Visualizing Age-Related Macular Degeneration

A white paper -- Deploying the Crowd and Human Computational Gaming to Train an Algorithm to Analyze Optical Coherence Tomography Scans to Diagnose and Track Treatment Effectiveness of Age-Related Macular Degeneration

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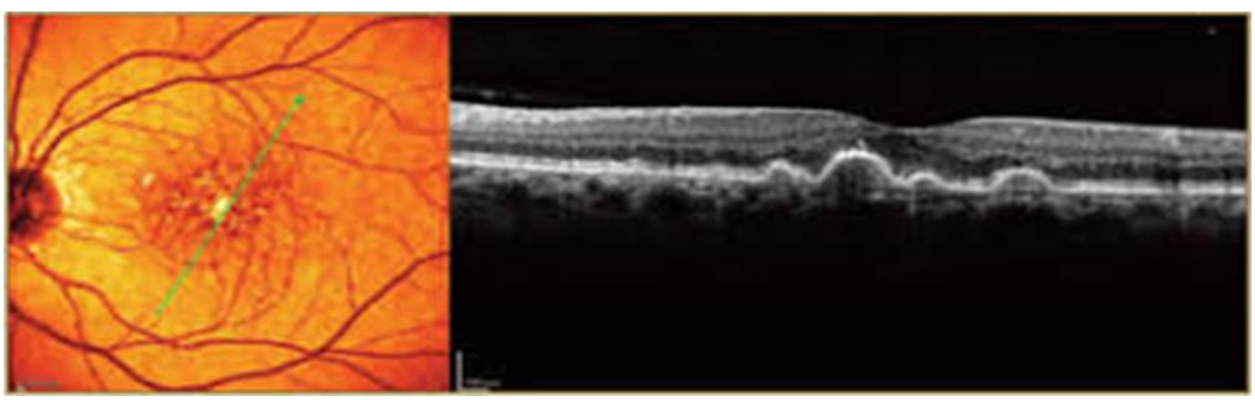
TABLE OF CONTENTS

INTRODUCTION

Age-related macular degeneration (AMD) is a disease of the retina for which there is no cure. It is the leading cause of vision impairment across the globe in those aged 50 and older. Optical coherence tomography (OCT) is a non-invasive imaging method that allows researchers and clinicians to identify the disease and track treatment effectiveness. Though automated tools to analyze OCT retinal scans are available, human evaluators are needed to confirm and modify the images before they can be used for diagnosis or treatment[i]. Referral of these scans to reading centers is time-consuming, expensive, and inefficient. In partnership with researchers from Southern Methodist University (SMU) Guildhall, Johns Hopkins University, and The Retina Foundation Southwest, BALANCED Media | Technology® (BALANCED) deployed its HEWMEN® platform behind an online video game built around OCT retinal scans to facilitate human guided artificial intelligence (AI) to train machine learning (ML) to improve an automated algorithm used to diagnose and track treatment effectiveness of AMD.

ABSTRACT

Working with researchers from SMU Guildhall and The Retina Foundation Southwest, BALANCED created an online video game that incorporated OCT retinal scan images into the game's environment. In the background, BALANCED deployed its HEWMEN platform to facilitate human guided AI to train ML to improve an automated algorithm used to diagnose and track treatment effectiveness of AMD. The players had no training to read or interpret OCT scans, but rather the game reinforced desired actions and results through usual gameplay mechanics of context and reward. Through this gameplay, BALANCED provided human guidance as an additional input to AI to train an existing image evaluation tool. Our research shows that despite the use of a small dataset, we can significantly improve the algorithm's image evaluation quality and robustness, with improvement in both accuracy and precision.



PROBLEM STATEMENT

Age related macular degeneration is a leading cause of blindness worldwide with more than 20% of the world's population likely afflicted[ii]. Currently, no cure exists, but treatment modalities are available and continue to emerge. Critical to slowing disease progression of AMD is the identification of those at risk for disease, early diagnosis, and the ability to track treatment effectiveness. Optical coherence tomography is a diagnostic tool shown to be effective in each of these areas. In the study of eye disease, OCT is the optical equivalent of ultrasound imaging. It is a non-invasive, painless imaging technique that uses light instead of sound to produce an image of the retina of the eye. During an OCT scan, a dim, short wavelength beam of light is directed through the pupil toward the retina. By measuring the scattering of the light, a cross-sectional image of the various layers of the retina, in particular the retinal pigment epithelium (RPE) and Bruch's membrane, is obtained and disease state can be evaluated[iii]. Certain features identified by OCT are predictive of those persons who are at greater risk for developing AMD. Those persons are then evaluated frequently with OCT and therapy initiated early in the course of the disease should it develop. Those diagnosed with AMD are followed by OCT scans to monitor disease progression and effectiveness of treatment to guide therapy.

