,[76] sarcoidosis-associated uveitis,[77] syphilitic uveitis,[78] tubercular uveitis,[79] serpiginous choroiditis,[80] birdshot choriorretinitis,[81] multifocal choroiditis with panuveitis,[82] punctate inner choroiditis,[83] sympathetic oftalmia,[84] Vogt-Koyanagi-Harada disease,[85] MEWDS,[86] APMPPE,[87] acute retinal necrosis syndrome,[88] toxoplasmic retinitis,[89] cytomegalovirus retinitis,[90] and tubulointerstitial nephritis with uveitis syndrome.[91]

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7. IMAGE PROCESSING IN ANIMAL MODELS

The use of animal models in uveitis has been fundamental to understand pathophysiology and evaluate new treatment strategies.[92] AI and computer vision has also been used in the study of uveitis animal models. Researches also used algorithms to grade AC inflammation with OCT in the case of rat model.[93, 94] Edmond et al. compared the OCT grading in a rabbit model with the clinical SUN score and aqueous cell density using a haemocytometer, showing that the correlation of the OCT score was better with the aqueous cell density than the clinical SUN score.[95] We need to take into account the anatomical differences between animal models and humans in order to extrapolate this techniques to human.

8. MEDICAL RETINA SEGMENTATION TOOLS AND UVEITIS APPLICATIONS

Some of the algorithms developed for OCT analysis in medical retina research could have a potential utility in uveitis. For example, algorithms developed to detect macular ischaemia in OCTA for diabetic retinopathy could be used for the assessment of macular ischaemia in retinal vasculitis.[96] Equally algorithms to conduct automated detection, segmentation, and quantification of macular fluid across exudative macular diseases (age-related macular degeneration, diabetic macular oedema, and/or retinal vein occlusions) could be equally applied to uveitic macular oedema.[97-99] choroidal segmentation has also been refined through AI in medical retina research as well, and as discussed above its use in uveitis could be fundamental in assessing activity of some uveitides.[100, 101] Nevertheless, uveitides have some particularities, like the presence of intraocular inflammation that could obscure retinal structures or reversibility (both functionally and structurally) of some of the lesions, that makes the translation of medical retina segmentation tools to uveitis challenging.

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9. COMPUTER VISION IN THE REAL WORLD

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All these tools are mainly applied in the research setting. However, their influence on treatment and diagnosis needs to be evaluated as well as their impact on the optimisation of the clinical workflow. In fact, in the real world dataset algorithms for diabetic retinopathy have shown to have very good negative predictive values, but the sensibility can vary significantly among algorithms, reaching values close to 50% of sensitivity for some algorithms.[102] Nowadays there are some initiatives to test AI tools in the routine clinical care, as the RAZORBILL study in neovascular age related macular degeneration.[103] Additionally, an attempt to standardise the reporting for clinical trials of artificial intelligence interventions has been published: the SPIRIT AI and CONSORT-AI guidelines.[104]

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10. CONCLUSION

Modern OCT devices incorporate their own image processing tools, and standardization of output metrics, such as central macular thickness. However, it is important to aggregate larger datasets and allow for longitudinal analysis. The use of image processing by computer vision will be fundamental in the development of objective and quantifiable scores of inflammation in uveitis, that could serve as more sensitive markers of disease activity than current SUN score and set more reliable outcomes for clinical trials in uveitides. However larger datasets and real-world experience of this techniques are warranted before its incorporation to the routine clinical care.

