AI in Medicine: the Test Case of Ophthalmology

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Take-Homes – AI and Medicine

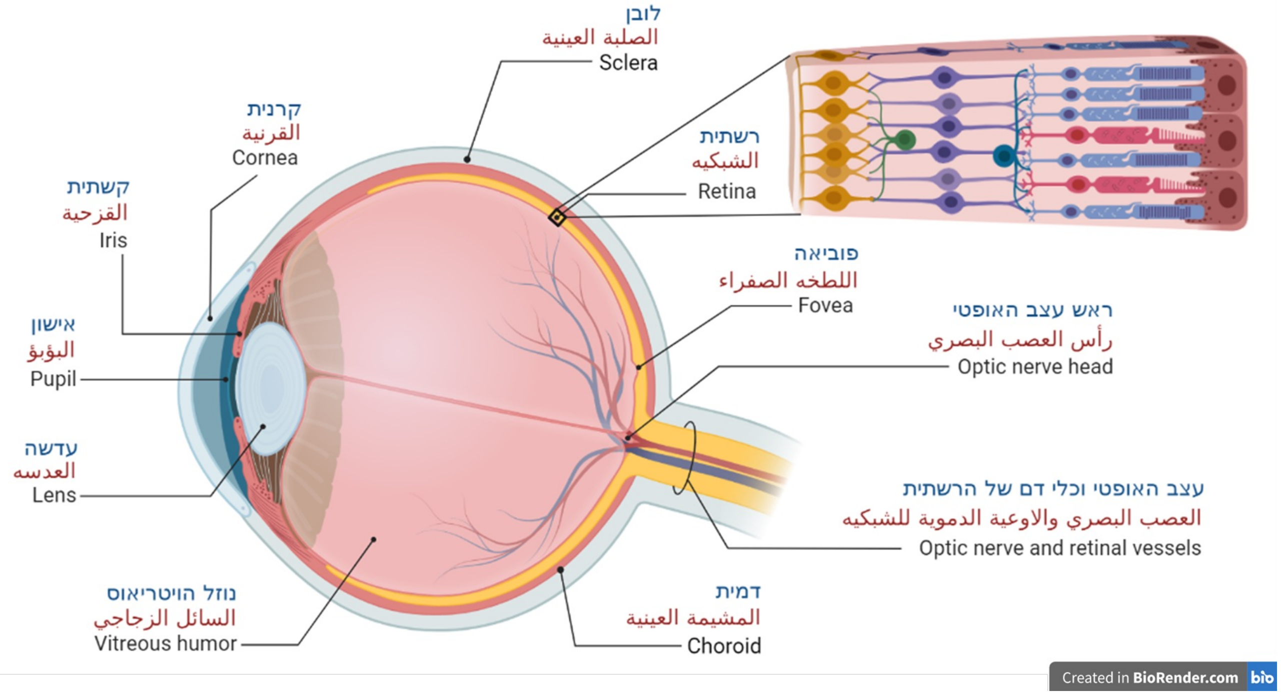
- New era
- Challenges for AI system development and integration
- Opportunities for:
  - Research
  - Entrepreneurship
  - Bringing value for our patients
- **You can do it!**

Talk Outline

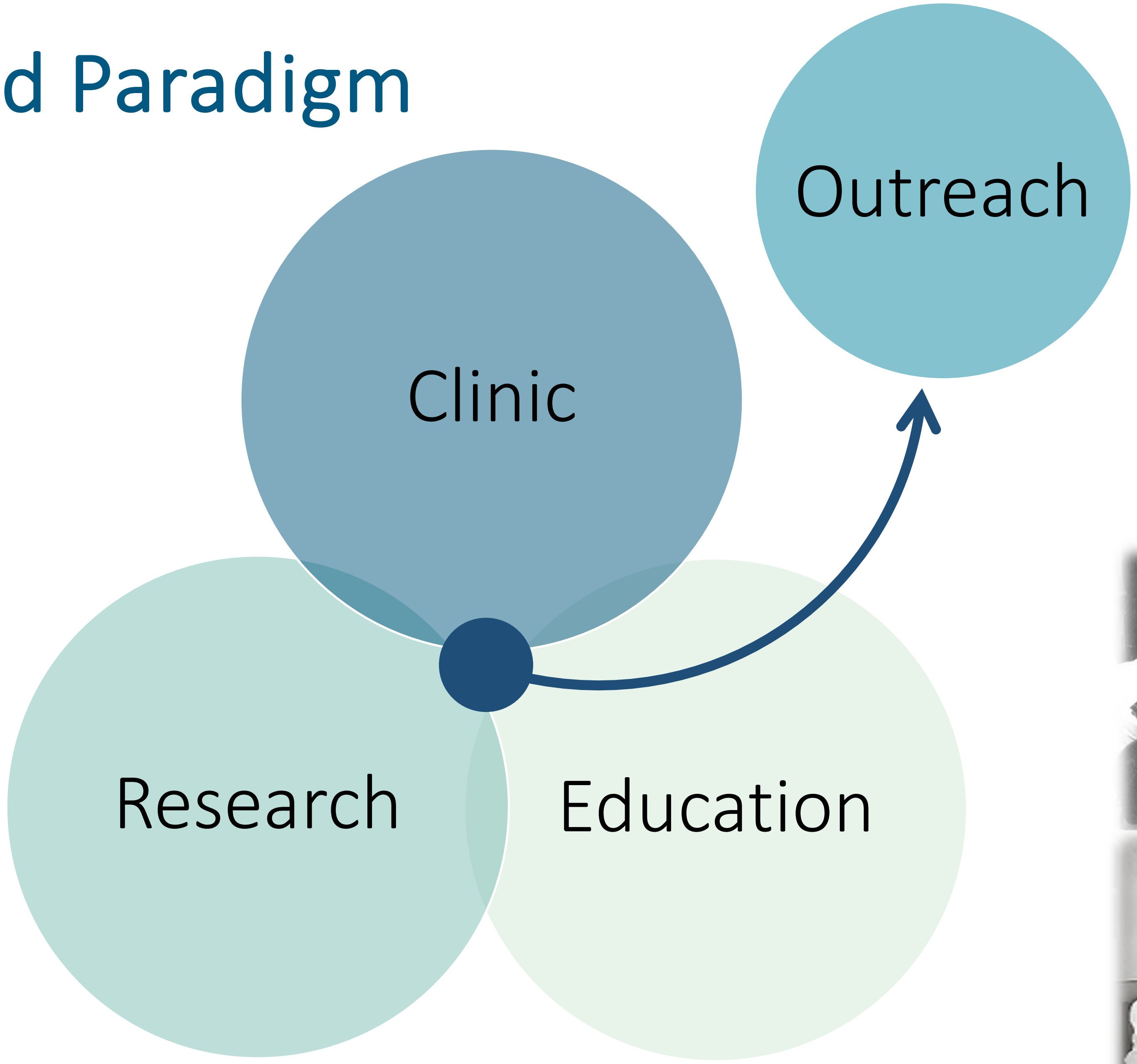
- Introduction
- What is Ophthalmology
- “Classical ophthalmology”
- “The Times They Are A-Changin”
- AI tools in the clinic
- Development of new AI tools in Ophthalmology

Ophthalmology

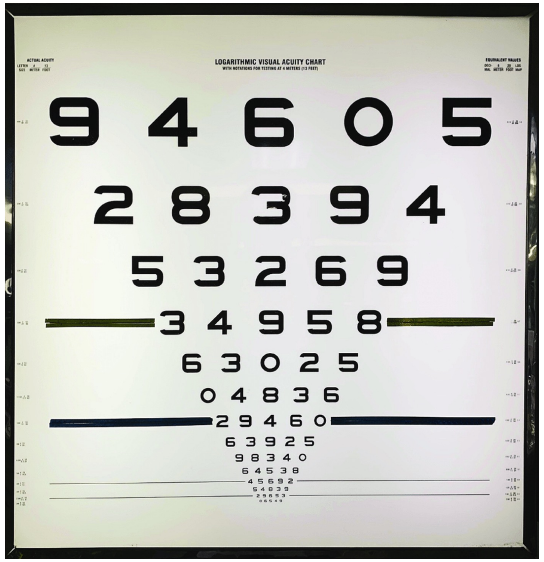
- Common diseases
- High impact (QUALY)
- Cutting-edge technologies (gene therapy, stem cells, AI)



Old Paradigm



“Classical Ophthalmology”



Eye (2019) 33:347–348
https://doi.org/10.1038/s41433-018-0252-7

The ROYAL COLLEGE of OPHTHALMOLOGISTS

COMMENT

Check for updates

Deskilling in ophthalmology is the inevitable controllable?

Jaime Levy [1] · Alan Jotkowitz [2] · Itay Chowers [1]

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The evolving art of medicine and the "problem" with technology

Medicine is an ever-changing art. The rate of change and its consequences bare important implications to patients and physicians alike. Ophthalmology is not an exception in that sense. Up until around the turn of the Millennium, an ophthalmologist had to develop diagnostic skills which were heavily dependent upon one's ability to identify correctly pathological findings. The ophthalmologist had then to determine the diagnosis and develop a treatment plan. These characteristics of the profession were similar in developed or developing countries. While major differences among such countries were availability of professionals and treatment equipment.

During the last few years, we have witnessed the increasing use of technology in the field of ophthalmology. Advances such as optical coherence tomography (OCT) and OCT-angiography, as well as sophisticated biometry and cornea photography, have and are revolutionizing daily practice in ophthalmology clinics worldwide.

For example, OCT surrogate end-points and biomarkers are displacing other historical measurements such as visual acuity and clinical examination in clinical trials and it routine practice. The use of this new technology has busted the diagnostic accuracy of retinal diseases, but, it also created a whole host of new challenges, such as data storage, interpretation, learning, cost and maintenance. An additional problem is the fact that ophthalmologists in training who begin to examine patients and learn various pathologies, may be prone to diagnose, treat or make decisions based solely on OCT and similar sophisticated technologies even without thoroughly examining the patient. In a short time, the "physical examination" of the patient can pass to the background or even to the dustbin history.

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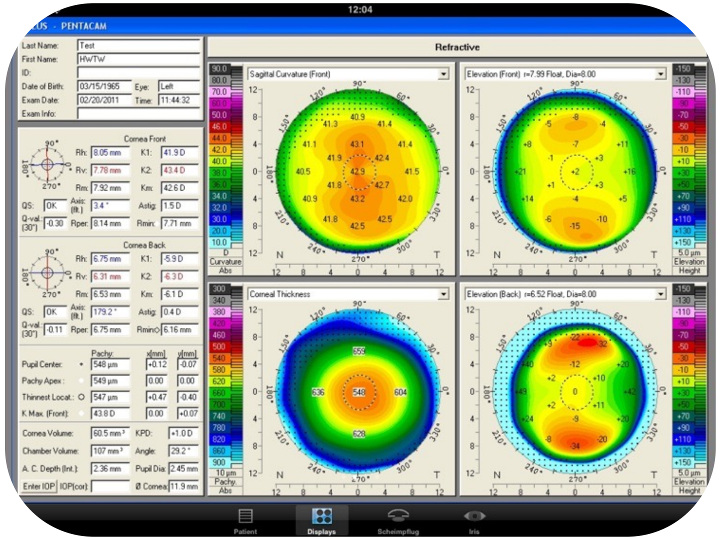
Deep learning

Deep learning algorithms applied to the field of the ophthalmology are bearing fruit. In the field of retina, deep learning builds upon the data generated by modern imaging modalities. Research on automatic detection of diabetes retinopathy, age-related macular degeneration (AMD), glaucoma, decision on whether to inject or not an eye with neovascular AMD, and many more, are appearing in the ophthalmological literature in recent years. The first system which autonomously screens diabetic patients for retinopathy was recently approved by the FDA. In other fields of medicine, such as radiology and pathology, which bear much resemblance to ophthalmology in which the diagnosis is visual and a large number of images must be reviewed to see if there is for example, a pulmonary embolus on computed tomography, an abnormal cell on the histological slide on minimal subretinal fluid on OCT, voices are emerging that advise specialists to become an "information specialist" to captain artificial intelligence and provide a better medical service [1].

Deskilling

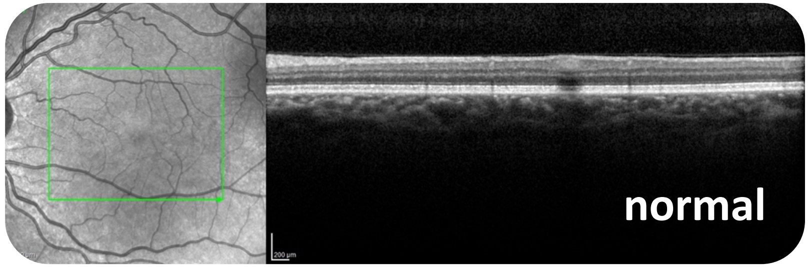
The origin of the term deskilling comes from Marx in the 19th century and the escalating labor force in factories, the decline of craft skills and its replacement with technological means [2]. Deskilling is the reduction of the level of skill required to complete a task when some or all components of the task are partly automated [3]. This process can affect physicians' ability to derive informed opinions on the basis of detectable signs, symptoms, and available data. Deskilling itself is rarely a problem; however, it becomes one if the technology fails or

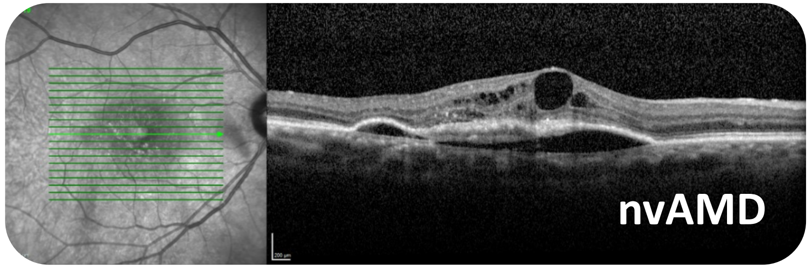
Current Practice



Optical Coherence Tomography

- Use light reflectance to illustrate structure
- Common use in Ophthalmology for retinal and anterior segment diseases
- Typical exam: 37-49 sections/eye
- Pt. often perform several OCT exams/year
- ~30 Million OCT exams performed worldwide every year (2017)





From: Foreword: 25 Years of Optical Coherence Tomography
Invest. Ophthalmol. Vis. Sci.. 2016;57(9):OCTi-OCTii. doi:10.1167/iovs.16-20269

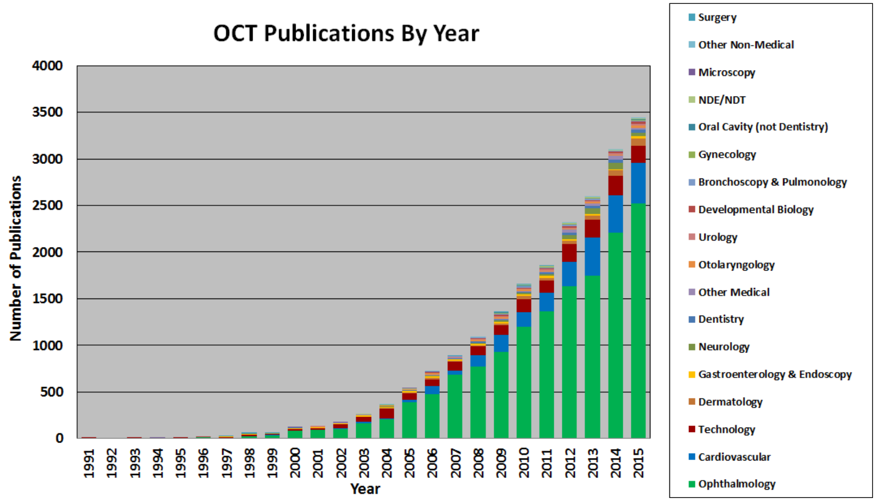
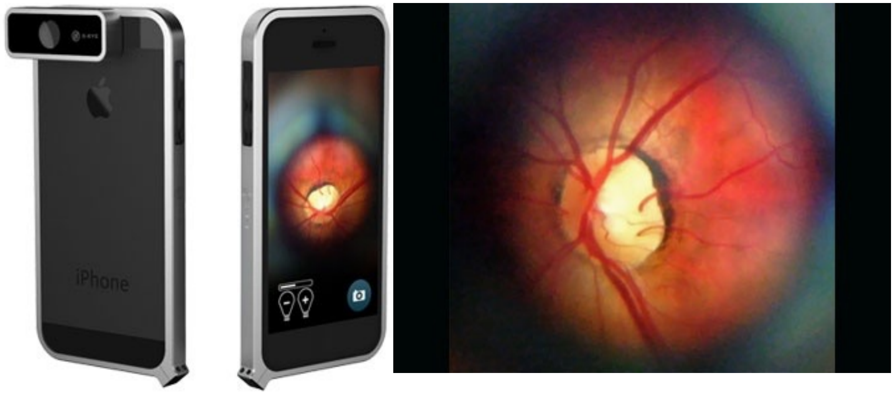


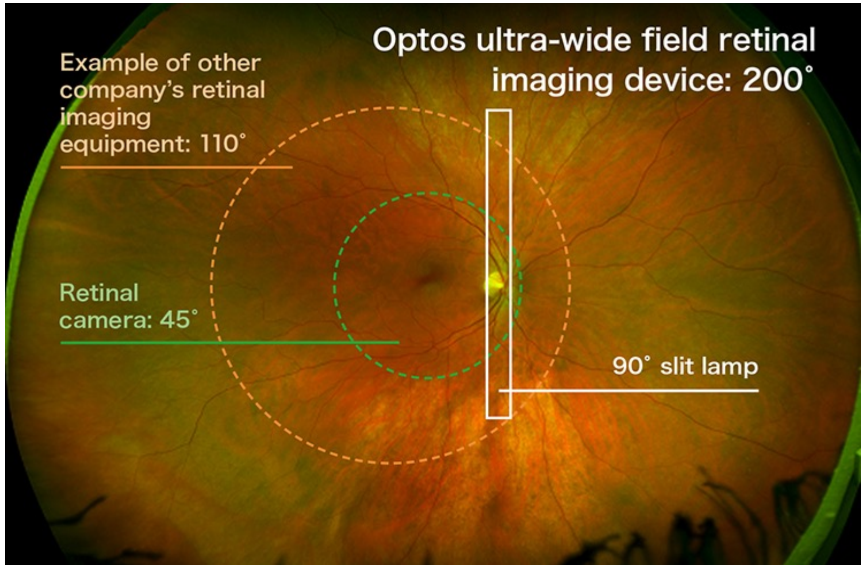
Figure Legend:

OCT publication volume according to research area. Ophthalmology has the largest volume of publications, attesting to the wide acceptance and impact of OCT in our field. OCT technology continues to make advances and applications in many medical specialities are being developed. Compiled from PubMed abstract search. Image courtesy of Eric Swanson, www.OCTNews.org.