In evaluating AMD, the OCT scan detects retinal thickening, abnormal blood vessel creation (neovascularization), and retinal anomalies called drusen. Drusen are either hard (low risk of disease) or soft (precursors of AMD)[iv] and can be differentiated via OCT. Optical coherence tomography scans the macular region of the retina to identify drusen and other pathology to predict, diagnose and track progression of disease and treatment effectiveness. Unfortunately, artifacts inherent in OCT scans detract from the precision of the technology. Optical coherence tomography artifacts can be patient related, operator-related, and / or software related. Patient and operator related artifacts can generally be controlled at the point of care (POC) during the scanning procedure. Inevitable software-related errors, however, are most common and must be addressed post-exam. Optical coherence tomography image analysis is automated via computer software algorithms. Software-related artifacts are mostly due to failed segmentation algorithms resulting in misidentification of inner and outer retinal boundaries, resulting in incomplete segmentation artifact[v]. Artifact secondary to segmentation failure occurs commonly in the evaluation of AMD. As these artifacts cannot be mitigated at the POC, subsequent manual adjustment of retinal segmentations by experts is required to correct the errors[vi]. Problems inherent in referral of these scans to the limited number of reading centers available for such manual correction include time-delay, expense, and inefficiency related to interoperator variability.

> Optical coherence tomography has become the most popular ophthalmologic imaging tool in use and is anticipated to grow significantly as the world's population ages. Though automation exist to analyze OCT scans, the tools are flawed as training of the algorithms is limited. New methods of training that can be effective using small data sets are needed to address these deficits, making automation accurate and efficient to meet the increased demand of OCT technology[vii]

BACKGROUND

Crowdsourcing and Citizen Science

From the early 20th century, researchers in the field of Collective Intelligence have shown that groups can outperform individuals when making decisions and predictions[viii]. A classic example is Sir Francis Galton's county fair experiment of 1907. Galton collected 800 cards from individuals who had participated in an ox weight-judging competition. Of the contestants, Galton wrote: "The competitors included butchers and farmers, some of whom were highly expert in judging the weight of cattle; others were probably guided by such information as they might pick up, and by their own fancies". The mean of 787 of those predictions (13 were illegible or otherwise defective) overestimated the actual weight by only nine pounds[ix].