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REFERENCES

1. Johnson J, McKee S, Vella A, et al. Artificial intelligence in mathematics. Oxford: Clarendon Press, 1994; x, 328 p.
2. Turing A, Copeland BJ. The essential Turing : seminal writings in computing, logic, philosophy, artificial intelligence, and artificial life plus the secrets of Enigma. Oxford: Oxford University Press,, 2020.
3. Turing A, Ince D. Mechanical intelligence. Amsterdam ; London: North-Holland, 1992; xix, 227 p.
4. Turing AM. Computing machinery and intelligence. Mind 1950;59:433-60.
5. McCarthy J, Lifschitz V. Artificial intelligence and mathematical theory of computation : papers in honor of John McCarthy. Boston ; London: Academic Press, 1991.
6. Knowles E. Oxford dictionary of phrase and fable, 2nd ed. ed. Oxford: Oxford University Press, 2005.
7. LeCun Y, Bengio Y, Hinton G. Deep learning. Nature 2015;521(7553):436-44.
8. Ting DSW, Pasquale LR, Peng L, et al. Artificial intelligence and deep learning in ophthalmology. Br J Ophthalmol 2019;103(2):167-75.
9. Islam MM, Poly TN, Walther BA, et al. Artificial Intelligence in Ophthalmology: A Meta-Analysis of Deep Learning Models for Retinal Vessels Segmentation. J Clin Med 2020;9(4).
10. Moraru AD, Costin D, Moraru RL, Branisteanu DC. Artificial intelligence and deep learning in ophthalmology - present and future (Review). Exp Ther Med 2020;20(4):3469-73.
11. Szeliski R. Computer vision : algorithms and applications. London: Springer, 2011.
12. Jabs DA, Nussenblatt RB, Rosenbaum JT, Standardization of Uveitis Nomenclature Working G. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. Am J Ophthalmol 2005;140(3):509-16.
13. Baghdasaryan E, Tepelus TC, Marion KM, et al. Analysis of ocular inflammation in anterior chamber-involving uveitis using swept-source anterior segment OCT. Int Ophthalmol 2019;39(8):1793-801.
14. Sharma S, Lowder CY, Vasanji A, et al. Automated Analysis of Anterior Chamber Inflammation by Spectral-Domain Optical Coherence Tomography. Ophthalmology 2015;122(7):1464-70.
15. Agarwal A, Ashokkumar D, Jacob S, et al. High-speed optical coherence tomography for imaging anterior chamber inflammatory reaction in uveitis: clinical correlation and grading. Am J Ophthalmol 2009;147(3):413-6 e3.
16. Invernizzi A, Marchi S, Aldigeri R, et al. Objective Quantification of Anterior Chamber Inflammation: Measuring Cells and Flare by Anterior Segment Optical Coherence Tomography. Ophthalmology 2017;124(11):1670-7.
17. Lu M, Wang X, Lei L, et al. Quantitative Analysis of Anterior Chamber Inflammation Using the Novel CASIA2 Optical Coherence Tomography. Am J Ophthalmol 2020;216:59-68.
18. Kang TS, Lee Y, Lee S, et al. Development of fully automated anterior chamber cell analysis based on image software. Sci Rep 2021;11(1):10670.
19. Ozer MD, Kebapci F, Batur M, et al. In vivo analysis and comparison of anterior segment structures of both eyes in unilateral Fuchs' uveitis syndrome. Graefes Arch Clin Exp Ophthalmol 2019;257(7):1489-98.
20. Zarei M, KhaliliPour E, Ebrahimiadib N, Riazi-Esfahani H. Quantitative Analysis of the Iris Surface Smoothness by Anterior Segment Optical Coherence Tomography in Fuchs Uveitis. Ocul Immunol Inflamm 2020:1-6.
21. Nussenblatt RB, Palestine AG, Chan CC, Roberge F. Standardization of vitreal inflammatory activity in intermediate and posterior uveitis. Ophthalmology 1985;92(4):467-71.
22. Madow B, Galor A, Feuer WJ, et al. Validation of a photographic vitreous haze grading technique for clinical trials in uveitis. Am J Ophthalmol 2011;152(2):170-6 e1.