Color Fundus Photography

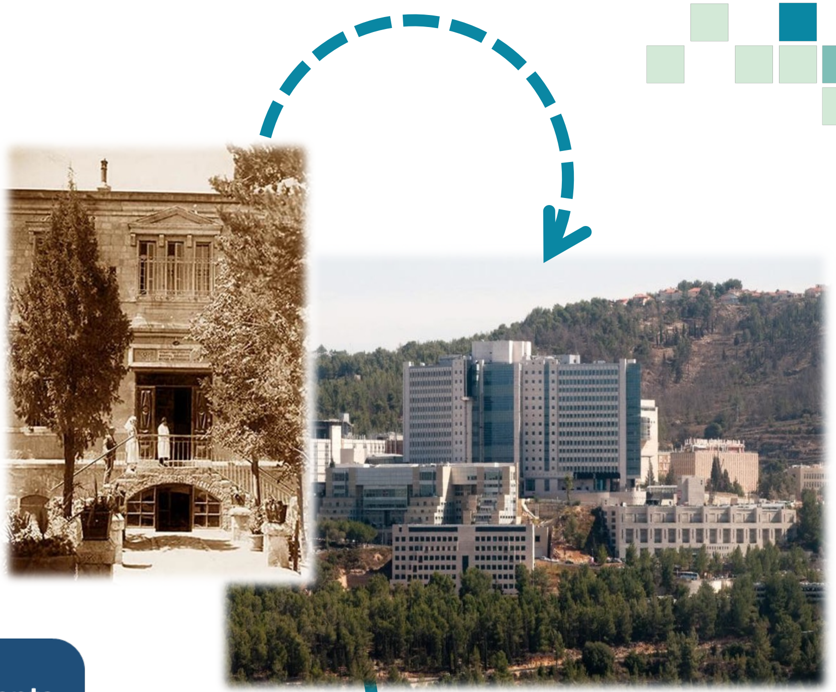
- Identify/document retinal findings- DR, AMD, retinal detachment, ROP
- Performed using variety of techniques
    - Conventional (30-60 degree)
    - Ultrawide field (200 degree)
    - Cell phone

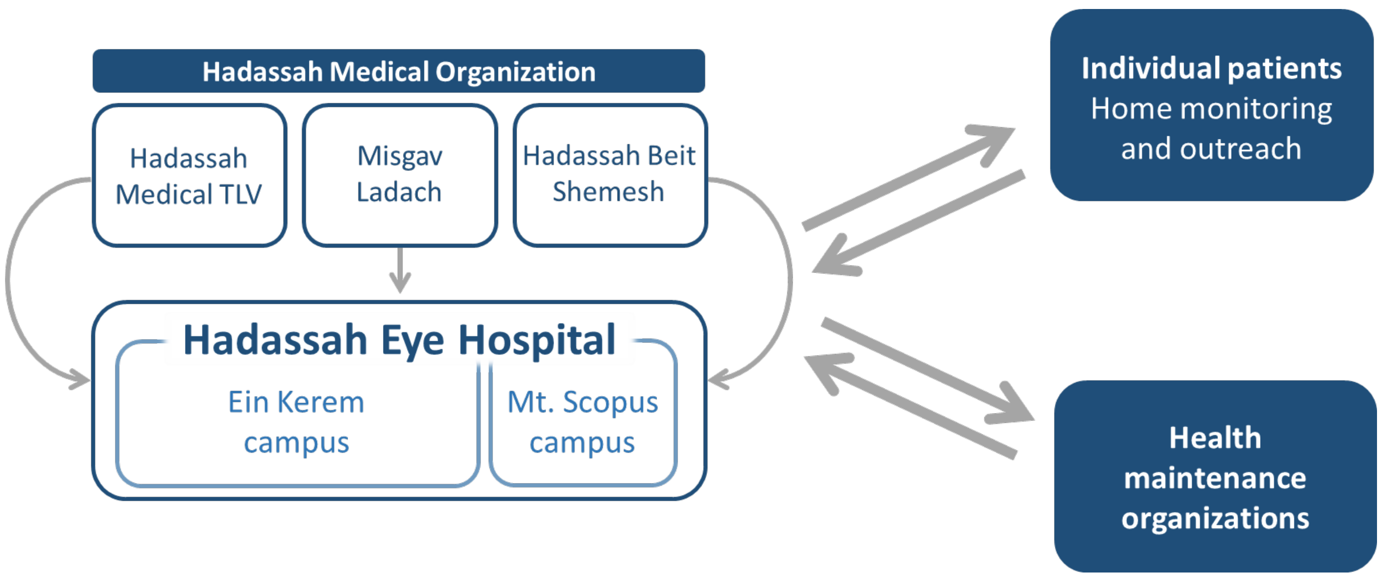




Hadassah Ophthalmology

- Since 1918
- Time to modernize paradigms





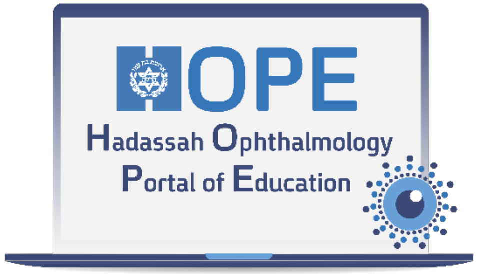
New Paradigm

Outreach
Innovation,
tele-ophthalmology

Clinic
AI-based care

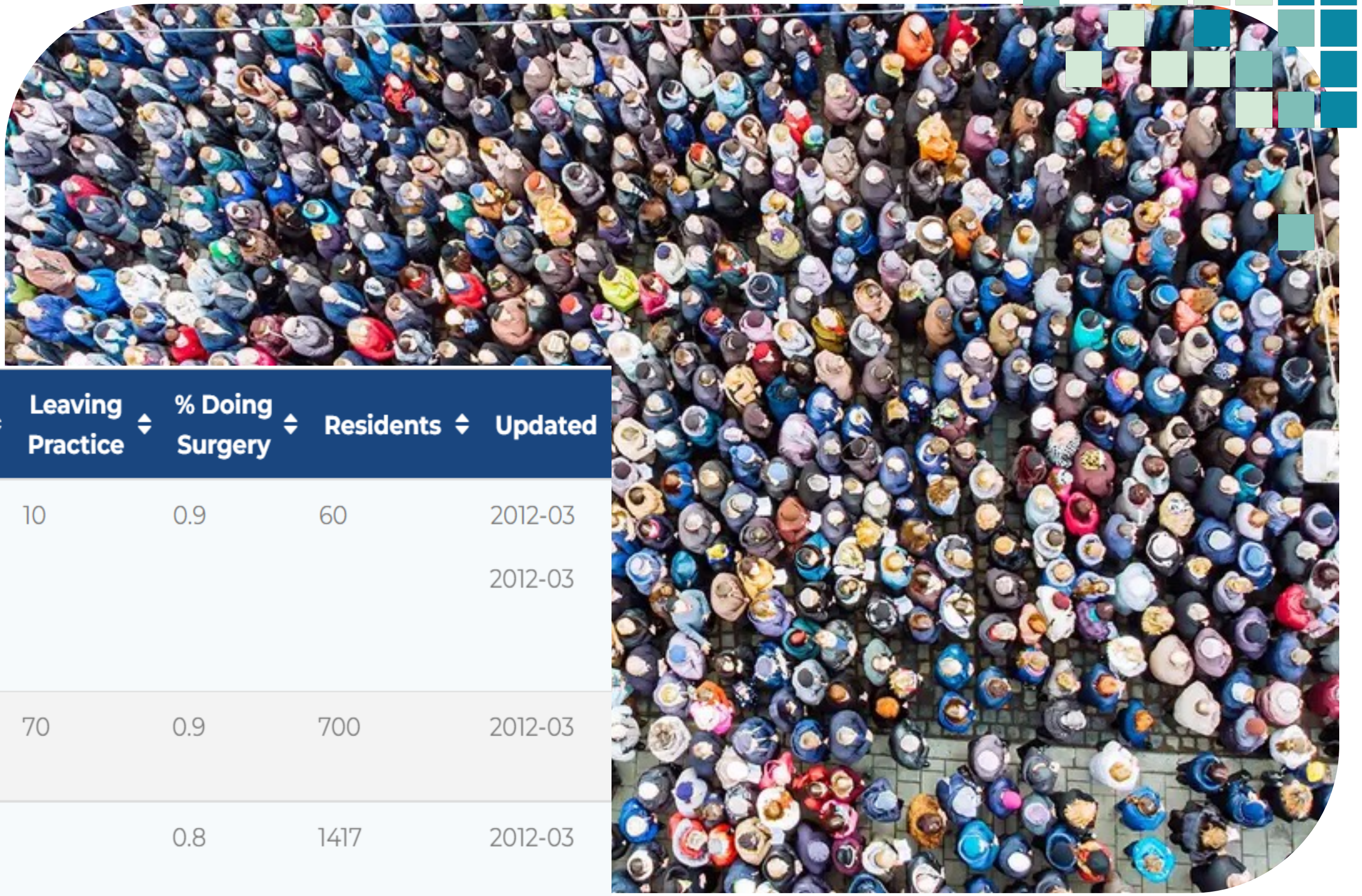
Research
Digital health, gene therapy

Education
Online, simulators



Why We Need AI

- Pt/MDs ratio



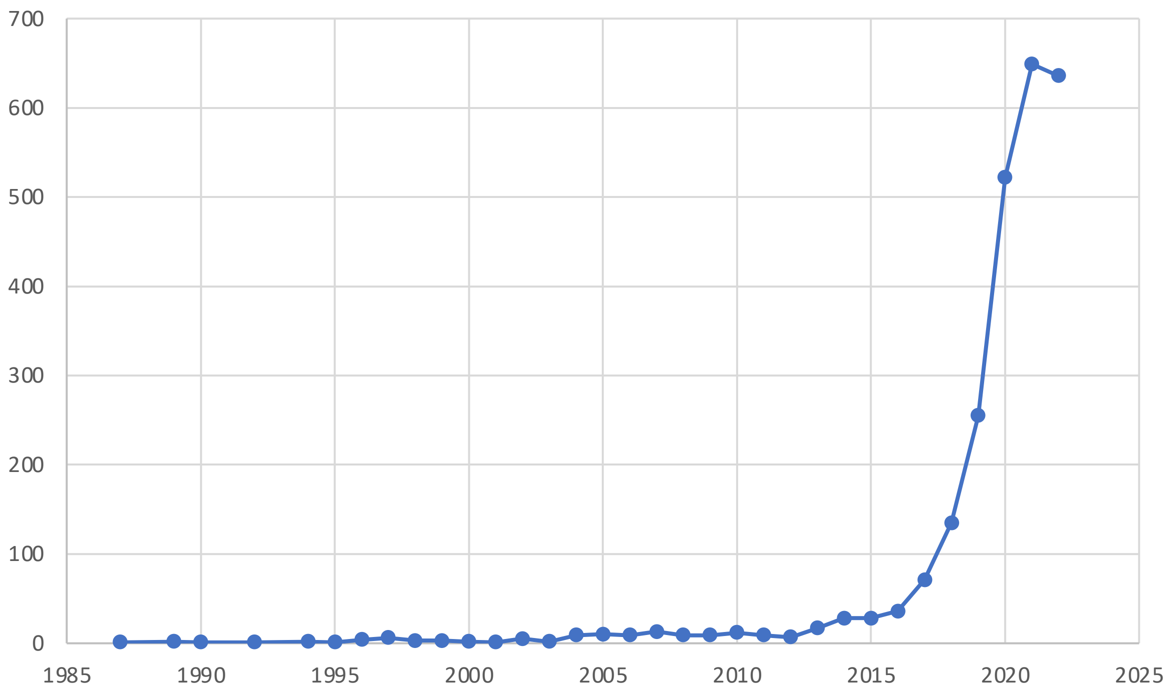
Country	Population	Ophthalmologists per million	Total	Entering Practice	Leaving Practice	% Doing Surgery	Residents	Updated
Israel	8064547	81	650	10	10	0.9	60	2012-03
United Arab Emirates	9154302	14	125					2012-03
United Kingdom	65397080	49	3200	100	70	0.9	700	2012-03
United States	319929162	59	18805	440		0.8	1417	2012-03
Afghanistan	33736494	4	140	6	3	0.7	50	2012-03
Albania	2923352	30	88				17	2012-03
Algeria	39871528	25	1000					2012-03
Angola	27859305	1	15					2012-03

Changing Paradigms

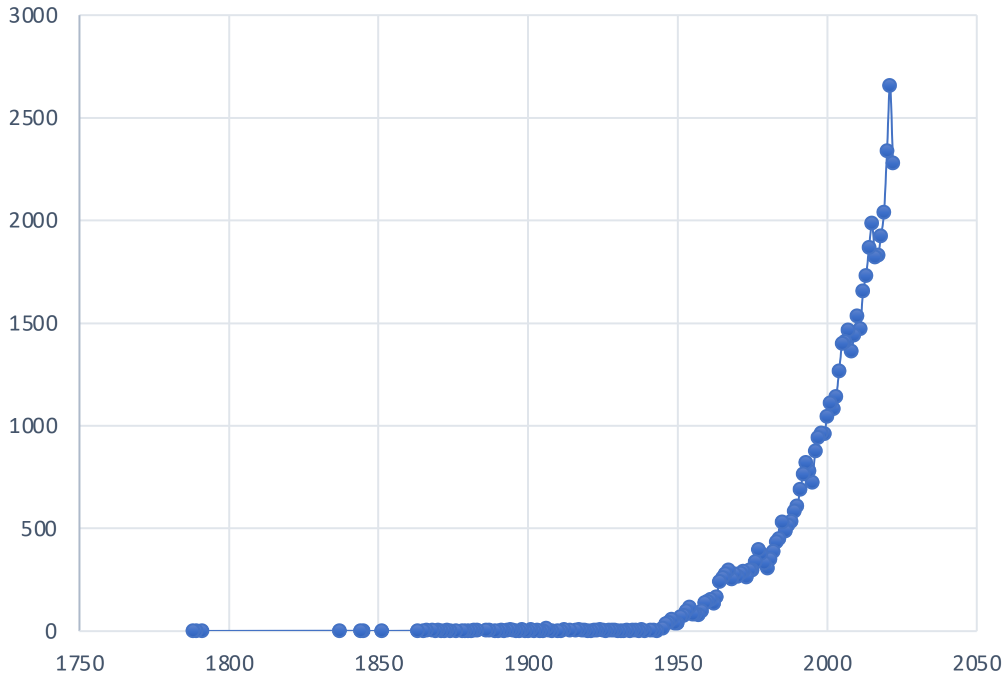
Task	Past	Current/Future
Produce data	Challenging	Easy
Analyze data	Easy	Challenging