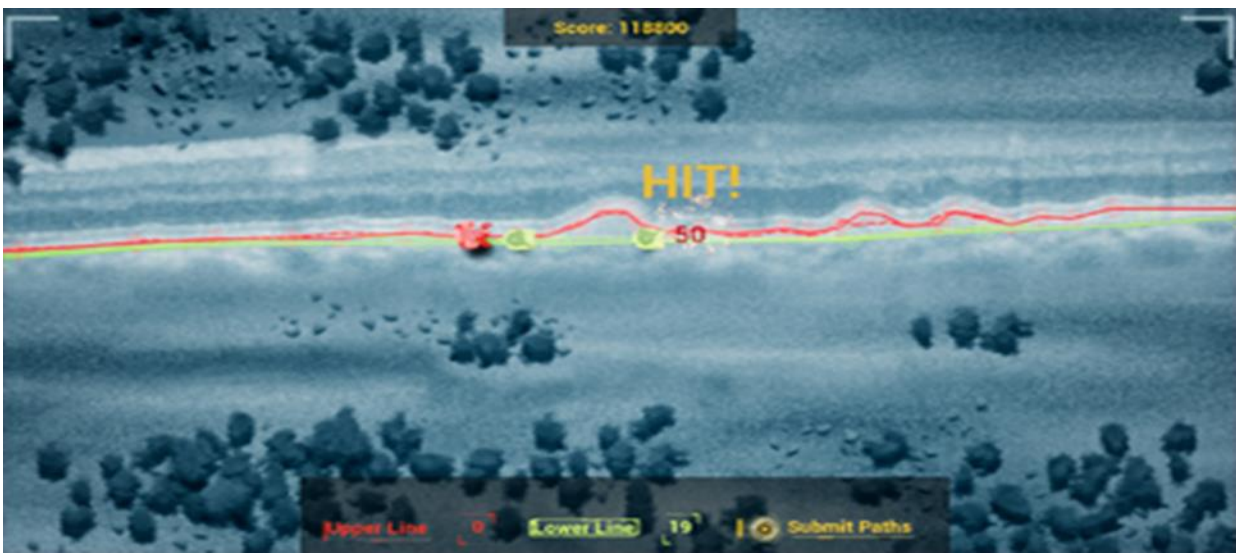
Crowdsourcing

Since Galton's experiment, fundamentally better ways to harness the intelligence of human groups have emerged. Crowdsourcing involves participants taking an active role in the tasks performed or supporting long-running computations in which tasks and results may be exchanged during intermittent connections[x]. Crowdsourcing is used in citizen science projects, where members of the public contribute to research despite not being formally trained experts in the topic of study[xi]. It is exactly these citizen scientists, particularly gamers, that BALANCED recruits for its projects. A recent notable example of crowdsourcing is SETI @ Home. SETI @ home, currently in hibernation, is a scientific experiment based at UC Berkeley. It uses internet-connected computers in the search for extraterrestrial intelligence (SETI). Volunteers run a program on their computer that downloads and analyzes radio telescope data. SETI @ home has been in operation for 20 years and more than 5.2 million people have participated in the project worldwide[xii].

Human Computational Gaming

Human computational gaming (HCG) has been used by researchers as a tool of human computing (HC). Gaming by its nature keeps players engaged, thereby providing long-term and enthusiastic participation. A notable example of HCG is Foldit. A game out of the University of Washington's center for Game Science in collaboration with the Department of Biochemistry, Foldit successfully used gamers to solve an HIV protein folding problem in three weeks that had eluded researchers for 15 years[xiii]. Though successful for their intended purposes, games for science have not been commercially successful or scientifically scalable as they are designed for a single problem alone. Clark, et. al. (2018) proposed a remedy in which scientist construct data into a five-step analysis structure that aligns with the game play loop in commercial video games[xiv]. This makes games for science scalable and portable to many different applications, being that they become problem and data agnostic.

At BALANCED, our mission is to bring purpose to play. We accomplish this by connecting the gaming community to data-centric problems, allowing us to crowdsource AI innovation through online gaming. Through HEWMEN, our proprietary technology, we have woven together the joy of play, the reward of problem solving, and the power of community to crowdsource real-world results. HEWMEN is an interactive AI platform designed to augment or enhance the work of ML and data science professionals through the selective inclusion of human intelligence in the training, operation, and refinement of ML models and the mining of data. By combining gamers' unstructured problem-solving skills with raw computational power, the HEWMEN Platform provides for improved model accuracy and precision while reducing model size, lowering computational requirements, and leveraging small data sets. The result of this human-centric approach is a refocusing of ML and data science talent towards model deployment and extracting insights and away from manipulating data. The HEWMEN Platform enables the worldwide gaming community to 'play out the problem' through specially designed game interfaces that are embedded with real-world data.



SOLUTION

In partnership with SMU Guildhall and The Retina Foundation Southwest, BALANCED deployed its HEWMEN platform behind an online video game, Eye in the Sky Defender (ESD), that was built around OCT retinal scans. ESD and HEWMEN combine HCG with distributed computing to facilitate human guided AI to train machine learning to improve an automated algorithm used to diagnose and track treatment effectiveness of AMD.

