

OPI-Lab

Laboratorio de Óptica y
Procesamiento de Imágenes

Medical Digital Image Processing in Ophthalmology: Successes and Current Challenges

Andrés G. Marrugo, Ph.D.

Dept. of Mechanical and Mechatronics
Engineering

opilab.utb.edu.co

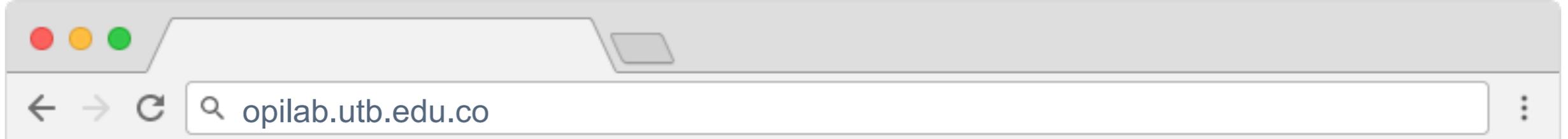
Terrassa, January 31st, 2019





- Founded in 1533
- UNESCO World Heritage Site





OPI·Lab

[Publicaciones](#)

[Personal](#)

[Proyectos](#)

[Seminario](#)

[Docencia](#)

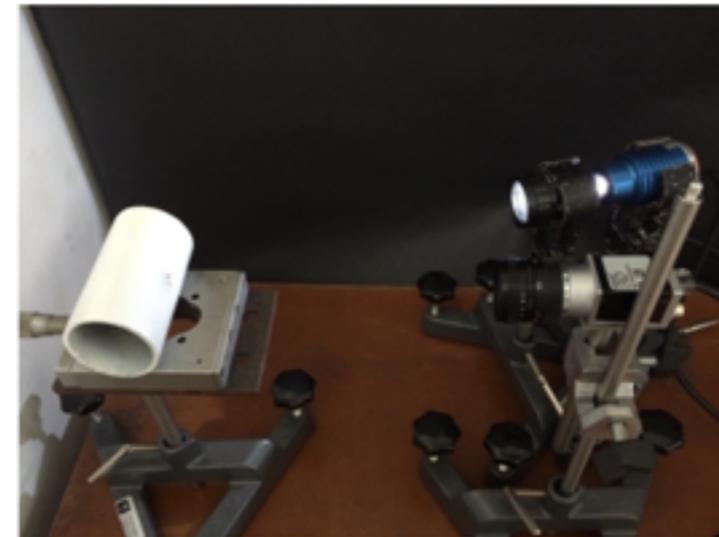
[Wiki](#)

[English](#)



OPI·Lab - Laboratorio de Óptica y Procesamiento de Imágenes.

Somos un laboratorio de óptica aplicada y procesamiento de imágenes enfocados en metrología óptica, imagenología médica, reconstrucción 3D, microscopía y procesamiento digital de imágenes.



Noticias

27. Noviembre 2018

Le otorgaron el reconocimiento **SPIE Rising Researcher** al prof. Andrés Marrugo. ¡Felicitaciones!

16. Noviembre 2018

Artículo aceptado en **Applied Optics**. Saldrá en el Vol 58, número 5 de febrero 2019. Felicitaciones a



Andrés Marrugo

Profesor asociado



Image Processing
Medical Imaging
Optical Metrology



Lenny Romero

Profesora asociada



Image Processing
Optical Metrology
Diffractive Optics

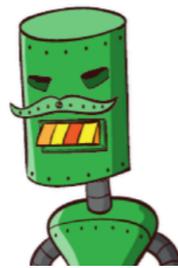


Hernando Altamar

*Profesor asistente /
Estudiante de doctorado*



Microscopy
Image Processing



Raul Vargas

Estudiante de maestría



Jesus Pineda

Estudiante de maestría



Enrique Sierra

Estudiante de maestría



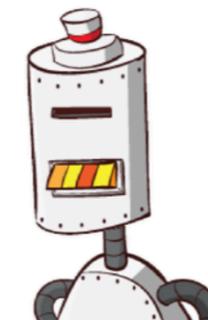
Erik Barrios

Estudiante de maestría



Jhacson Meza

Estudiante de pregrado



Juan Sierra

Estudiante de pregrado



I'm going to talk about **three** things:

1. How **medical imaging** has dramatically changed in recent years.
2. **New technologies in digital image processing** are enabling **computer-aided diagnostics**, treatment, etc.
3. **Still many challenges** in the underlying technology.