Publication in Ophthalmology Per Year

AI



Cataract Surgery



AI in Ophthalmology

Two main categories:

- Ophthalmic data analysis
- Ophthalmic image analysis

  →Detection and grading of disease

  →Automated image segmentation

Goals: Identify and predict

The AAO IRIS® Registry (Intelligent Research in Sight)

- World's largest specialty clinical data registry (Sept. 2020)
- De-identified data on over 349.37 million patient visits from 59.99 million unique patients
- Enables big-data studies

IRIS
INTELLIGENT REGISTRY
INFORMATION SYSTEM

AI for Ophthalmic Image Analysis

- Input: color fundus images (Poplin et al., 2018)
- Predicted characteristics:
  - Age, gender, smoker/non-smoker, HbA1c, BMI, BP

ARTICLES
https://doi.org/10.1038/s41551-018-0195-0
nature biomedical engineering

Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning

Ryan Poplin[1,4], Avinash V. Varadarajan[1,4], Katy Blumer[1], Yun Liu[1], Michael V. McConnell[2,3], Greg S. Corrado[1], Lily Peng[1,4]* and Dale R. Webster[1,4]

Traditionally, medical discoveries are made by observing associations, making hypotheses from them and then designing and running experiments to test the hypotheses. However, with medical images, observing and quantifying associations can often be difficult because of the wide variety of features, patterns, colours, values and shapes that are present in real data. Here, we show that deep learning can extract new knowledge from retinal fundus images. Using deep-learning models trained on data from 284,335 patients and validated on two independent datasets of 12,026 and 999 patients, we predicted cardiovascular risk factors not previously thought to be present or quantifiable in retinal images, such as age (mean absolute error within 3.26 years), gender (area under the receiver operating characteristic curve (AUC) = 0.97), smoking status (AUC = 0.71), systolic blood pressure (mean absolute error within 11.23 mmHg) and major adverse cardiac events (AUC = 0.70). We also show that the trained deep-learning models used anatomical features, such as the optic disc or blood vessels, to generate each prediction.

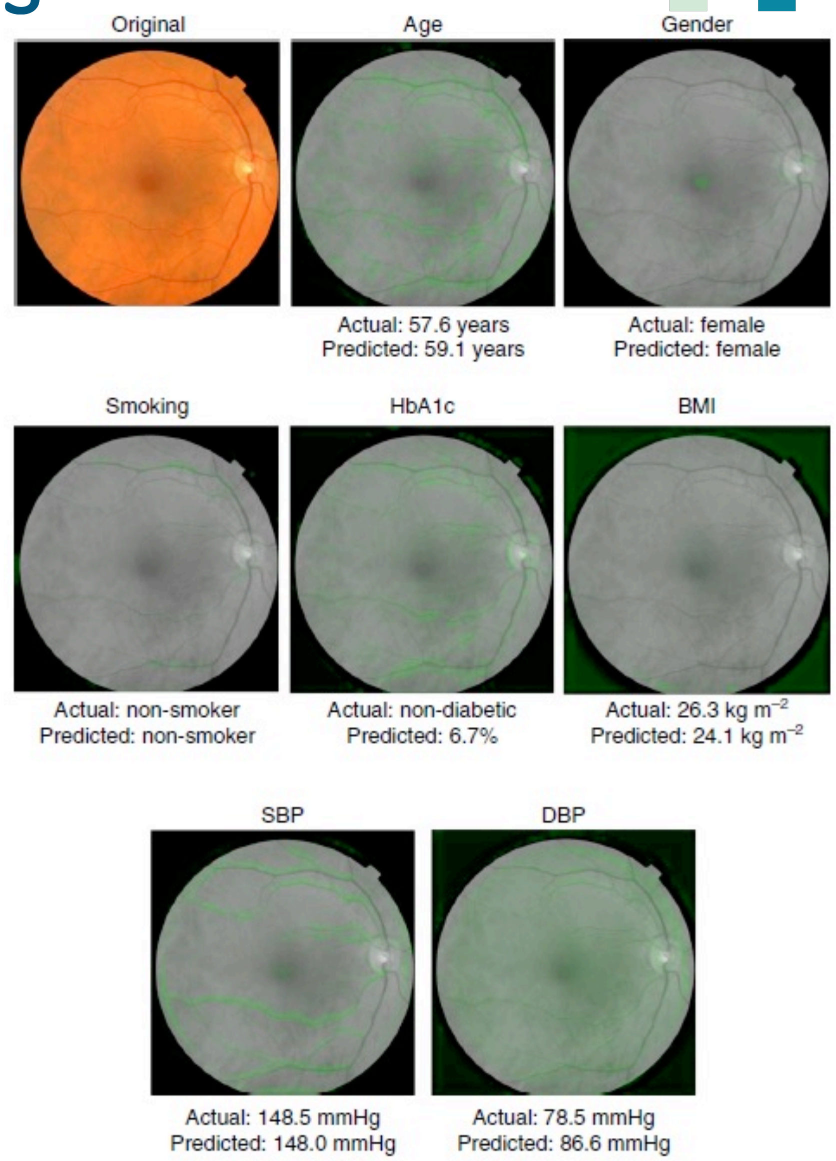
Poplin, R., Varadarajan, A.V., Blumer, K. et al. Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning. Nat Biomed Eng 2, 158–164 (2018).

AI for Ophthalmic Image Analysis

Table 1 | Baseline characteristics of patients in the development and validation sets

Characteristics	Development set		Clinical validation set	
	UK Biobank	EyePACS	UK Biobank	EyePACS-2K
Number of patients	48,101	236,234	12,026	999
Number of images	96,082	1,682,938	24,008	1,958
Age: mean, years (s.d.)	56.8 (8.2), $n=48{,}101$	53.6 (11.6), $n=234{,}140$	56.9 (8.2), $n=12{,}026$	54.9 (10.9), $n=998$
Gender (% male)	44.9, $n=48{,}101$	39.2, $n=236{,}212$	44.9, $n=12{,}026$	39.2, $n=999$
Ethnicity	1.2% Black, 3.4% Asian/PI, 90.6% White, 4.1% Other $n=47{,}785$	4.9% Black, 5.5% Asian/PI, 7.7% White, 58.1% Hispanic, 1.2% Native American, 1.7% Other $n=186{,}816$	1.3% Black, 3.6% Asian/PI, 90.1% White, 4.2% Other $n=11{,}926$	6.4% Black, 5.7% Asian/PI, 11.3% White, 57.2% Hispanic, 0.7% Native American, 2% Other $n=832$
BMI: mean (s.d.)	27.31 (4.78), $n=47{,}847$	n/a	27.37 (4.79), $n=11{,}966$	n/a
Systolic BP: Mean, mmHg (s.d.)	136.82 (18.41), $n=47{,}918$	n/a	136.89 (18.3), $n=11{,}990$	n/a
Diastolic BP: Mean, mmHg (s.d.)	81.78 (10.08), $n=47{,}918$	n/a	81.76 (9.87), $n=11{,}990$	n/a
HbA1c: mean, % (s.d.)	n/a	8.23 (2.14), $n=141{,}715$	n/a	8.2 (2.13), $n=737$
Current Smoker: %	9.53%, $n=47{,}942$	n/a	9.87%, $n=11{,}990$	n/a

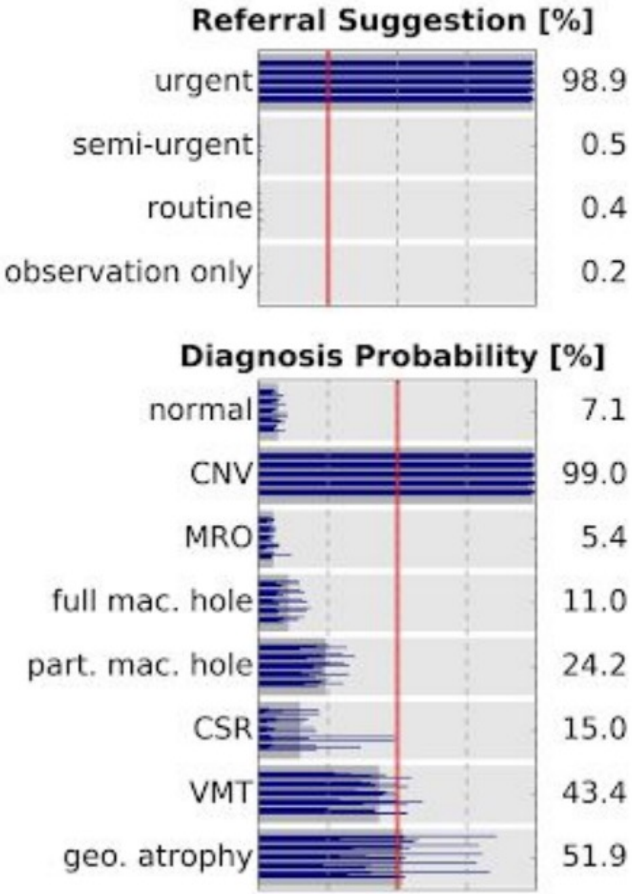
n/a indicates that the characteristic was not available for that dataset. *n* is the number of patients for whom that measurement was available. PI, Pacific Islander.



Poplin, R., Varadarajan, A.V., Blumer, K. et al. Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning. Nat Biomed Eng 2, 158–164 (2018).

DeepMind (Google)

- Developing an AI product capable of diagnosing 50 retinal pathologies based on OCT scans
- Identify retinal diseases with 94% accuracy
- Referral suggestions on par with retinal experts
- Explanation of how decision was made – no ‘black box’



De Fauw, J., Ledsam, J.R., Romera-Paredes, B. et al. Clinically applicable deep learning for diagnosis and referral in retinal disease. Nat Med 24, 1342–1350 (2018).

DeepMind (Google)

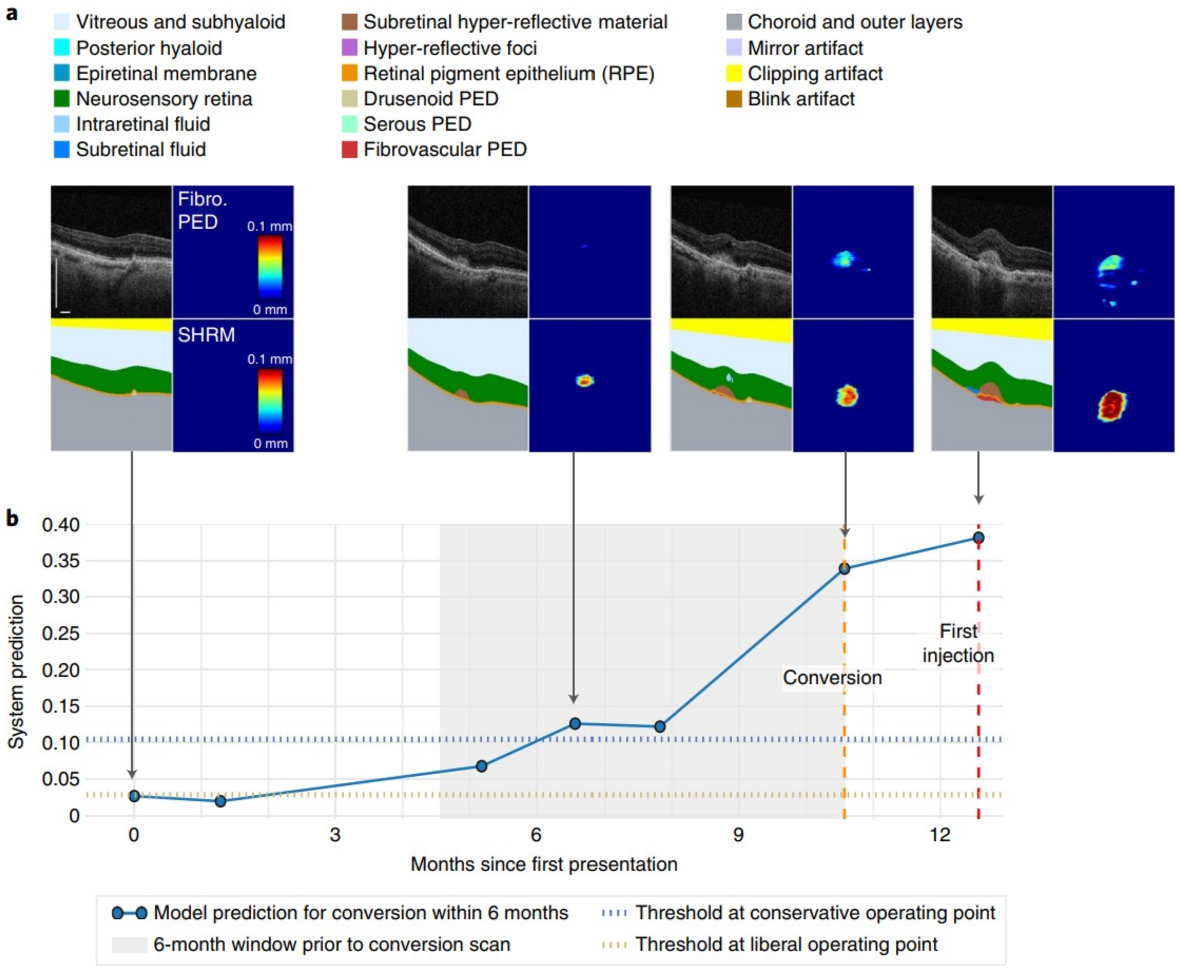
- Early warning system for conversion to nvAMD: OCT → risk for nvAMD within 6 months
- Combined models based on 3D OCT and corresponding automatic tissue segmentation
- Automatic tissue segmentation identified anatomical changes before conversion
- Predicted better than five out of six experts

nature medicine ARTICLES
https://doi.org/10.1038/s41591-020-0867-7
Check for updates

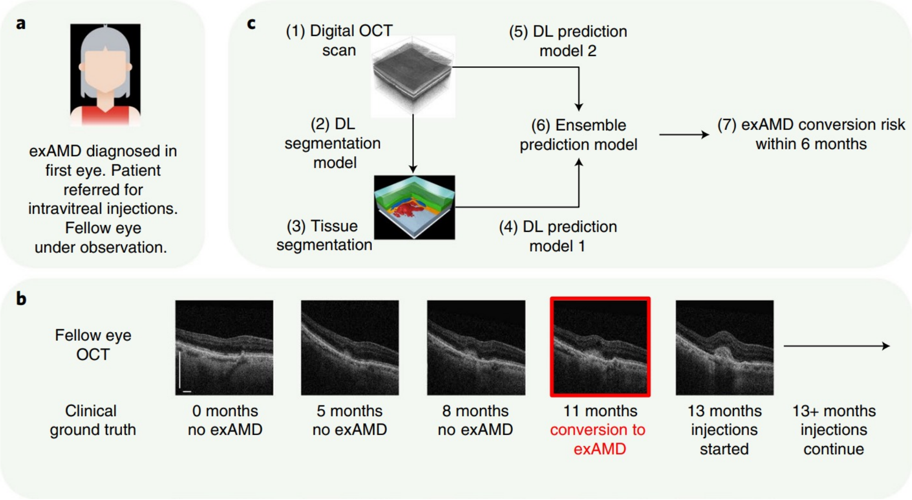
Predicting conversion to wet age-related macular degeneration using deep learning

Yim, J., Chopra, R., Spitz, T. et al. Predicting conversion to wet age-related macular degeneration using deep learning. Nat Med 26, 892–899 (2020).

DeepMind (Google)



Example of a correct prediction by the AI system



Clinical setup and proposed system

nature medicine

ARTICLES

https://doi.org/10.1038/s41591-020-0867-7

Check for updates

Predicting conversion to wet age-related macular degeneration using deep learning

Yim, J., Chopra, R., Spitz, T. et al. Predicting conversion to wet age-related macular degeneration using deep learning. Nat Med 26, 892–899 (2020).