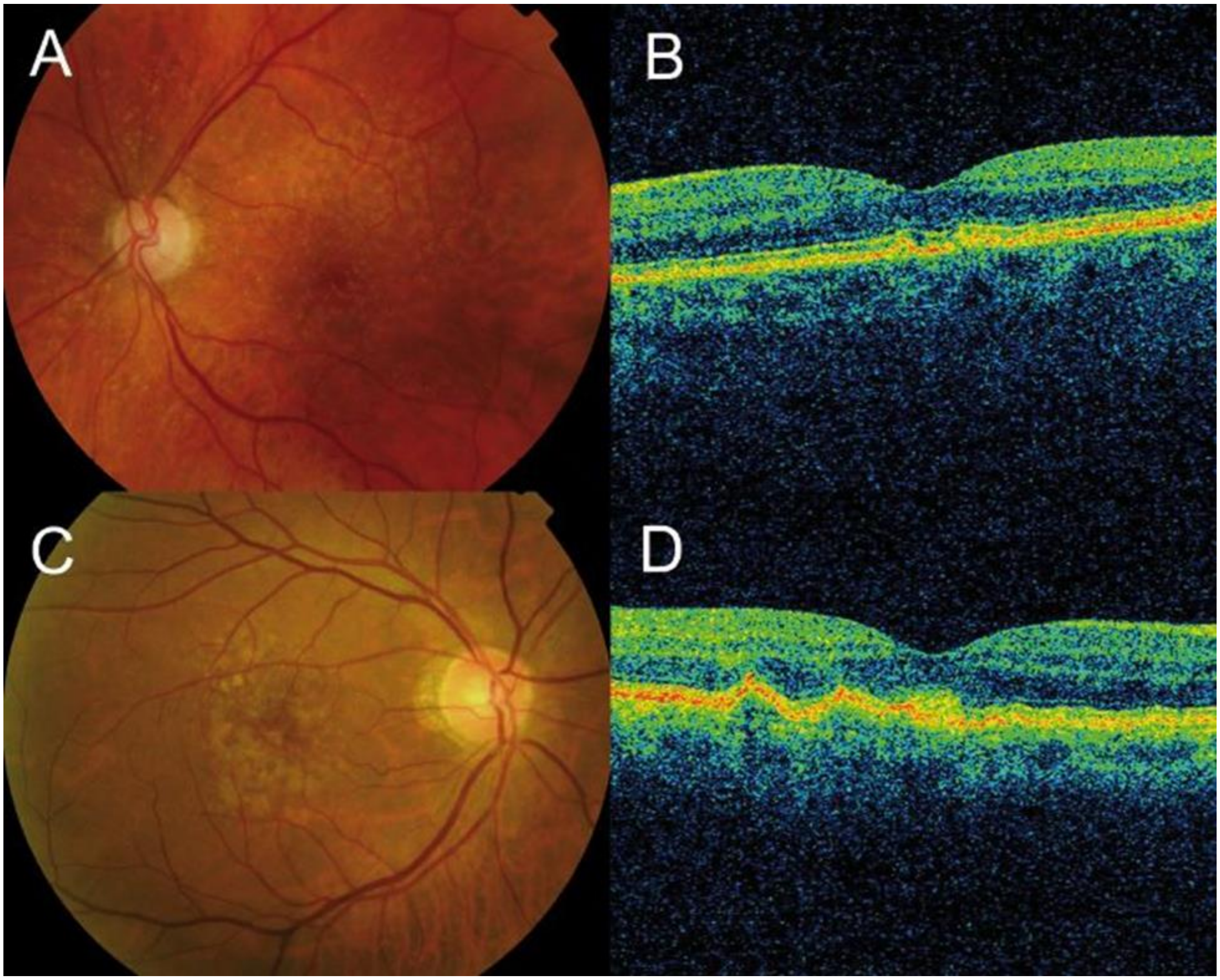
Game design

Eye in the Sky Defender was built as a traditional tower defense game. Images obtained from OCT scans of the retina are reminiscent of satellite images of topography where the retinal layers look like roads or trails. These "trails" were inserted at the center of game play and we added trees and buildings to the landscape on either side for visual enhancement. The goal, through game play, is for the player to identify the RPE and Bruch's membrane. In doing so, the volume any drusen occupied between those two layers is determined. To identify the layers, the players place "defensive towers" along the path that they anticipate enemy tanks and robots will travel. The game instructions inform that the tanks will take the lower route (Bruch's membrane) and the robots the upper undulating route (RPE). In the background, the towers (nodes) that the players place, determine the route the artificial intelligence (AI) algorithm will follow. Once the player submits his tower placement selection, he then watches the robots and tanks progress along their respective paths, seeing the effectiveness of his defenses. As they travel the route, the enemy leaves behind a trail to visually train players on the types of features (RPE and Bruch's membrane) to follow in future levels of play. The closer the player's anticipated paths are to the RPE and Bruch's membrane line, the more effective they are in defeating the enemies and, thus, identifying the retinal layers. After completing an image, players receive a final scoring report detailing their accuracy. Players then proceed to the next level, which is a new OCT scan[xv].

