Deep Learning Artificial Intelligence Evaluation of Optical Coherence Tomography Scans in a Non-infectious Pan-uveitis Cohort

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Abstract

BACKGROUND: To evaluate Deep Learning (DL) Artificial Intelligence (AI) application to optical coherence tomography scans of non-infectious pan-uveitis patients.

METHODS: Consecutive patients with non-infectious pan-uveitis were included in the study if they had an OCT scan (Zeiss, Germany) of the macula. Inflammation was graded on the Nussenblatt scoring system by a uveitis specialist. A DL AI system developed using Python 3.9 and open source TensorFlow software was then trained to classify inflammation as high, low, or none. Performance was assessed by AUC scores. Training to cross-validation used an 80:20 split with 2000 iterations in all evaluations.

RESULTS: 154 scans of 52 patients were analyzed. 38 (70.4%) of patients were female and the mean age of participants was 50.3 ± 15.5 years. 58 (37.7%) of OCT scans were graded as no inflammation, 61 (39.6%) scans as mild inflammation, and 35 (22.7%) scans as high inflammation. The AUC for OCT images was 0.830 (CI95: 0.784 to 0.876).

CONCLUSION: Deep Learning AI can be applied in the grading of non-infectious pan-uveitis OCT scans in a precise manner.

Introduction

The field of Artificial Intelligence (AI) applied to image recognition, colloquially known as Deep Learning (DL), has shown considerable promise when applied to various medical tasks.[1,2,3] Ophthalmology as a medical specialty, with its reliance on high precision imaging modalities for both diagnosis and monitoring of disease progression, is particularly amicable to DL AI initiatives. Application of AI initiatives have already been implemented for multiple ophthalmic conditions including glaucoma[4], Age Related Macular Degeneration[5], Retinopathy of Prematurity[6], and ptosis[7] with a high degree of precision.

Uveitis, a disease characterized by iris, ciliary body, or choroidal inflammation, is in need of a reliable and quantifiable metric of disease severity. At present, one of the gold standards for quantifying vitreous inflammation is the Nussenblatt scale; an ordinal metric that ranges from 0 to 4 using indirect ophthalmoscopy.[8] In spite of rigid grading criteria, Nussenblatt scoring is only moderately reliable (□ = 0.53) and highly rater dependent.[9] Recent work has demonstrated that Optical Coherence Tomography (OCT) scans of pan-uveitis patients can be analyzed in such a manner as to reliably correlate with both Nussenblatt scoring and visual impairment as captured by the National Eye Institute condensed Visual Function Questionnaire.[10] The signal to noise ratio of disease manifestation captured by OCT may be amenable to DL AI application for a precise gradation of uveitis extent. Herein, we seek to determine if DL AI may be applied to OCT scans in the non-infectious pan-uveitis population to precisely quantify disease extent.

Methods

Consecutive patients seen at Kresge Eye Institute from December 9th, 2021 to April 26th, 2022 with non-infectious pan-uveitis were included in the study if they had OCT scans taken at a given visit within the study timeframe, a vision greater than no light perception, and the extent of uveitis was graded by a uveitis specialist using the Nussenblatt scale. Patients were excluded from the study if they had a known infectious etiology for their uveitis or if they had prior surgery in the study eye. IRB approval was obtained from the local institution's ethics board (20-12-4279). This study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice. Patient age, sex, eye, visual acuity (VA) in LogMAR units, were recorded as was OCT signal strength. Use of immunosuppressive agents at the time of visit was documented as either biological disease modifying anti-rheumatic drugs (DMARDs), non-biological DMARS, oral steroids, or steroid drops.

OCT scans were obtained using the Zeiss (Cirrus HD-OCT, Carl Zeiss Meditec Inc., Dublin, CA) Macular Cube 512x128 scans centered on the fovea. Both *en face* foveal thickness and a single B scan centred through the fovea were extracted for each distinct visit for each eye and saved as a jpg file (See Fig. 1).

Image of right eye in patient with Grade II Vitreous Inflammation

A DL AI system developed using Python 3.9 and open source TensorFlow software was then trained to recognize images as either no inflammation, (Nussenblatt score of 0), low inflammation (Nussenblatt score of 0.5 to 1), and high inflammation (Nussenblatt score of 2,3, or 4). Performance was assessed by AUC scores. Training to cross-validation used an 80:20 split with 2000 iterations in all evaluations.

Statistical Analysis

Continuous variables were summarized and means and standard deviation while categorical variables were summarized and percentages and counts. The AUC with 95% confidence interval was calculated to assess the accuracy of the DL models.