Quantification of Atrophy

- Objective quantification of retinal atrophy associated with AMD
- Based on the classification of light scattering patterns with a custom column-based convolutional neural network (CNN)

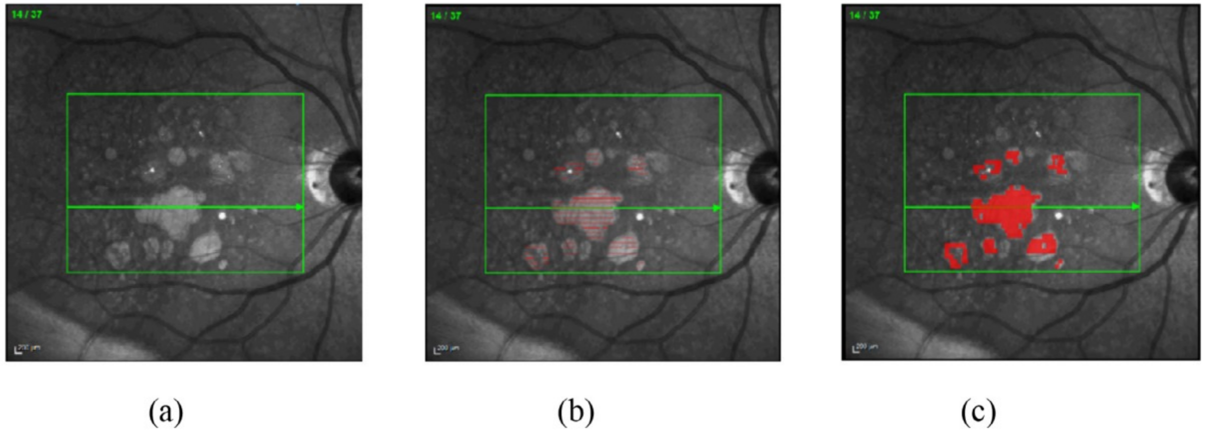
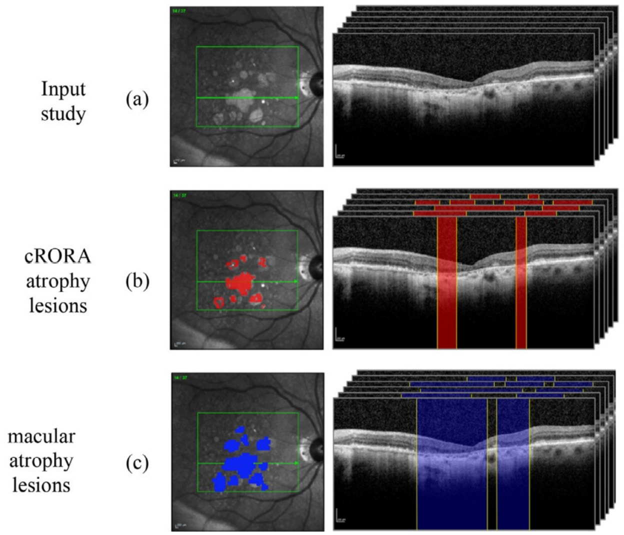


Fig. 3. Illustration of the computation and visualization of cRORA atrophy: (a) IR image with OCT scan FOV (green rectangle); (b) IR image with overlaid atrophy segments (red) identified in the OCT slices; (c) IR image with overlaid atrophy lesions segmentations (red).



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Medical Image Analysis
journal homepage: www.elsevier.com/locate/media

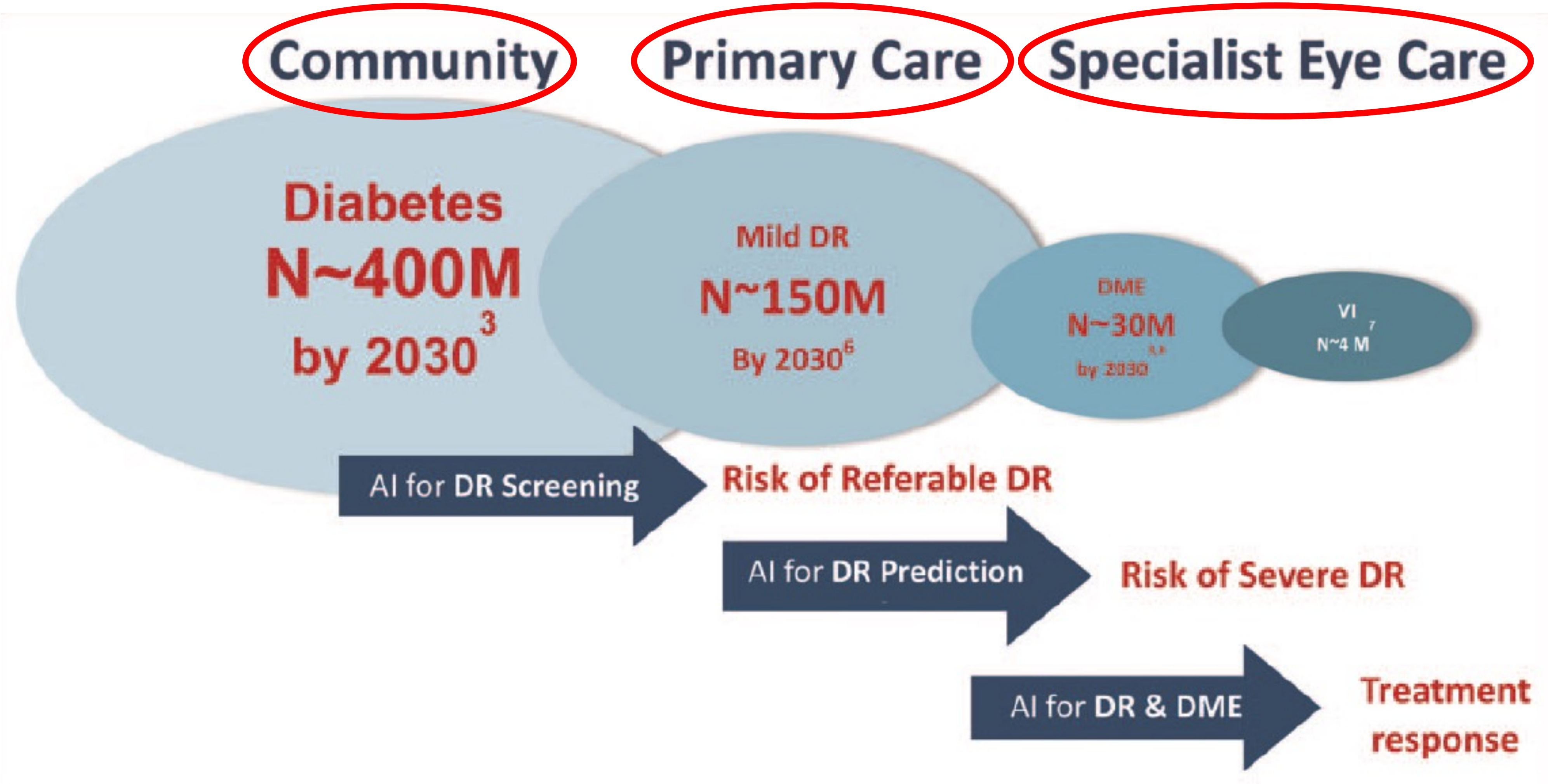
A column-based deep learning method for the detection and quantification of atrophy associated with AMD in OCT scans

Adi Szeskin[a], Roei Yehuda[a], Or Shmueli[b], Jaime Levy[b], Leo Joskowicz[a,*]

[a] School of Computer Science and Engineering, The Hebrew University of Jerusalem, Israel
[b] Department of Ophthalmology, Hadassah Medical Center, Jerusalem, Israel

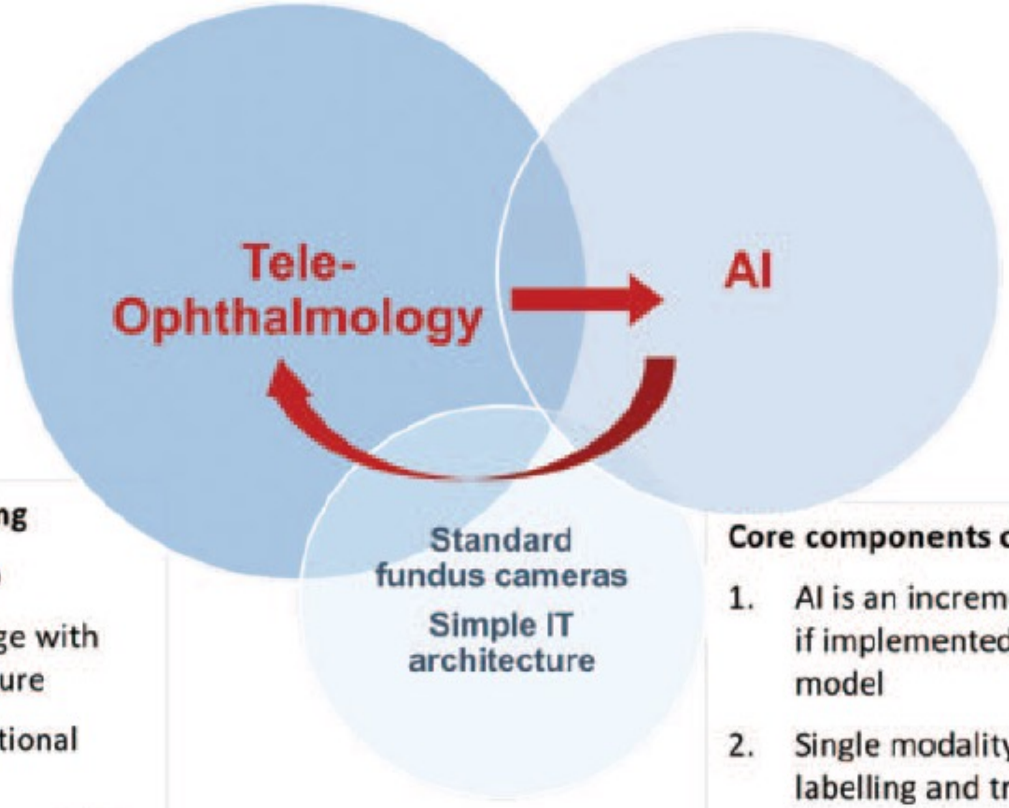
Szeskin A, Yehuda R, Shmueli O, Levy J, Joskowicz L. A column-based deep learning method for the detection and quantification of atrophy associated with AMD in OCT scans. Med Image Anal. 2021

AI for DR screening, prediction and management



Curr Opin Ophthalmol 2020, 31:357–365

Key components for AI-assisted DR tele-screening



Core components of DR tele-screening

1. Clearly defined public health gap
2. Uses single modality fundus image with standard camera & IT infrastructure
3. Diagnosis of DR requires no additional patient or clinical data
4. Robust outcome and cost-effective studies
5. Impact of change: primary care providers, none for ophthalmologists

Core components of AI assisted DR tele-screening

1. AI is an incremental (*not* disruptive) technology if implemented as part of DR tele-screening model
2. Single modality fundus image allows easier labelling and training of AI algorithm
3. Availability of existing large and diverse "real-world" datasets to test AI algorithm
4. Clear pathway for regulatory (FDA, CE) approval
5. Impact of change: none for ophthalmologists

Curr Opin Ophthalmol 2020, 31:357–365

Summary of AI algorithms for DR screening

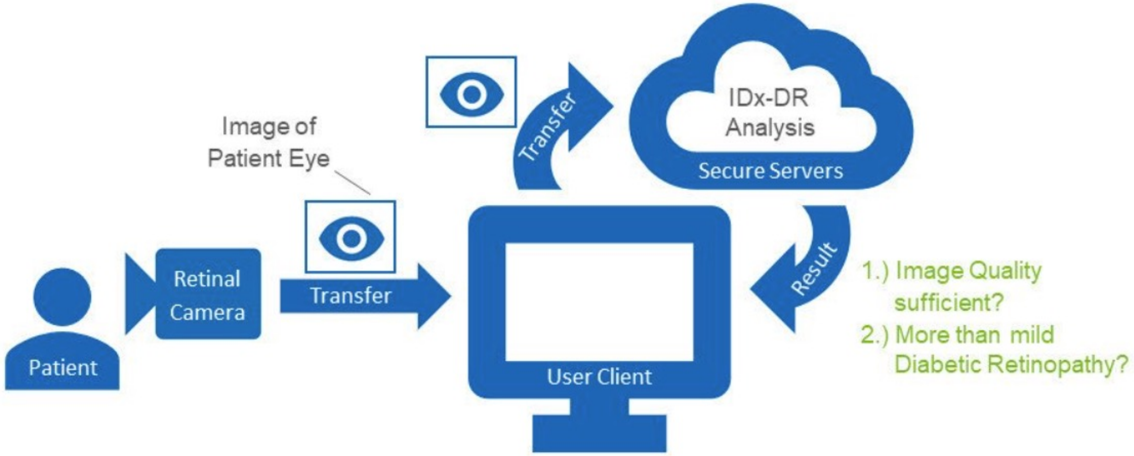
Study	Year	AI techniques	Dataset for development	Dataset for external test/validation	AUC	Sensitivity	Specificity
Abràmoff *et al.*	2016 [38] 2018 [21]	Ensemble of AlexNet & VGGNet	1748 Images	Primary care clinics: 819 patients Primary care clinics: 1616 patients	**0.98** **NR** **NR**	96.8% 87.2% 100%	87.0% 90.7% 97.8%
Gulshan *et al.*	2016 [19] 2019 [42]	Inception-V3 Inception-V4	128 175 Images 103 634 Images	EyePACS-1: 9963 images Messidor-2: 1748 images South India: 3049 patients	**99.1** **99.0** **96.3–98.0**	97.5% 96.1% 88.9–92.1%	93.4% 93.9% 92.2–95.2%
Li *et al.*	2018 [37]	Inception V3	71 043 Images	3 Datasets: 35 201 images	**95.5**	92.5%	98.5%
Raumvib-oonsuk *et al.*	2019 [43]	Inception-V4	1665 151 Images	EyePACS-2: 1958 images	**98.7**	96.8%	95.6%
Lim *et al.*	2019 [39]	VGGNet	40 542 Images	EyePACS-1: 101 710 images	**96.5**	91.3%	91.1%
Ting *et al.*	2017 [20] 2019 [41]	VGGNet Ensemble of VGGNet with ResNet	76 370 Images	SiDRP: 71 896 images 10 datasets: 40 752 images Zambia: 4504 images	**93.6** **0.89–0.98** **97.3**	90.5% 91.8–100% 92.3%	91.6% 73.3–92.2% 89.0%
Son *et al.*	2020 [44]	Customized regional CNN	95 350 Images	IDRiD: 143 images e-ophtha: 434 images	**95.7–98.0** **94.7–96.5**	88.9–92.6 89.2–93.6	94.0–100.0 91.4–97.1

AI, artificial intelligence; AUC, Area Under the receiver operating characteristic Curve (AUC).