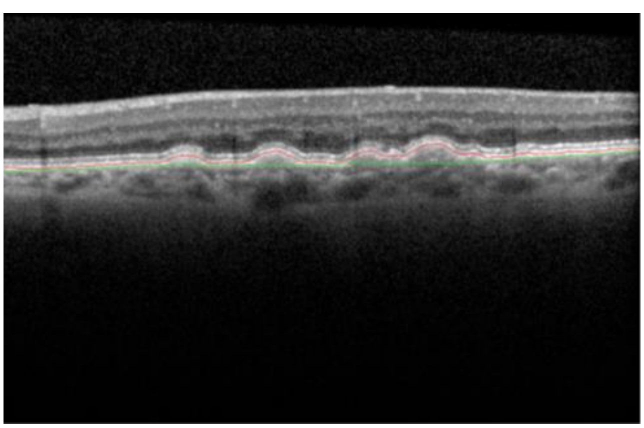
Results

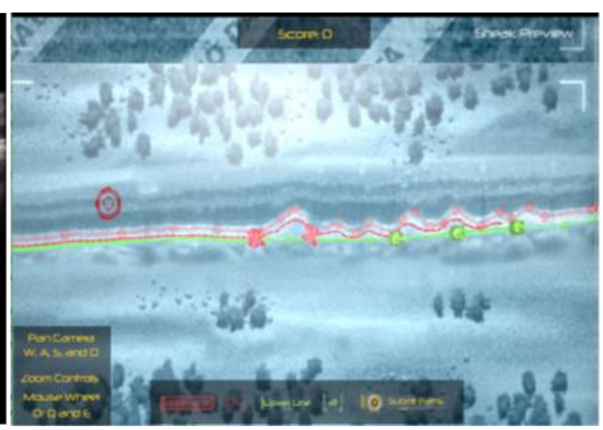
Utilizing learning models inherit in the gameplay mechanics of ESD, we trained individual players to identify the retinal boundaries of OCT retina scans. We then evaluated the individual player results and the collective averages of all the players. Over seven (7) levels of play, we found that players had an improvement in accuracy of 81% to 93% in identifying retinal layers. This is of particular importance as Bruch's membrane, in particular, is often miss-defined in automated analysis. When looking at the collective averages of all players, we found it to be within 3% of the lines corrected manually by trained evaluators. This is well within the acceptable 10-15% margin of error for such analysis[xvi]. In turn the players, through HCG, enhanced the OCT retinal images, and effectively trained an existing deep learning algorithm to identify the retinal layers. This HEWMEN enabled deep learning algorithm increased the precision (+78%) and accuracy (+38%) of retinal layer identification within OCT images. Furthermore, this was done with a very small, crowdsourced data set[xvii]. Because HEWMEN is agnostic to both data and algorithm, we are able to use this human in the loop (HiTL) approach to tackle other problems, such as co-medication discovery for recurrent cancer and drug treatment for COVID-19 disease.

Visual Data



A and B represent a normal retina. C and D represent drusen formation. Drusen are seen as undulations and elevations in the hyperreflective band of the RPE with less reflective material beneath them, while the inner retinal layers remain generally intact[xviii].





Example Automatic (top) and Manually Corrected (bottom) OCT Scans

Eye in the Sky: Defender Gameplay Image

Images Courtesy Clark, Ouellette (2018)

CONCLUSION

Through HCG and crowdsourcing, BALANCED in partnership with SMU Guildhall and The Retina Foundation Southwest, was able to show that an untrained user can accurately identify retinal layers simply by playing a video game. By utilizing HEWMEN, this HiTL technique was able to train and improve an existing deep learning algorithm to identify retinal layers and pathology more precisely. This will have significant impact in the diagnosis and management of AMD and decrease the need for referral of OCT retinal scans to reading centers, saving time, and reducing expense while allowing experts to concentrate efforts on less routine images. Extending beyond that, because HEWMEN is data and algorithm agnostic, HiTL via HCG and HEWMEN can train algorithms for automation in many fields to be more efficient without having expertise in those fields of interest.

References:

[i] C. Clark, M. Ouellette and K. Csaky, "Training Players to Analyze Age-Related Macular Degeneration Optical Coherence Tomography Scans using a Human Computation Game," 2019 IEEE 7th International Conference on Serious Games and Applications for Health (SeGAH), Kyoto, Japan, 2019, pp. 1-7, doi: 10.1109/SeGAH.2019.8882430.

[ii] Lim, L. S., Mitchell, P., Seddon, J. M., Holz, F. G., & Wong, T. Y. (2012). Age-related macular degeneration. The Lancet, 379(9827), 1728-1738. doi:10.1016/s0140-6736(12)60282-7.

[iii] Fujimoto JG, Pitris C, Boppart SA, Brezinski ME. Optical coherence tomography: an emerging technology for biomedical imaging and optical biopsy. Neoplasia. 2000;2(1-2):9-25. doi:10.1038/sj.neo.7900071.