23. Davis JL, Madow B, Cornett J, et al. Scale for photographic grading of vitreous haze in uveitis. Am J Ophthalmol 2010;150(5):637-41 e1.
24. Keane PA, Karampelas M, Sim DA, et al. Objective measurement of vitreous inflammation using optical coherence tomography. Ophthalmology 2014;121(9):1706-14.
25. Coric D, Ometto G, Montesano G, et al. Objective quantification of vitreous haze on optical coherence tomography scans: no evidence for relationship between uveitis and inflammation in multiple sclerosis. Eur J Neurol 2020;27(1):144-e3.
26. Montesano G, Way CM, Ometto G, et al. Optimizing OCT acquisition parameters for assessments of vitreous haze for application in uveitis. Sci Rep 2018;8(1):1648.
27. Keane PA, Balaskas K, Sim DA, et al. Automated Analysis of Vitreous Inflammation Using Spectral-Domain Optical Coherence Tomography. Transl Vis Sci Technol 2015;4(5):4.
28. Barbosa J, Syeda S, Rodriguez-Torres Y, et al. Quantifying vitreous inflammation in uveitis: an optical coherence tomography prospective study. Can J Ophthalmol 2020;55(5):352-8.
29. Zarranz-Ventura J, Keane PA, Sim DA, et al. Evaluation of Objective Vitritis Grading Method Using Optical Coherence Tomography: Influence of Phakic Status and Previous Vitrectomy. Am J Ophthalmol 2016;161:172-80 e1-4.
30. Terheyden JH, Ometto G, Montesano G, et al. Automated quantification of posterior vitreous inflammation: optical coherence tomography scan number requirements. Sci Rep 2021;11(1):3271.
31. Yan H, Li J, Zhang J, Yang L. Retinal and Choroidal Thickness in Patients with Uveitis. Ocul Immunol Inflamm 2017;25(2):202-9.
32. Fabro F, Herbort CP. Need for Quantitative Measurement Methods for Posterior Uveitis: Comparison of Dual FA/ICGA Angiography, EDI-OCT Choroidal Thickness and SUN Vitreous Haze Evaluation in Stromal Choroiditis. Klin Monbl Augenheilkd 2018;235(4):424-35.
33. Nishisho R, Kusuhara S, Sotani N, et al. Changes in choroidal imaging parameters following adalimumab therapy for refractory noninfectious uveitis. Graefes Arch Clin Exp Ophthalmol 2021;259(5):1273-80.
34. Takahashi H, Takase H, Ishizuka A, et al. Choroidal thickness in convalescent vogt-koyanagi-harada disease. Retina 2014;34(4):775-80.
35. Szepessy Z, Barsi A, Kranitz K, Nagy ZZ. The Evolution of Central Retinal and Choroidal Thickness in Acute Anterior Uveitic Patients with Spondyloarthropathy. J Ophthalmol 2018;2018:9136017.
36. Karampelas M, Sim DA, Keane PA, et al. Choroidal assessment in idiopathic panuveitis using optical coherence tomography. Graefes Arch Clin Exp Ophthalmol 2013;251(8):2029-36.
37. Mehta H, Sim DA, Keane PA, et al. Structural changes of the choroid in sarcoid- and tuberculosis-related granulomatous uveitis. Eye (Lond) 2015;29(8):1060-8.
38. Agrawal R, Salman M, Tan KA, et al. Choroidal Vascularity Index (CVI)--A Novel Optical Coherence Tomography Parameter for Monitoring Patients with Panuveitis? PLoS One 2016;11(1):e0146344.
39. Agrawal R, Ding J, Sen P, et al. Exploring choroidal angioarchitecture in health and disease using choroidal vascularity index. Prog Retin Eye Res 2020;77:100829.
40. Agarwal A, Agrawal R, Khandelwal N, et al. Choroidal Structural Changes in Tubercular Multifocal Serpiginoid Choroiditis. Ocul Immunol Inflamm 2018;26(6):838-44.
41. Liu S, Du L, Zhou Q, et al. The Choroidal Vascularity Index Decreases and Choroidal Thickness Increases in Vogt-Koyanagi-Harada Disease Patients During a Recurrent Anterior Uveitis Attack. Ocul Immunol Inflamm 2018;26(8):1237-43.
42. Spaide RF, Fujimoto JG, Waheed NK, et al. Optical coherence tomography angiography. Prog Retin Eye Res 2018;64:1-55.
43. Invernizzi A, Cozzi M, Staurenghi G. Optical coherence tomography and optical coherence tomography angiography in uveitis: A review. Clin Exp Ophthalmol 2019;47(3):357-71.