IDx-DR

- First FDA-approved autonomous diagnostic system
- Detects DR and ME
- Input: color fundus images

  Output: negative/referable/vision threatening



Xu, Feng, D.; Mi, H. Deep Convolutional Neural Network-Based Early Automated Detection of Diabetic Retinopathy Using Fundus Image. Molecules 2017, 22, 2054

npj | Digital Medicine

www.nature.com/npjdigitalmed

ARTICLE OPEN

Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices

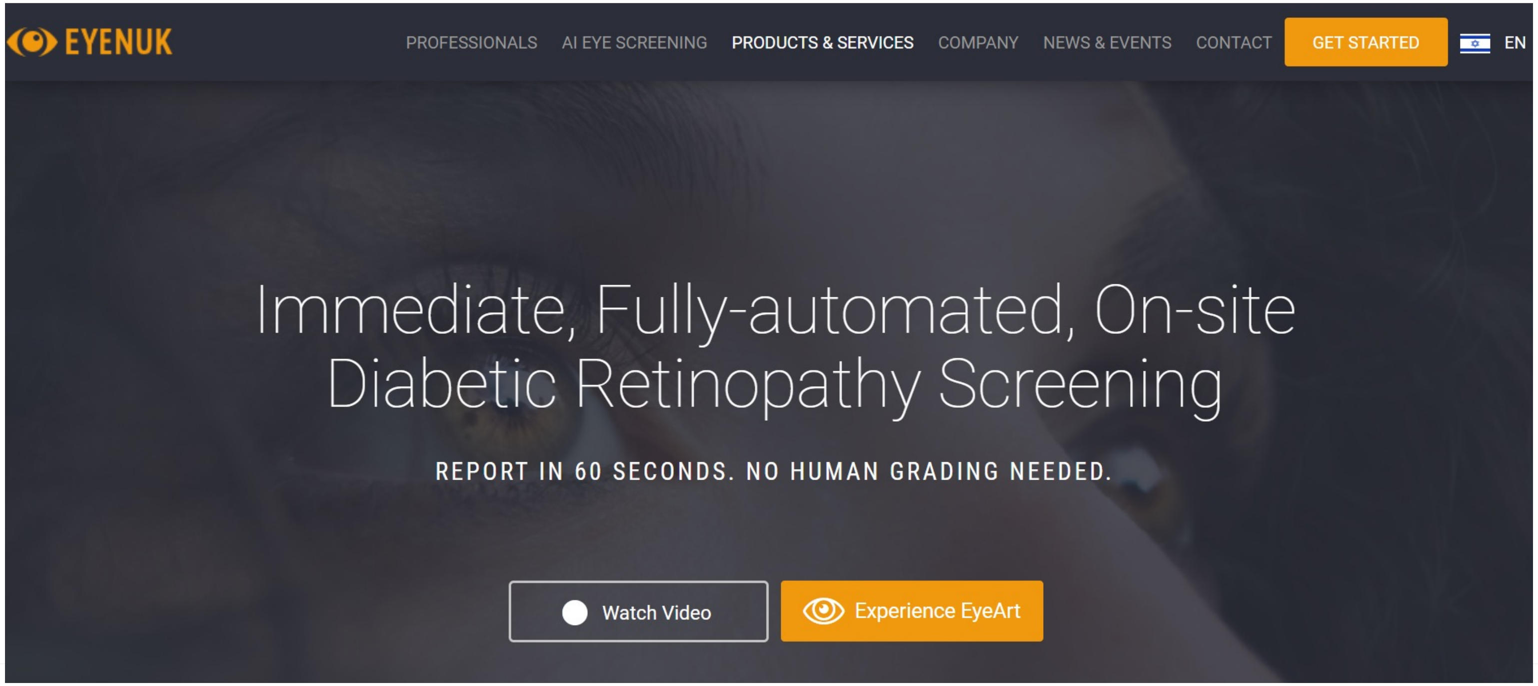
Michael D. Abràmoff[1,2,3,4], Philip T. Lavin[5], Michele Birch[6], Nilay Shah[7] and James C. Folk[1,2,3]

Artificial Intelligence (AI) has long promised to increase healthcare affordability, quality and accessibility but FDA, until recently, had never authorized an autonomous AI diagnostic system. This pivotal trial of an AI system to detect diabetic retinopathy (DR) in people with diabetes enrolled 900 subjects, with no history of DR at primary care clinics, by comparing to Wisconsin Fundus Photograph Reading Center (FPRC) widefield stereoscopic photography and macular Optical Coherence Tomography (OCT), by FPRC certified photographers, and FPRC grading of Early Treatment Diabetic Retinopathy Study Severity Scale (ETDRS) and Diabetic Macular Edema (DME). More than mild DR (mtmDR) was defined as ETDRS level 35 or higher, and/or DME, in at least one eye. AI system operators underwent a standardized training protocol before study start. Median age was 59 years (range, 22–84 years); among participants, 47.5% of participants were male; 16.1% were Hispanic, 83.3% not Hispanic; 28.6% African American and 63.4% were not; 198 (23.8%) had mtmDR. The AI system exceeded all pre-specified superiority endpoints at sensitivity of 87.2% (95% CI, 81.8–91.2%) (>85%), specificity of 90.7% (95% CI, 88.3–92.7%) (>82.5%), and imageability rate of 96.1% (95% CI, 94.6–97.3%), demonstrating AI's ability to bring specialty-level diagnostics to primary care settings. Based on these results, FDA authorized the system for use by health care providers to detect more than mild DR and diabetic macular edema, making it, the first FDA authorized autonomous AI diagnostic system in any field of medicine, with the potential to help prevent vision loss in thousands of people with diabetes annually. ClinicalTrials.gov NCT02963441

npj Digital Medicine (2018)1:39 ; doi:10.1038/s41746-018-0040-6

https://youtu.be/zF2uhO7Wuag

Autonomic AI based DR Screening



STEP 1

Capture color retinal fundus images of the patient's eyes

STEP 2

Submit images to the cloud for analysis

STEP 3

Download DR screening results and export PDF report.

- Challenges?

EYENUK

EyeArt
Diabetic Retinopathy Screening Report

Patient Information

Patient ID: 123-45-6789
Patient Name: Michelle L. Roddy
Date of Birth: 04-Mar-1963
Gender: Female
Submission Date: 2019/03/15 12:41

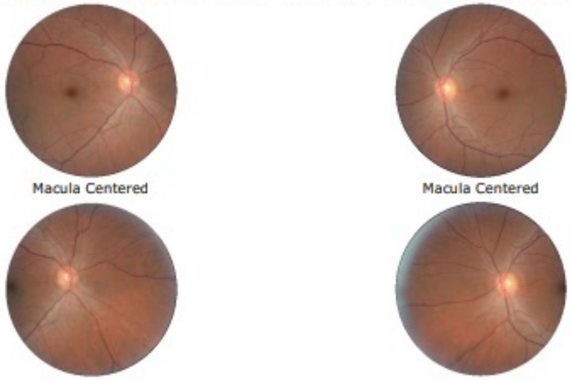
General Information

Referring Location: St. Lucy's
Referring Provider: Dr. Charlie Hallock
Encounter ID: 0987-abc-d1k
EyeArt Control ID: 560144
Dilation Status: Non Dilated

Diabetic Retinopathy Screening Summary

Screening Result: Negative for referable diabetic retinopathy.

Right Eye: No apparent signs of DR detected [0.0]
Left Eye: No apparent signs of DR detected [0.0]



Macula Centered | Macula Centered
ONH Centered | ONH Centered

*Do not use the above thumbnail images for diagnostic purposes.

ICD-10 Diagnosis Codes

E11.9 Type 2 diabetes mellitus without complications

Plan and Recommendations

Return for retinal imaging within 12 months.

As per ADA recommendations, emphasize the importance of controlling blood sugar, cholesterol and blood pressure as well the importance of routine follow-up with an ophthalmologist regardless of whether visual symptoms are present or absent.

Report Date: 2019/03/15 12:46

Warning: This report is automatically generated using EyeArt and only provides a Diabetic Retinopathy (DR) screeningassessment. This screening does not take place of a regular eye examination for the purpose of assessing the presence of age-related macular degeneration, glaucoma, cataract, anterior segment diseases or other possible vision threatening conditions. For customer support, please email support@eyenuk.com 1/1

ID:123-45-6789 | NAME:Michelle L. Roddy | DOB:04-Mar-1963

EYENUK

EyeAr
Diabetic Retinopathy Screening Report

Patient Information

Patient ID: 123-45-6791
Patient Name: Benny S. Jones
Date of Birth: 22-Nov-1951
Gender: Male
Submission Date: 2019/03/15 12:45

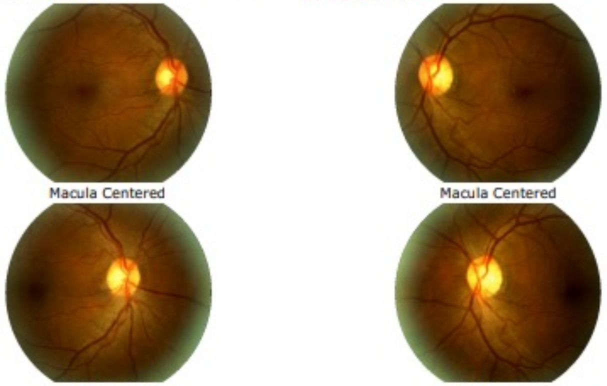
General Information

Referring Location: St. Lucy's
Referring Provider: Dr. Charlie Hallock
Encounter ID: 0987-abc-d1m
EyeArt Control ID: 560145
Dilation Status: Non Dilated

Diabetic Retinopathy Screening Summary

Screening Result: Positive for vision threatening diabetic retinopathy.

Right Eye: Signs of Moderate NPDR [2.3] without macular edema detected
Left Eye: Signs of Moderate NPDR [2.9] with macular edema detected



Macula Centered | Macula Centered
ONH Centered | ONH Centered

*Do not use the above thumbnail images for diagnostic purposes.

ICD-10 Diagnosis Codes

E11.3391 Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, right eye

E11.3312 Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye

Plan and Recommendations

Immediate referral to ophthalmologist for evaluation of vision threatening diabetic retinopathy.

As per ADA recommendations, emphasize the importance of controlling blood sugar, cholesterol and blood pressure as well the importance of routine follow-up with an ophthalmologist regardless of whether visual symptoms are present or absent.

Report Date: 2019/03/15 12:47

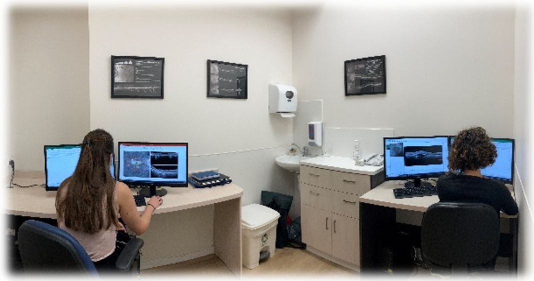
Warning: This report is automatically generated using EyeArt and only provides a Diabetic Retinopathy (DR) screeningassessment. This screening does not take place of a regular eye examination for the purpose of assessing the presence of age-related macular degeneration, glaucoma, cataract, anterior segment diseases or other possible vision threatening conditions. For customer support, please email support@eyenuk.com 1/1

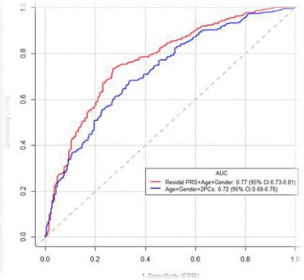
ID:123-45-6791 | NAME:Benny S. Jones | DOB:22-Nov-1951

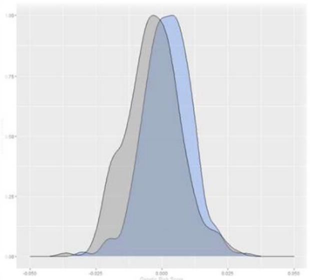
Our Wild Journey into the New Era

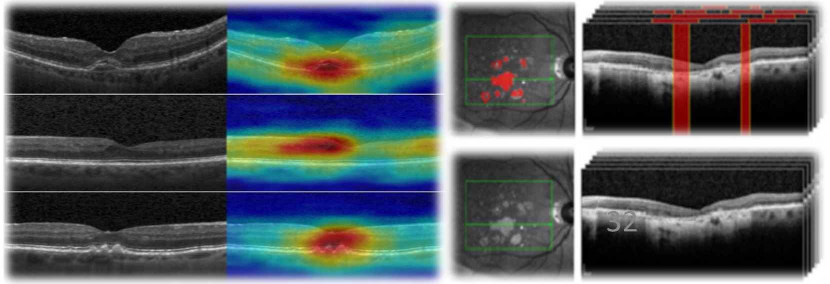
Hadassah Ophthalmology AMD AI project

0. Preliminary work
1. Regulatory approval
2. Data generation and extraction
3. Data preparation
4. Data sharing and analysis
5. Developing AI models
6. Implementing AI tools in the clinic

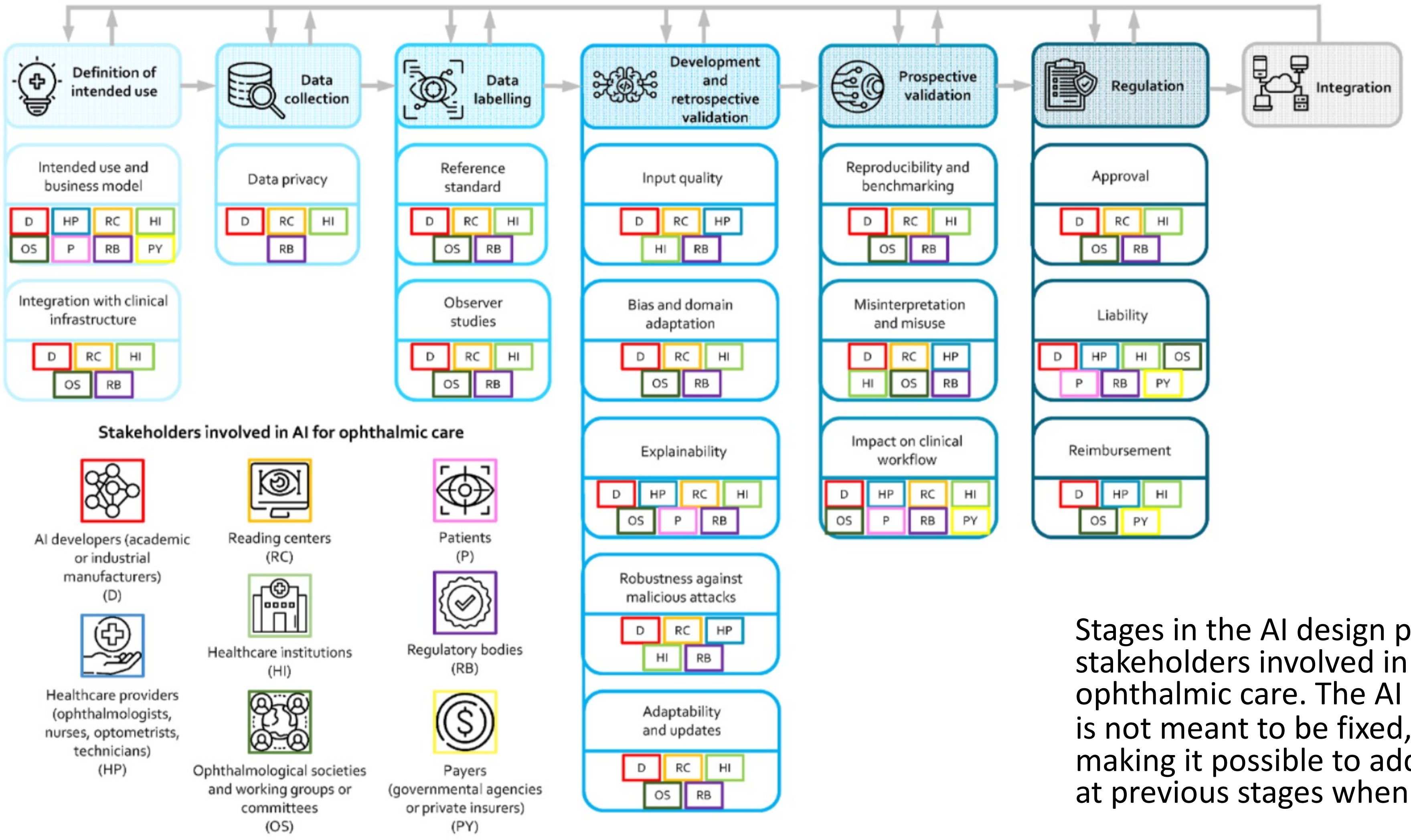








AI Systems in Ophthalmic Practice



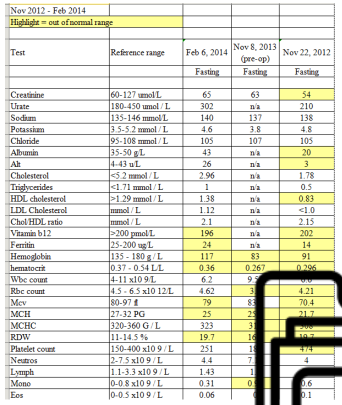
Stages in the AI design pipeline and the stakeholders involved in AI for ophthalmic care. The AI design pipeline is not meant to be fixed, but cyclic, making it possible to address challenges at previous stages when necessary.