Results

52 patients with 154 unique image sets were included in the study. 38 (70.4%) of patients were female and the mean age of participants was 50.3 ± 15.5 years. 58 (37.7%) (See Table 1). Mean visual acuity was 0.563 ± 0.627 LogMAR. OCT image quality was 7.17 ±2.63 units. 58 (37.7%) of OCT scans were graded as no inflammation, 61 (39.6%) scans as mild inflammation, and 35 (22.7%) scans as high inflammation. Half (50.0%) of the study cohort had pan-uveitis from an unknown etiology while the remainder of participants had a diagnosis of Sarcoidosis (28.8%), HLAB27 genotype (7.7%) Systemic Lupus Erythematosus or juvenile idiopathic arthritis (7.7%), Crohn's disease or Ulcerative Colitis (5.8%), Rheumatoid Arthritis, Vogt-Koyanagi-Harada syndrome, and Blau Syndrome. The AUC for uveitis score of none, low, or high inflammation from OCT images was 0.830 (CI95: 0.784 to 0.876).

Table 1. Demographics and Baseline Characteristics

Variable	Mean	Standard Deviation
Age	50.25 (years)	15.5 (years)
LogMAR Visual Acuity	0.563	0.627
OCT Signal Strength	7.17 out of 10	2.63
	Count	Frequency
Sex		
Male	16	29.6%
Female	38	70.4%
Diagnosis		
Idiopathic	21	50.0%
Sarcoidosis	15	28.8%
HLAB27	4	7.7%
SLE/JIA	4	7.7%
Crohn’s/Ulcerative Colitis	3	5.8%
Other (VKH, Blau’s, RA)	5	9.6%
Cell Grading		
Grade 0	58	37.7%
Grade 0.5	41	26.6%
Grade 1	20	13.0%
Grade 2	20	13.0%
Grade 3	11	7.1%
Grade 4	4	2.6%
Medications		
DMARDs (non-biologicals)		58.6%
DMARDS (biologicals)		15.7%
Oral Steroids		42.9%
Topical Steroids (gtts)		80.0%

Discussion

Uveitis represents a significant cause of morbidity and blindness in the working age population. Some 35% of uveitis patients become clinically blind.[11] Progression in developing appropriate therapeutics agents to treat uveitis is limited by conventional metrics of assessing disease state. When rater reliability is poor, its use as a sufficiently discriminatory measure in a trial endpoint is compromised resulting in an increased likelihood of Type II error.[12]

Much progress could be made in our understanding and alleviation of uveitis first by developing a more sensitive and valid measure of disease state. Here, DL AI holds promise. To the best of our knowledge, this is the first study to date to evaluate precision of AI assisted grading of OCT scans in a non-infectious pan-uveitis cohort. We found the AUC of an AI DL model classifying uveitis as none, low, and high on OCT scans relative to convention grading methods to be 0.830 (CI95: 0.784 to 0.876). AUC between 0.8 and 0.9 are generally considered excellent in discriminating into categories. Such finding are comparable to other attempts to segment and automate vitreous inflammation.[13] Future work will focus on expanding scale sensitivity and validating DL AI grading of the non-infectious pan-uveitis disease process.

Declarations

Meeting Presentations

None

Financial Support

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Conflict of Interest

No conflicting relationship exists for any of the authors.

Ethical approval and consent to participate

IRB approval was obtained from the institutional ethics review board and approved under study number 20-12-4279. This study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice

Consent for publication

Not applicable retrospective study design

Availability of data and materials

The authors ensure the integrity of the data and it is available upon request

Competing interests

None of the authors have competing interests to declare

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Authors' contributions

JB and PZ contributed to manuscript writing, study design, and analysis. PG, KL, and XL contributed to study design and manuscript review

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Not applicable

Authors' information (Optional)

Not applicable

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Figures

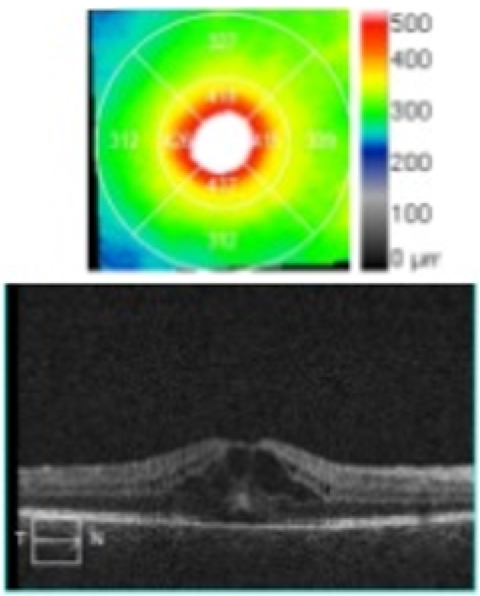

Figure 1

Optical Coherence Tomography *en face* Image and B Scan Segmented for Deep Learning Analysis