[iv] Garcia-Layana, A., et.al. (2017, July). Optical Coherence Tomography in Age-related Macular Degeneration. Retrieved July 26, 2020, from https://amdbook.org/content/optical-coherence-tomography-age-related-macular-degeneration.

[v] Bhende M, Shetty S, Parthasarathy MK, Ramya S. Optical coherence tomography: A guide to interpretation of common macular diseases [published correction appears in Indian J Ophthalmol. 2018 Mar;66(3):485]. Indian J Ophthalmol. 2018;66(1):20-35. doi:10.4103/ijo.IJO_902_17.

[vi] Giani A, Cigada M, Esmaili DD, Salvetti P, Luccarelli S, Marziani E, et al. Artifacts in automatic retinal segmentation using different optical coherence tomography instruments. Retina. 2010; 30:607–16.

[vii] C. Clark, M. Ouellette and K. Csaky, "Training Players to Analyze Age-Related Macular Degeneration Optical Coherence Tomography Scans using a Human Computation Game," 2019 IEEE 7th International Conference on Serious Games and Applications for Health (SeGAH), Kyoto, Japan, 2019, pp. 1-7, doi: 10.1109/SeGAH.2019.8882430.

[viii] L. Rosenberg, D. Baltaxe and N. Pescetelli, "Crowds vs swarms, a comparison of intelligence," 2016 Swarm/Human Blended Intelligence Workshop (SHBI), Cleveland, OH, 2016, pp. 1-4, doi: 10.1109/SHBI.2016.7780278.

[ix] GALTON, F. *Vox Populi*. *Nature* **75,** 450–451 (1907). https://doi.org/10.1038/075450a0.

[x] Lavoie, E., Hendren, L., "*Personal Volunteer Computing*," April 2019, Proceedings of the 16th ACM International Conference on Computing Frontiers, Pages 240–246https://doi.org/10.1145/3310273.3322819.

[xi] Swan, M. 2012. 'Crowdsourced Health Research Studies: An Important Emerging Complement to Clinical Trials in the Public Health Research Ecosystem.' *Journal of Medical Internet Research* 14 (2): e46. doi:10.2196/jmir.1988.

[xii] "SETI@Home Going into Hibernation." SETI Institute, SETI Institute, 4 Mar. 2020, www.seti.org/setihome-going-hibernation.

[xiii] F. Khatib, F. DiMaio, Foldit Contenders Group, Foldit Void Crushers Group, S. Cooper, M. Kazmierczyk, M. Gilski, S. Krzywda, H. Zabranska, I. Pichova, J. Thompson, Z. Popović, M. Jaskolski, D. &
Baker (2011). Crystal structure of a monomeric retroviral protease solved by protein folding game players.
Nature Structural & Molecular Biology volume 18, 1175–1177. https://doi.org/10.1038/nsmb.2119.

[xiv] C. Clark, I. Greenberg, and M. Ouellette, "A model for integrating human computing into commercial video games," 2018 IEEE 6th International Conference on Serious Games and Applications for Health (SeGAH), Vienna, 2018, pp. 1-8, doi: 10.1109/SeGAH.2018.8401316.

[xv] C. Clark, M. Ouellette and K. Csaky, "Training Players to Analyze Age-Related Macular Degeneration Optical Coherence Tomography Scans using a Human Computation Game," 2019 IEEE 7th International Conference on Serious Games and Applications for Health (SeGAH), Kyoto, Japan, 2019, pp. 1-7, doi: 10.1109/SeGAH.2019.8882430.

[xvi] C. Clark, M. Ouellette and K. Csaky, "Training Players to Analyze Age-Related Macular Degeneration Optical Coherence Tomography Scans using a Human Computation Game," 2019 IEEE 7th International Conference on Serious Games and Applications for Health (SeGAH), Kyoto, Japan, 2019, pp. 1-7, doi: 10.1109/SeGAH.2019.8882430.

[xvii] C. Clark, M. Ouellette, "Using Human Computation Game-Based Input to Enhance DNN Image Segmentation of Age-Related Macular Degeneration OCT Images with Small Datasets," *Under Review.* 2020.

[xviii] Garcia-Layana, A., et.al. (2017, July). Optical Coherence Tomography in Age-related Macular Degeneration. Retrieved July 26, 2020, from https://amdbook.org/content/optical-coherence-tomography-age-related-macular-degeneration.