Gonzalez-Gonzalo et al., PRER 2022

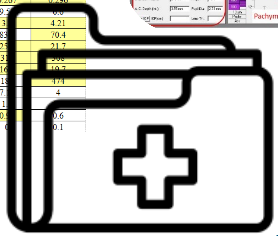
Challenges - Research

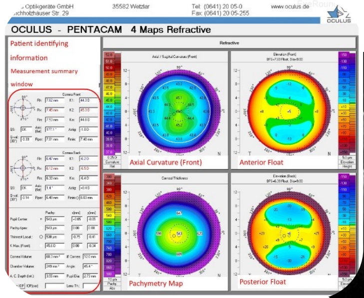
- Accessing EMR/imaging data
- Downloading data - generating DB
- Anonymization according to the MOH guidelines
- Regulatory approvals - ethics, data committee
- Computation resources - cloud/on site

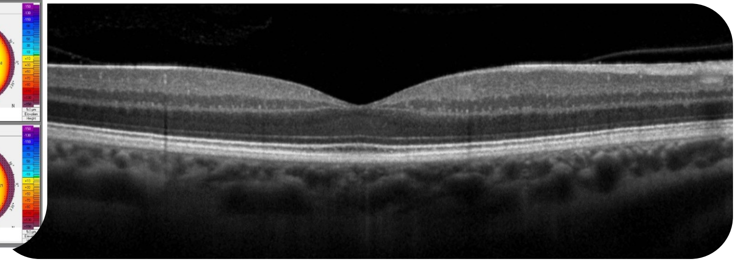
Challenges - Interdisciplinary Collaboration

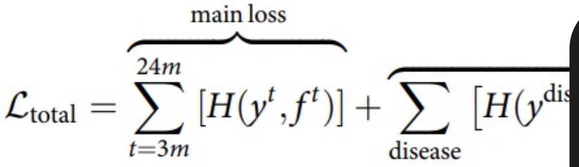


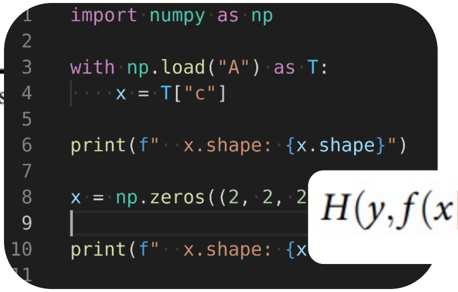
Nov 2012 - Feb 2014				
Highlight = out of normal range				
Test	Reference range	Feb 6, 2014	Nov 8, 2013 (pre-op)	Nov 22, 2012
		Fasting	Fasting	Fasting
Creatinine	60-127 umol/L	65	63	54
Urate	180-450 umol / L	302	n/a	210
Sodium	135-146 mmol/L	140	137	138
Potassium	3.5-5.2 mmol / L	4.6	3.8	4.8
Chloride	95-108 mmol / L	105	107	105
Albumin	35-50 g/L	43	n/a	20
Alt	4-43 u/L	26	n/a	3
Cholesterol	<5.2 mmol / L	2.96	n/a	1.78
Triglycerides	<1.71 mmol / L	1	n/a	0.5
HDL cholesterol	>1.29 mmol / L	1.38	n/a	0.83
LDL Cholesterol	mmol / L	1.12	n/a	<1.0
Chol/HDL ratio	mmol / L	2.1	n/a	2.15
Vitamin b12	>200 pmol/L	196	n/a	202
Ferritin	25-200 ug/L	24	n/a	14
Hemoglobin	135 - 180 g / L	117	83	91
hematocrit	0.37 - 0.54 L/L	0.36	0.267	0.296
Wbc count	4-11 x10 9/L	6.2	[illegible]	[illegible]
Rbc count	4.5 - 6.5 x10 12/L	4.62	[illegible]	4.21
Mcv	80-97 fl	79	[illegible]	70.4
MCH	27-32 PG	25	[illegible]	21.7
MCHC	320-360 G / L	323	[illegible]	[illegible]
RDW	11-14.5 %	19.7	[illegible]	19.7
Platelet count	150-400 x10 9 / L	251	[illegible]	474
Neutros	2-7.5 x10 9 / L	4.4	[illegible]	4
Lymph	1.1-3.3 x10 9 / L	1.43	[illegible]	[illegible]
Mono	0-0.8 x10 9 / L	0.31	[illegible]	0.6
Eos	0-0.5 x10 9 / L	0.06	[illegible]	0.1

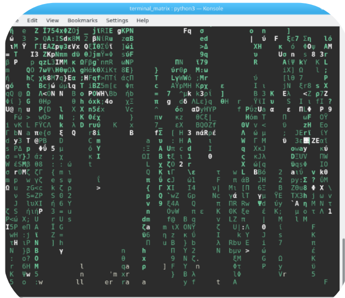












$$H(y, f(x|\theta)) = \sum_{k=1}^{K} -y_k \log(f_k(x|\theta))$$

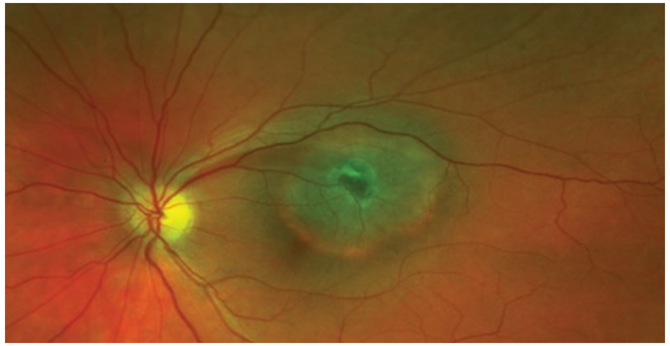
Challenges - Integrating AI into the Clinic

- Regulatory approval
- Technical challenges
- The business case

Clinical and technical challenges in building and deploying DL techniques from 'bench to bedside'

Steps	Potential challenges
1. Identification of training data sets	1. Patients' consent and confidentiality issues. 2. Varying standards and regulations between the different institutional review boards. 3. Small training data sets for rare disease (eg, ocular tumours) or common diseases that are not captured in routine (eg, cataracts).
2. Validation and testing data sets	1. Lack of sample size—not sufficiently powered. 2. Lack of generalisability—not tested widely in different populations or on data collected from different devices.
3. Explainability of the results	1. Demonstration of the regions 'deemed' abnormal by DL. 2. Methods to generate heat maps—occlusion tests, class activation, integrated gradient method, soft attention map and so on.
4. Clinical deployment of DL Systems	1. Recommendation of the potential clinical deployment sites. 2. Application of regulatory approval from health authorities (eg, US Food and Drug Administration, Europe CE marking and so on). 3. Conducting prospective clinical trials. 4. Medical rebate scheme and medicolegal requirement. 5. Ethical challenges.

Ting DSW, *et al*. *Br J Ophthalmol* 2019;**103**:167–175. doi:10.1136/bjophthalmol-2018-313173



OCT devices, protocols, resolution, format,…

KEY COMPANIES

Abbott HAAG-STREIT SURGICAL TOMEY NIDEK

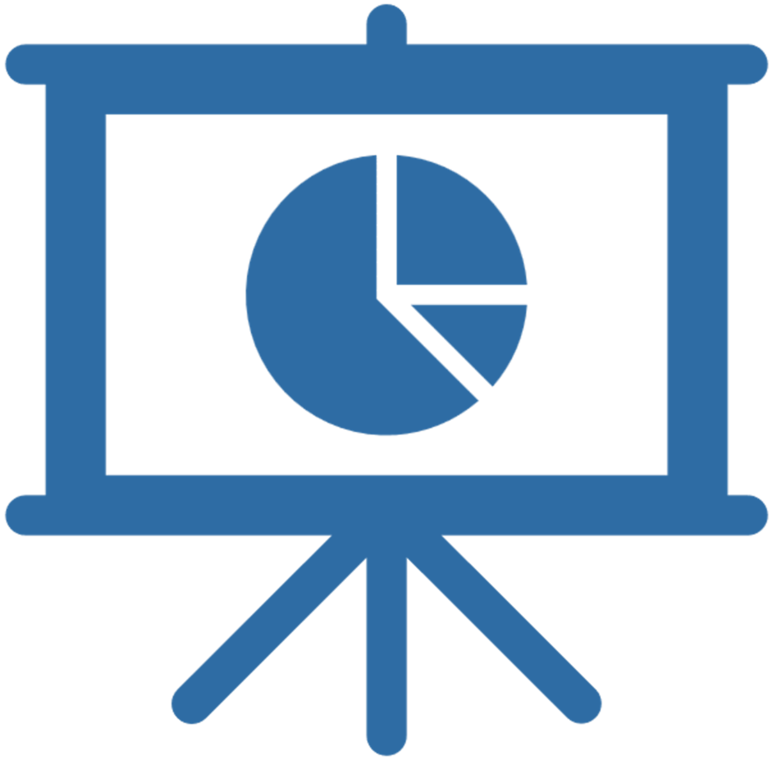
TERUMO optos santec

OPTOPOL technology LUMEDICA OPTOVUE TOPCON

ZEISS Leica MICROSYSTEMS Canon CANON MEDICAL CSO NOVACAM

And Many Others

Figure 1. OCT angiography (OCTA) devices

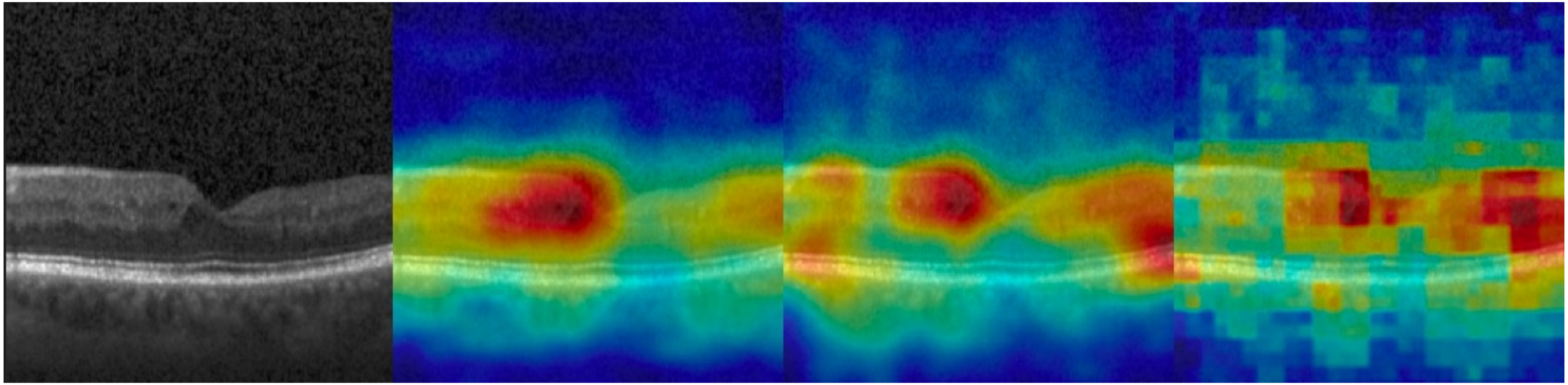


Our Project Results (so far)

Anomaly Detection Results

Developing a novel state-of-the-art model using localization **self supervised**

DL algorithm for detecting retinal diseases and biomarkers

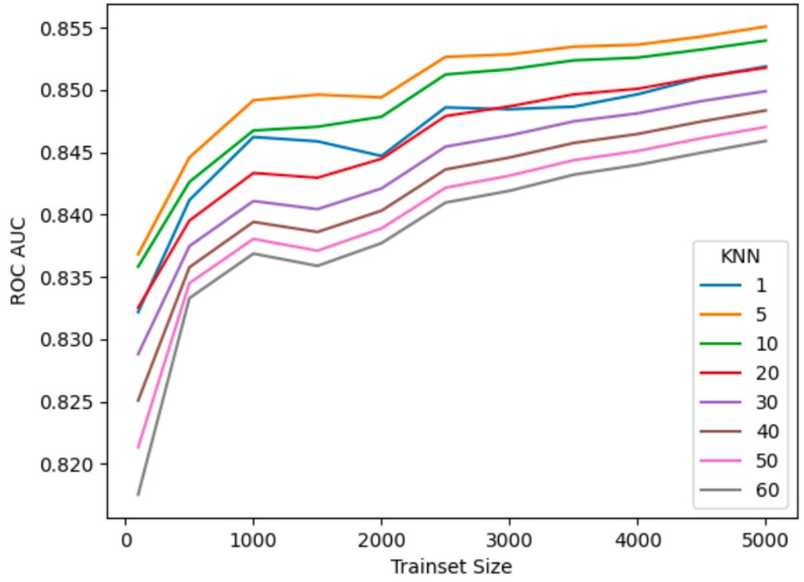


Collaborators: Ron Abutbul, Yedid Hoshen

Anomaly Detection Results

Table 1: Image-level anomaly detection accuracy (Average ROCAUC%)

Model	SPADE (R50)	SPADE (R152)	PaDiM (R50)	PaDiM (R152)	PatchCore (R50)	PANDA (R50 EWC)	PANDA (R152 EWC)	PaDiM (R50 EWC)	PaDiM (R152 EWC)	PatchCore (R50 EWC)
CNV	89.9	93.9	84.9	84.3	96.8	94.5	95.2	85.8	85.2	**97**
DME	80.5	85.9	81.1	85.1	91.7	87.9	85.9	81.9	82.6	**91.8**
DRUSEN	70	76.4	72.2	74.2	84.1	77.3	77.3	70.9	70	**84.5**
Average	80.13	85.4	79.4	81.2	90.8	86.5	86.1	79.5	79.2	**91.1**



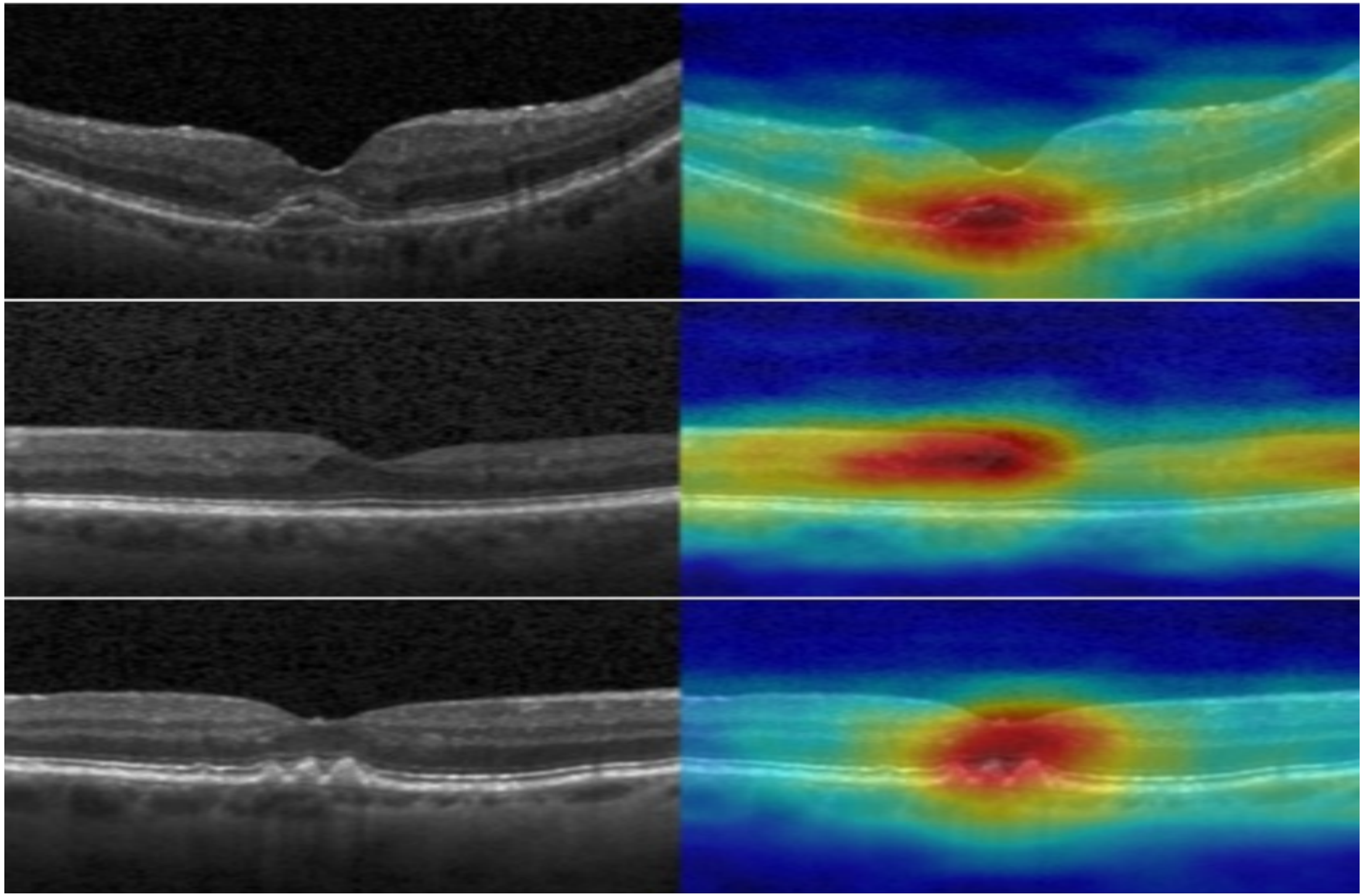
Collaborators: Ron Abutbul, Yedid Hoshen