44. Burke TR, Chu CJ, Salvatore S, et al. Application of OCT-angiography to characterise the evolution of chorioretinal lesions in acute posterior multifocal placoid pigment epitheliopathy. Eye (Lond) 2017;31(10):1399-408.
45. Pepple KL, Chu Z, Weinstein J, et al. Use of En Face Swept-Source Optical Coherence Tomography Angiography in Identifying Choroidal Flow Voids in 3 Patients With Birdshot Chorioretinopathy. JAMA Ophthalmol 2018;136(11):1288-92.
46. Hernanz I, Horton S, Burke TR, et al. Acute Macular Neuroretinopathy Phenotype in Behcet's Disease. Ophthalmic Surg Lasers Imaging Retina 2018;49(8):634-8.
47. Casalino G, Arrigo A, Romano F, et al. Acute macular neuroretinopathy: pathogenetic insights from optical coherence tomography angiography. Br J Ophthalmol 2019;103(3):410-4.
48. Pichi F, Srvivastava SK, Chexal S, et al. EN FACE OPTICAL COHERENCE TOMOGRAPHY AND OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY OF MULTIPLE EVANESCENT WHITE DOT SYNDROME: New Insights Into Pathogenesis. Retina 2016;36 Suppl 1:S178-S88.
49. Mandadi SKR, Agarwal A, Aggarwal K, et al. Novel Findings on Optical Coherence Tomography Angiography in Patients with Tubercular Serpiginous-Like Choroiditis. Retina 2017;37(9):1647-59.
50. Agarwal A, Aggarwal K, Deokar A, et al. Optical Coherence Tomography Angiography Features of Paradoxical Worsening in Tubercular Multifocal Serpiginoid Choroiditis. Ocul Immunol Inflamm 2016;24(6):621-30.
51. Aggarwal K, Agarwal A, Mahajan S, et al. The Role of Optical Coherence Tomography Angiography in the Diagnosis and Management of Acute Vogt-Koyanagi-Harada Disease. Ocul Immunol Inflamm 2018;26(1):142-53.
52. Wintergerst MWM, Pfau M, Muller PL, et al. Optical Coherence Tomography Angiography in Intermediate Uveitis. Am J Ophthalmol 2018;194:35-45.
53. Kim AY, Rodger DC, Shahidzadeh A, et al. Quantifying Retinal Microvascular Changes in Uveitis Using Spectral-Domain Optical Coherence Tomography Angiography. Am J Ophthalmol 2016;171:101-12.
54. Pakzad-Vaezi K, Khaksari K, Chu Z, et al. Swept-Source OCT Angiography of Serpiginous Choroiditis. Ophthalmol Retina 2018;2(7):712-9.
55. McKay KM, Chu Z, Kim JB, et al. Automated Quantification of Choriocapillaris Lesion Area in Patients with Posterior Uveitis. Am J Ophthalmol 2021.
56. Chu Z, Weinstein JE, Wang RK, Pepple KL. Quantitative Analysis of the Choriocapillaris in Uveitis Using En Face Swept-Source Optical Coherence Tomography Angiography. Am J Ophthalmol 2020;218:17-27.
57. Pecen PE, Petro KF, Baynes K, et al. Peripheral Findings and Retinal Vascular Leakage on Ultra-Widefield Fluorescein Angiography in Patients with Uveitis. Ophthalmol Retina 2017;1(5):428-34.
58. Karampelas M, Sim DA, Chu C, et al. Quantitative analysis of peripheral vasculitis, ischemia, and vascular leakage in uveitis using ultra-widefield fluorescein angiography. Am J Ophthalmol 2015;159(6):1161-8 e1.
59. Venkat AG, Sharma S. Automated measurement of leakage on wide-field angiography in the assessment of retinal vasculitis. J Ophthalmic Inflamm Infect 2020;10(1):4.
60. Passaglia CL, Arvaneh T, Greenberg E, et al. Automated Method of Grading Vitreous Haze in Patients With Uveitis for Clinical Trials. Transl Vis Sci Technol 2018;7(2):10.
61. Parra R, Ojeda V, Vazquez Noguera JL, et al. Automatic Diagnosis of Ocular Toxoplasmosis from Fundus Images with Residual Neural Networks. Stud Health Technol Inform 2021;281:173-7.
62. Gegundez-Fernandez JA, Fernandez-Vigo JI, Diaz-Valle D, et al. Uvemaster: A Mobile App-Based Decision Support System for the Differential Diagnosis of Uveitis. Invest Ophthalmol Vis Sci 2017;58(10):3931-9.