Localization results:

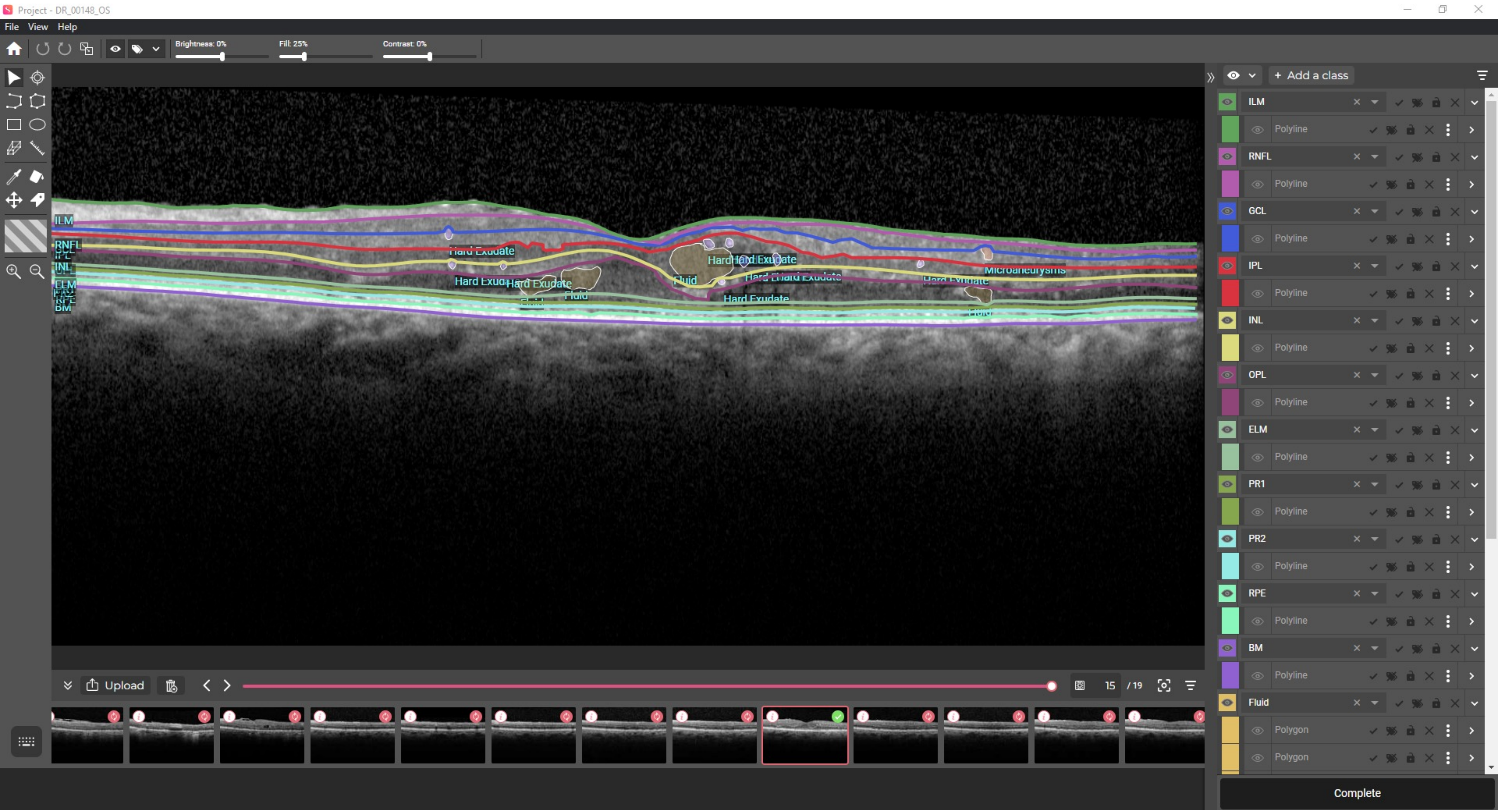
CNV

DME

DRUSEN



Collaborators: Ron Abutbul, Yedid Hoshen


Project - DR_00148_OS
File
View
Help
Brightness: 0%
Fill: 25%
Contrast: 0%
+ Add a class
ILM
Polyline
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RPE
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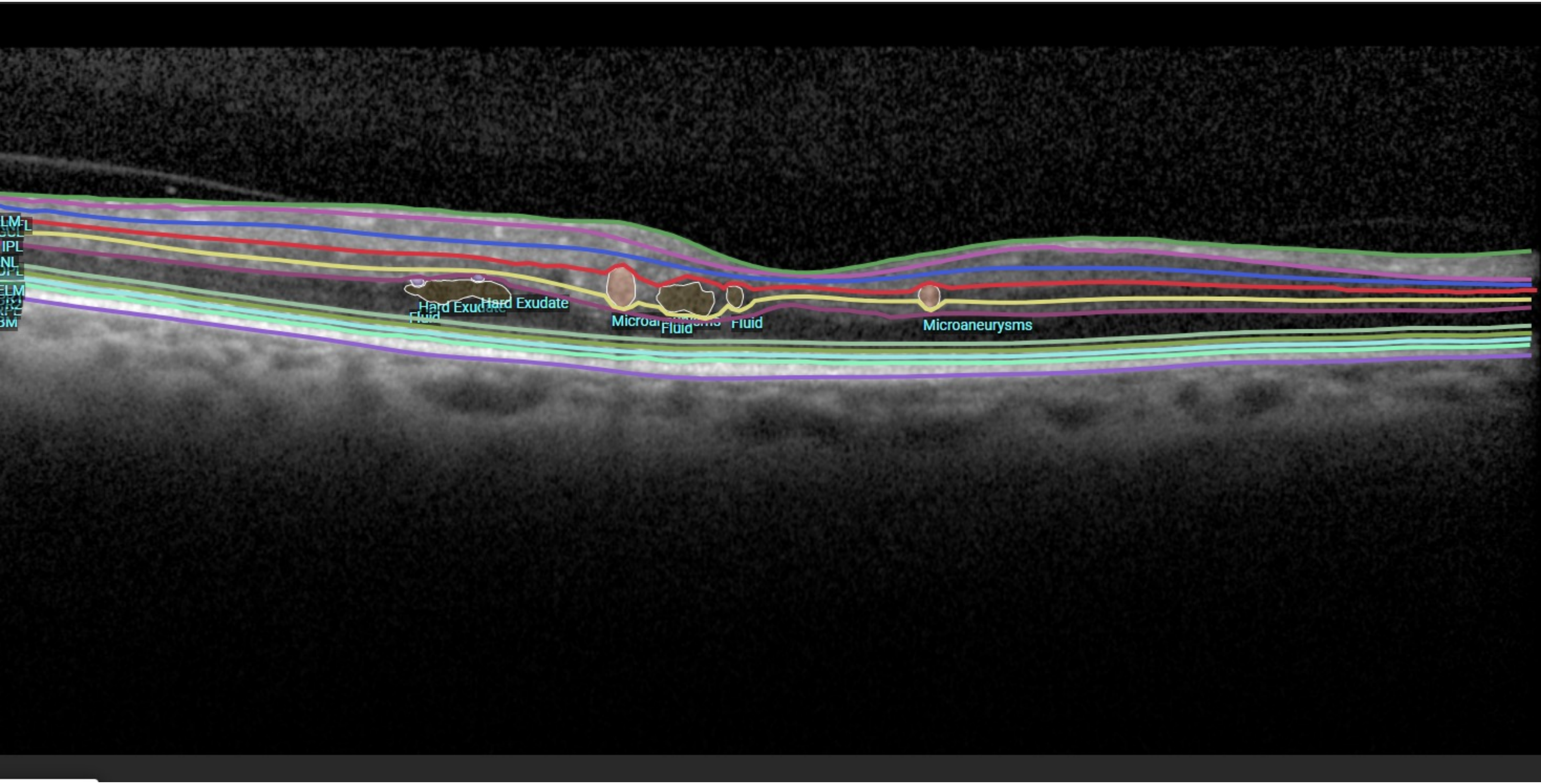
Microaneurysms


IPL
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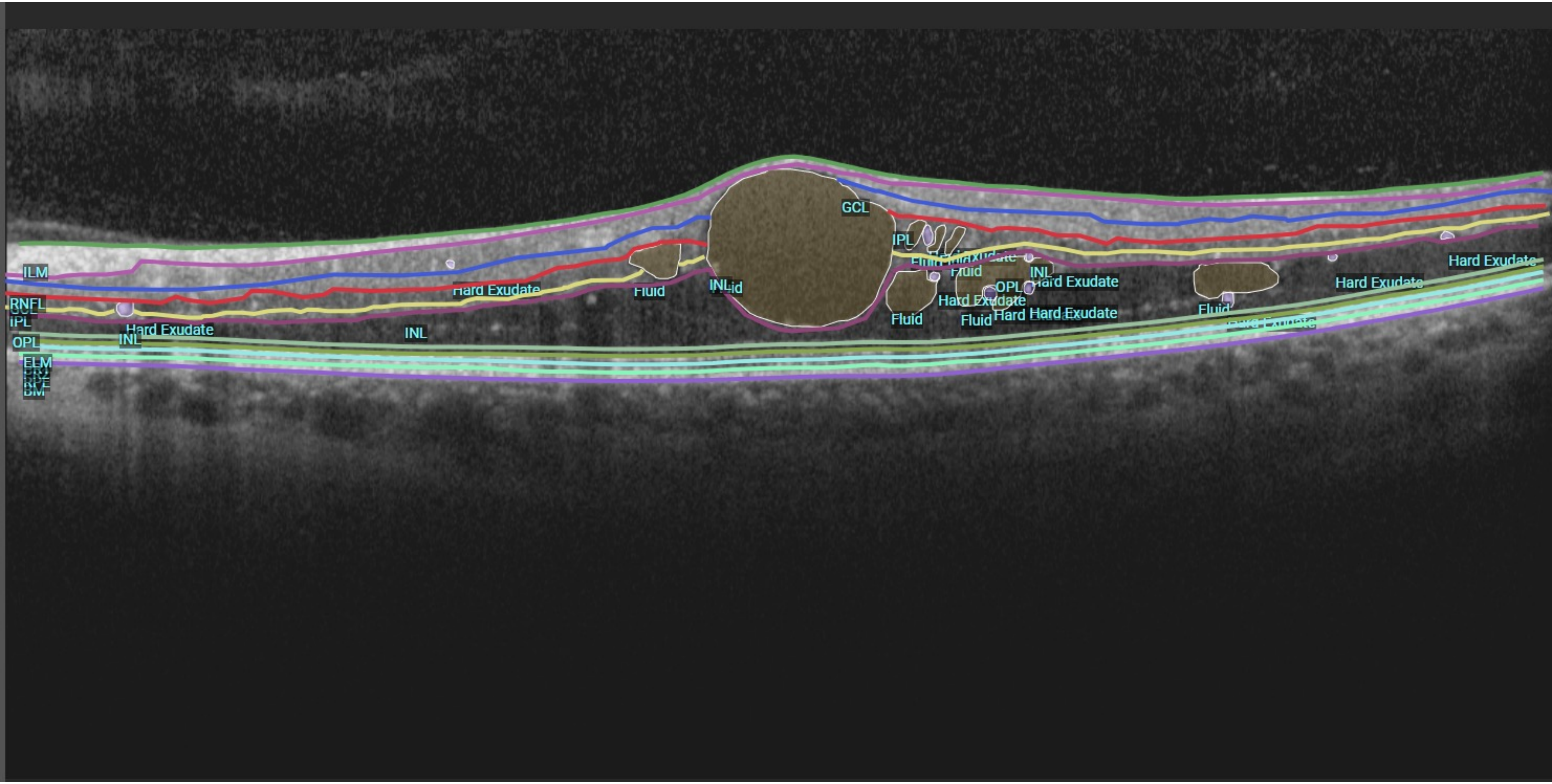
Fluid
Microaneurysms



ILM
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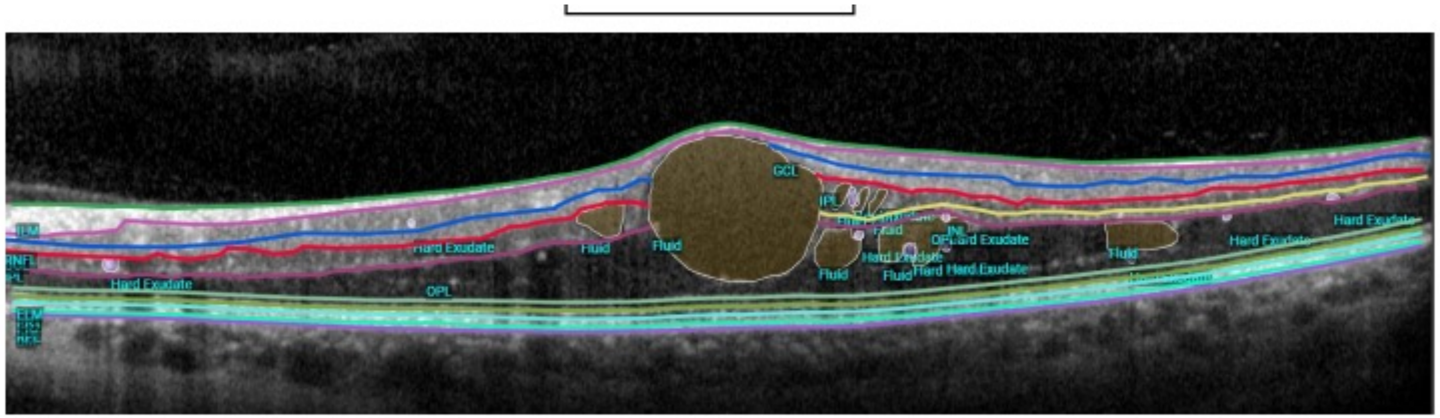
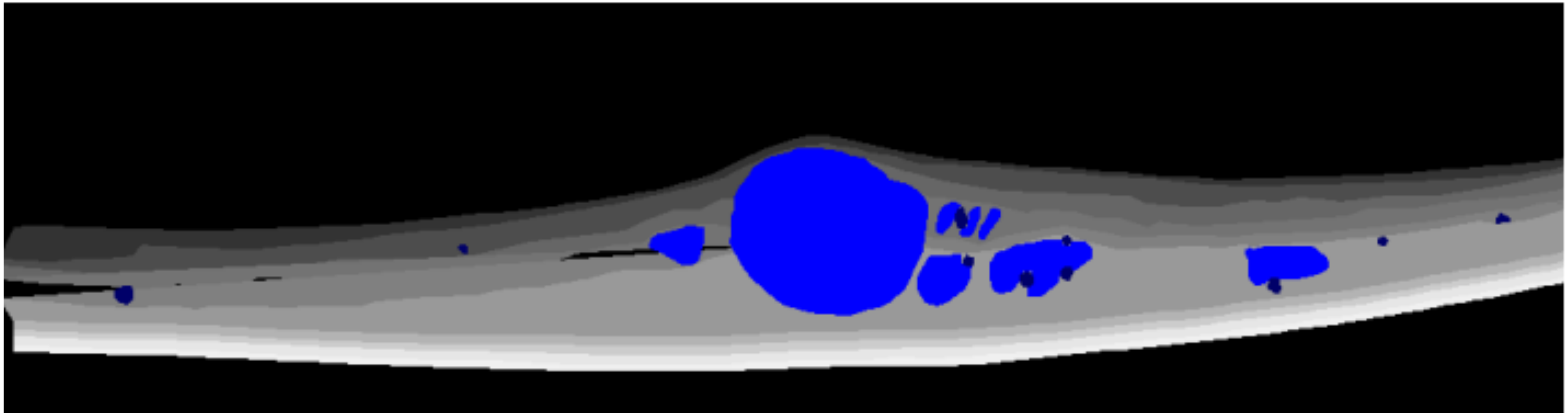
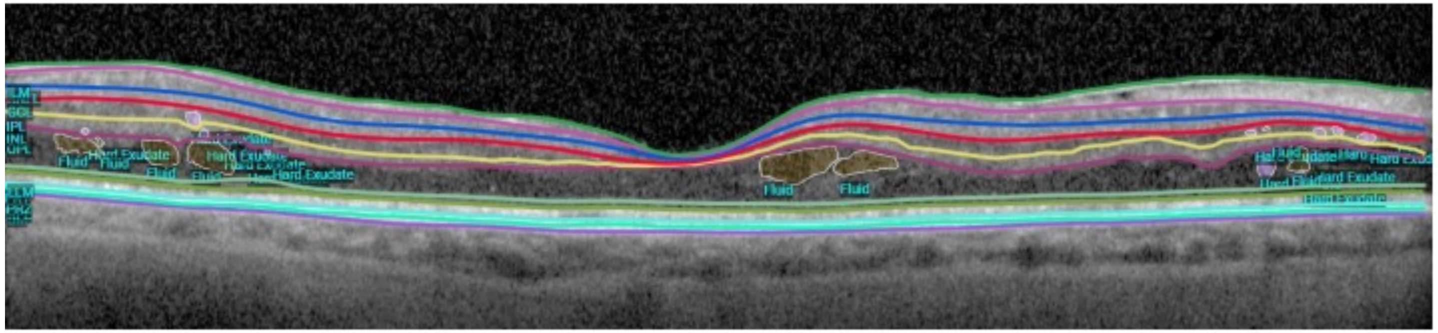
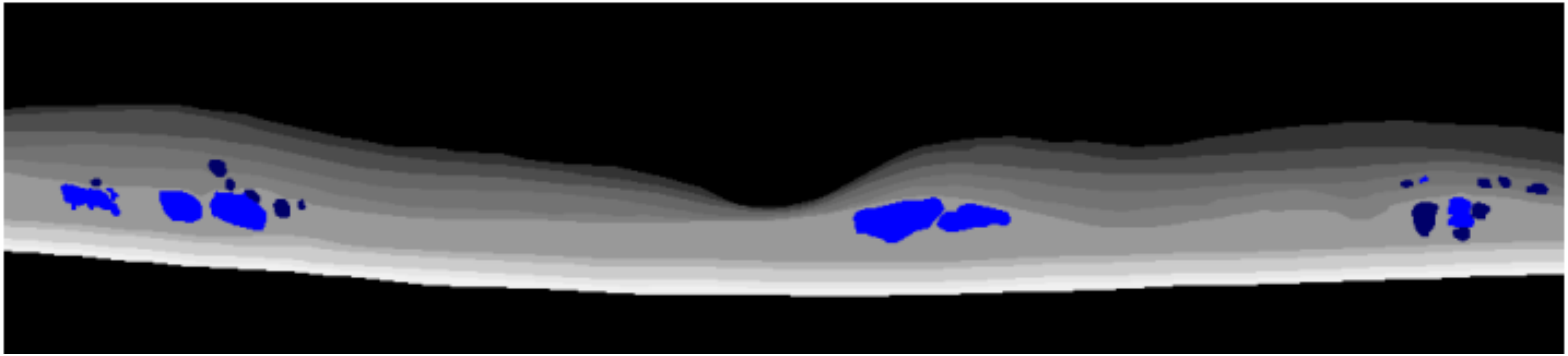