63. Trusko B, Thorne J, Jabs D, et al. The Standardization of Uveitis Nomenclature (SUN) Project. Development of a clinical evidence base utilizing informatics tools and techniques. Methods Inf Med 2013;52(3):259-65, S1-6.
64. Jabs DA, Dick A, Doucette JT, et al. Interobserver Agreement Among Uveitis Experts on Uveitic Diagnoses: The Standardization of Uveitis Nomenclature Experience. Am J Ophthalmol 2018;186:19-24.
65. Van Gelder RN, Sen HN, Tufail A, Lee AY. Here Comes the SUN (Part 2): Standardization of Uveitis Nomenclature for Disease Classification Criteria. Am J Ophthalmol 2021.
66. Standardization of Uveitis Nomenclature Working G. Development of Classification Criteria for the Uveitides. Am J Ophthalmol 2021;228:96-105.
67. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Spondyloarthritis/HLA-B27-Associated Anterior Uveitis. Am J Ophthalmol 2021;228:117-25.
68. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Juvenile Idiopathic Arthritis-Associated Chronic Anterior Uveitis. Am J Ophthalmol 2021;228:192-7.
69. Working Group T, Jabs DA, Acharya NR, et al. Classification criteria for Fuchs uveitis syndrome. Am J Ophthalmol 2021.
70. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Varicella Zoster Virus Anterior Uveitis. Am J Ophthalmol 2021;228:165-73.
71. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Herpes Simplex Virus Anterior Uveitis. Am J Ophthalmol 2021;228:231-6.
72. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Cytomegalovirus Anterior Uveitis. Am J Ophthalmol 2021;228:89-95.
73. The Standardization Of Uveitis Nomenclature Sun Working G, Jabs DA, Denniston AK, et al. Classification criteria for pars planitis. Am J Ophthalmol 2021.
74. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Multiple Sclerosis-Associated Intermediate Uveitis. Am J Ophthalmol 2021;228:72-9.
75. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Intermediate Uveitis, Non-Pars Planitis Type. Am J Ophthalmol 2021;228:159-64.
76. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Behcet Disease Uveitis. Am J Ophthalmol 2021;228:80-8.
77. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Sarcoidosis-Associated Uveitis. Am J Ophthalmol 2021;228:220-30.
78. Jabs DA, Belfort R, Jr., Bodaghi B, et al. Classification Criteria for Syphilitic Uveitis. Am J Ophthalmol 2021;228:182-91.
79. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Tubercular Uveitis. Am J Ophthalmol 2021;228:142-51.
80. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Serpiginous Choroiditis. Am J Ophthalmol 2021;228:126-33.
81. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Birdshot Chorioretinitis. Am J Ophthalmol 2021;228:65-71.
82. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Multifocal Choroiditis With Panuveitis. Am J Ophthalmol 2021;228:152-8.
83. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Punctate Inner Choroiditis. Am J Ophthalmol 2021.
84. Standardization of Uveitis Nomenclature Working G. ClassificationCriteriaforSympatheticOphthalmia. Am J Ophthalmol 2021;228:212-9.
85. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Vogt-Koyanagi-Harada Disease. Am J Ophthalmol 2021;228:205-11.
86. Standardization of Uveitis Nomenclature Working G. Classification Criteria For Multiple Evanescent White Dot Syndrome. Am J Ophthalmol 2021;228:198-204.
87. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Acute Posterior Multifocal Placoid Pigment Epitheliopathy. Am J Ophthalmol 2021;228:174-81.

88. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Acute Retinal Necrosis Syndrome. Am J Ophthalmol 2021;228:237-44.
89. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Toxoplasmic Retinitis. Am J Ophthalmol 2021;228:134-41.
90. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Cytomegalovirus Retinitis. Am J Ophthalmol 2021;228:245-54.
91. Standardization of Uveitis Nomenclature Working G. Classification Criteria for Tubulointerstitial Nephritis With Uveitis Syndrome. Am J Ophthalmol 2021;228:255-61.
92. Caspi RR. Understanding autoimmune uveitis through animal models. The Friedenwald Lecture. Invest Ophthalmol Vis Sci 2011;52(3):1872-9.
93. Pepple KL, Choi WJ, Wilson L, et al. Quantitative Assessment of Anterior Segment Inflammation in a Rat Model of Uveitis Using Spectral-Domain Optical Coherence Tomography. Invest Ophthalmol Vis Sci 2016;57(8):3567-75.
94. Choi WJ, Pepple KL, Wang RK. Automated three-dimensional cell counting method for grading uveitis of rodent eye in vivo with optical coherence tomography. J Biophotonics 2018;11(9):e201800140.
95. Edmond M, Yuan A, Bell BA, et al. The Feasibility of Spectral-Domain Optical Coherence Tomography Grading of Anterior Chamber Inflammation in a Rabbit Model of Anterior Uveitis. Invest Ophthalmol Vis Sci 2016;57(9):OCT184-8.
96. Yang D, Sun Z, Shi J, et al. A multi-task deep-learning system for assessment of diabetic macular ischemia on optical coherence tomography angiography images. Retina 2021.
97. Schmidt-Erfurth U, Vogl WD, Jampol LM, Bogunovic H. Application of Automated Quantification of Fluid Volumes to Anti-VEGF Therapy of Neovascular Age-Related Macular Degeneration. Ophthalmology 2020;127(9):1211-9.
98. Moraes G, Fu DJ, Wilson M, et al. Quantitative Analysis of OCT for Neovascular Age-Related Macular Degeneration Using Deep Learning. Ophthalmology 2021;128(5):693-705.
99. De Fauw J, Ledsam JR, Romera-Paredes B, et al. Clinically applicable deep learning for diagnosis and referral in retinal disease. Nat Med 2018;24(9):1342-50.
100. Masood S, Fang R, Li P, et al. Automatic Choroid Layer Segmentation from Optical Coherence Tomography Images Using Deep Learning. Sci Rep 2019;9(1):3058.
101. Kugelman J, Alonso-Caneiro D, Read SA, et al. Automatic choroidal segmentation in OCT images using supervised deep learning methods. Sci Rep 2019;9(1):13298.
102. Lee AY, Yanagihara RT, Lee CS, et al. Multicenter, Head-to-Head, Real-World Validation Study of Seven Automated Artificial Intelligence Diabetic Retinopathy Screening Systems. Diabetes Care 2021;44(5):1168-75.
103. Holz FG, Abreu-Gonzalez R, Bandello F, et al. Does real-time artificial intelligence-based visual pathology enhancement of three-dimensional optical coherence tomography scans optimise treatment decision in patients with nAMD? Rationale and design of the RAZORBILL study. Br J Ophthalmol 2021.
104. Ibrahim H, Liu X, Rivera SC, et al. Reporting guidelines for clinical trials of artificial intelligence interventions: the SPIRIT-AI and CONSORT-AI guidelines. Trials 2021;22(1):11.