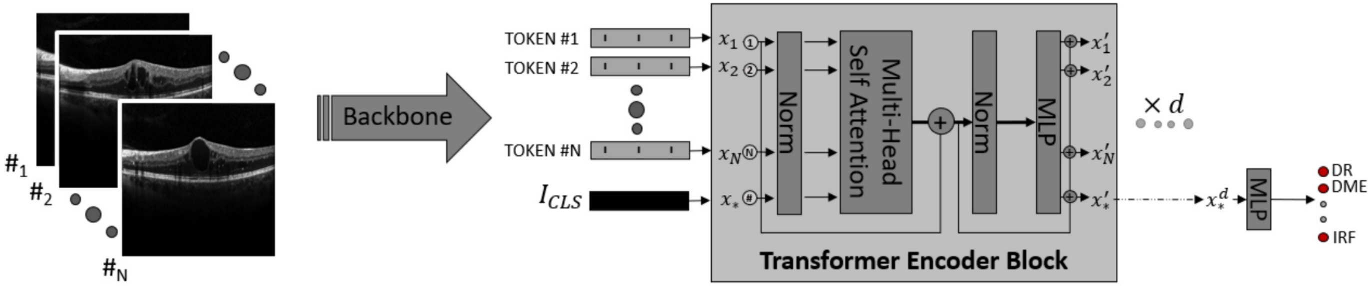
In collaboration with Meirav Galun, Danny Harari, Shimon Ulman; The Weitzman Institute of Science



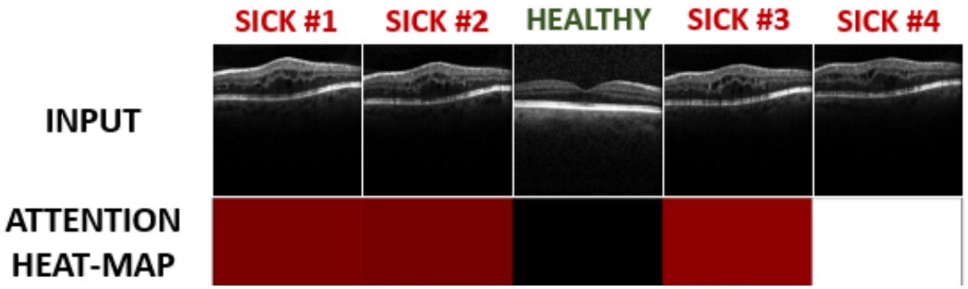


In collaboration with Meirav Galun, Danny Harari, Shimon Ulman; The Weitzman Institute of Science

Attention Based Classification of DR



OCT-Transformer architecture.



Synthetically composed volume and its corresponding attention heat-map. The brighter the color the higher the attention-score, with black and white at the ends and shades of red in between.

F1-Score	**SliverNet**	**Equivariant**	**OCT-Transformer**
DR	42.62%	65.45%	**75.56%**
DME	52.63%	64.52%	**81.48%**
IRF	72.73%	68.42%	**83.33%**
Normal	82.49%	89.95%	**94.47%**
Macro-F1	65.75%	73.13%	**83.8%**

Classification F1-Score Results on the Hadassah dataset; our models compared to previous method SliverNet.

Collaborators: Meirav Galun, Danny Harari, Dan Segev

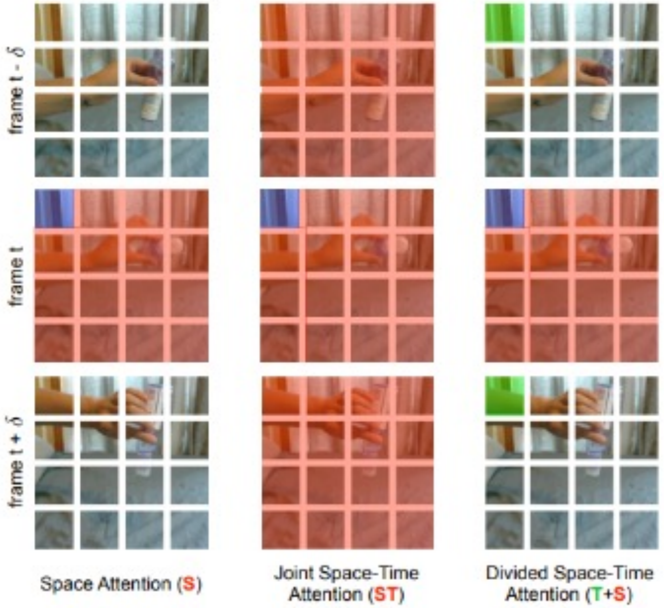
WEIZMANN INSTITUTE OF SCIENCE

DL Methods Results

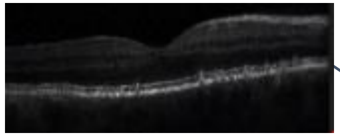
- Goal #1 (predict AMD stage from volume OCT/IR):
  - Model: Based on Timesformer -> Video with Transformers (same as large language models)

    https://arxiv.org/pdf/2102.05095.pdf

    https://github.com/facebookresearch/TimeSformer

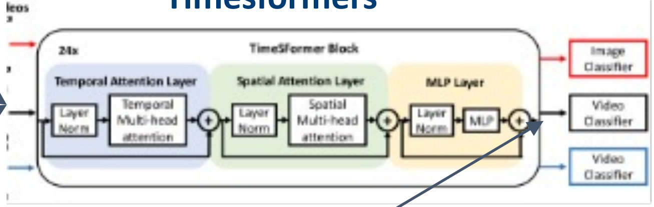


Full OCT scan

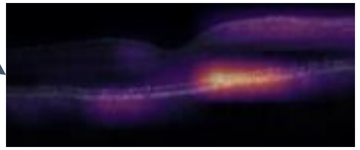


IR

Timesformers



AMD stage (3-9 classes)
Confidence

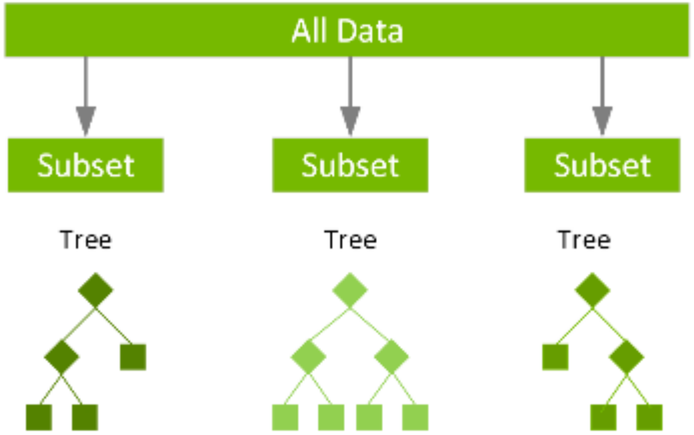


Annotations: AMDstage, Dry St, Drusen, age

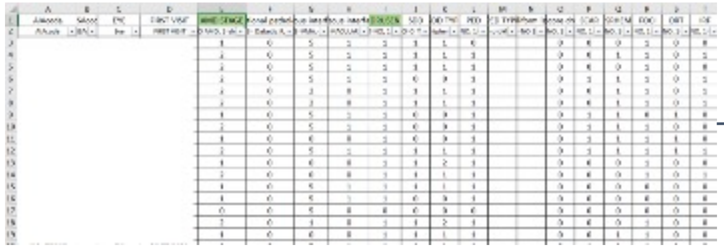
Collaborators: Intel

DL Methods Results

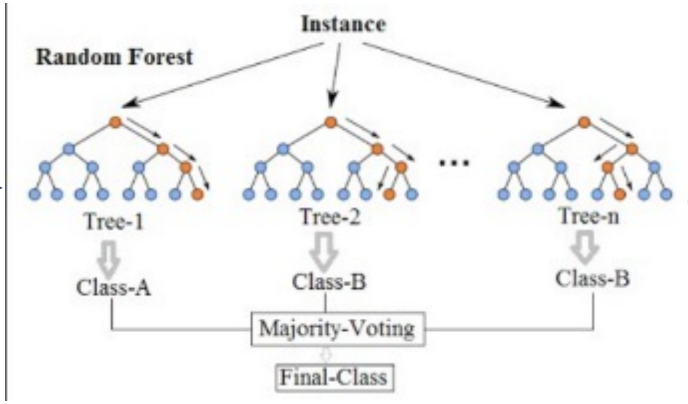
- Goal #2 (predict time to converting to neovascular disease):
- Model: Under development.
  - Tring XGBosst, Random-Forest
  - In the future: Vision+Tabular



Tabular data



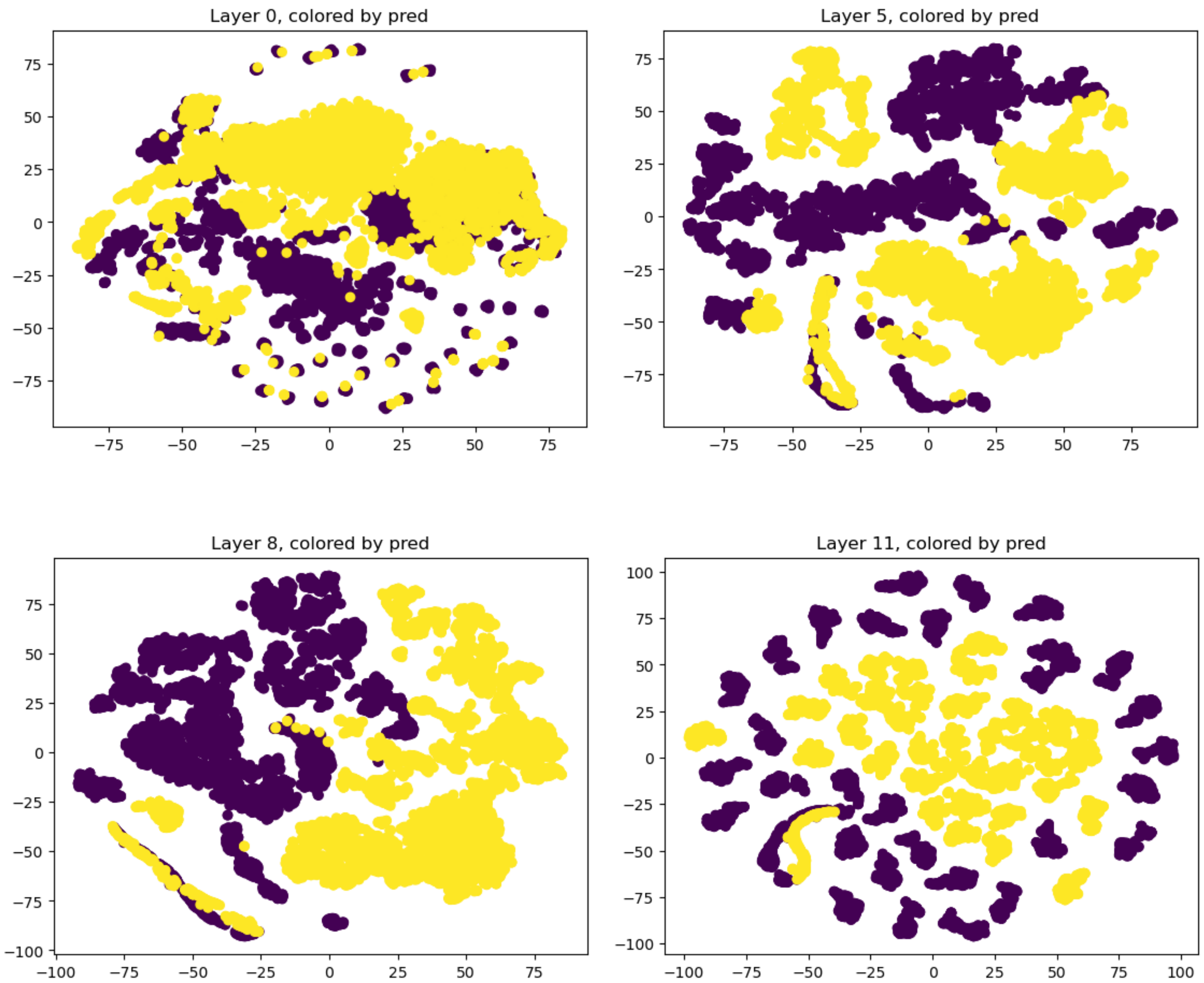
Machine learning model



Time to wet class:
0-4 Months
5-18 Months
>18 months

Collaborators: Intel

DL Methods Results



Progression in the CNN layers more easily separates and better predicts better the different AMD stages

Purple – neovascular AMD
Yellow – non-neovascular AMD

Collaborators: Intel

Take-Homes

- New era
- Challenges for AI integration in the clinic/outreach setting
- Opportunities for:
  - Research
  - Entrepreneurship
  - Bringing value for our patients
- **You can do it!**

Thank you for your attention!

- Dr. Liran Tiosano, tiosano@hadassah.org.il
- Prof. Jaime Levi, ljaime@hadassah.org.il
- Prof. Itay Chowers, chowers@hadassah.org.il

THE HEBREW UNIVERSITY OF JERUSALEM

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