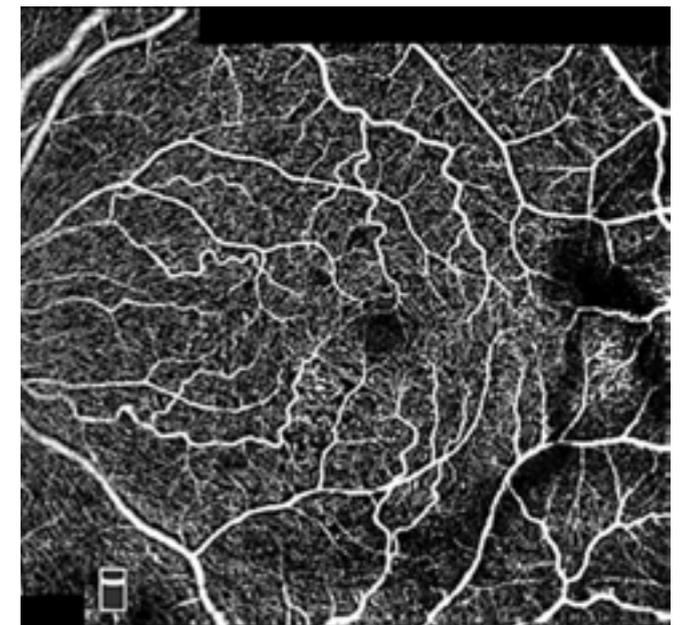
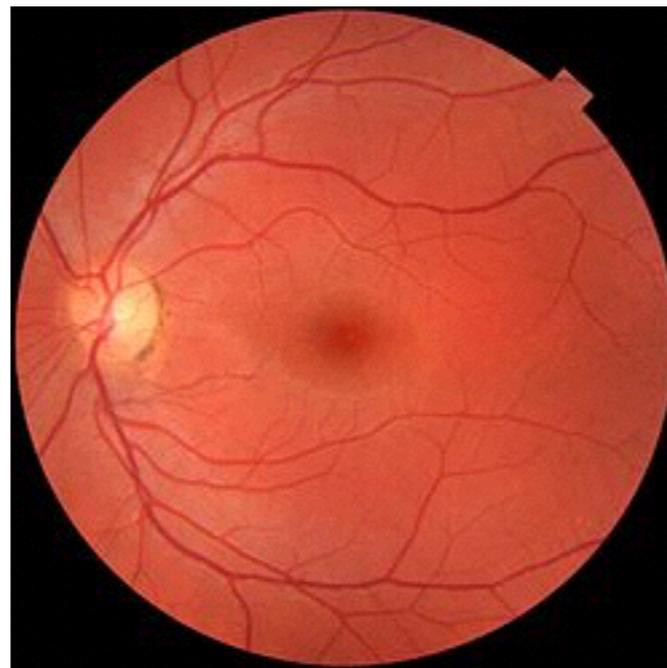
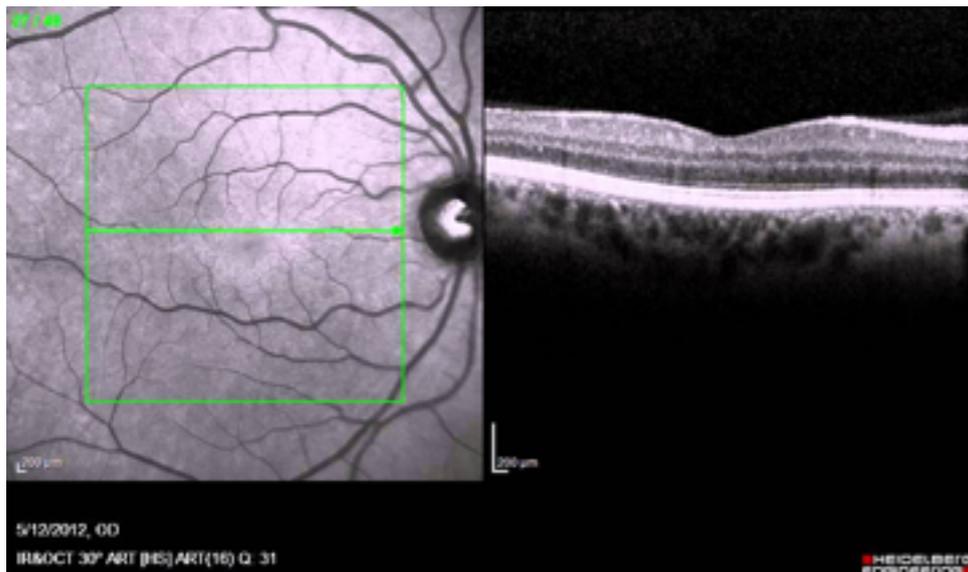
Caveats

- This talk does not intend to be a comprehensive review of ophthalmic imaging.
- The topics presented here have come to our attention due to our research interests.

1. Medical Imaging



Ophthalmology is a field heavily dependent on images.



1. Medical Imaging



Ophthalmology is a field heavily dependent on images

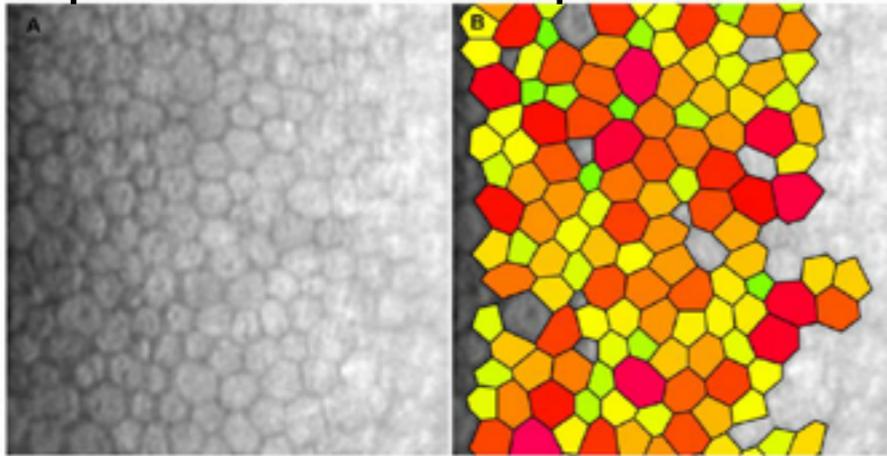
Diagnostic / screening purposes.

Disease progression assessment.

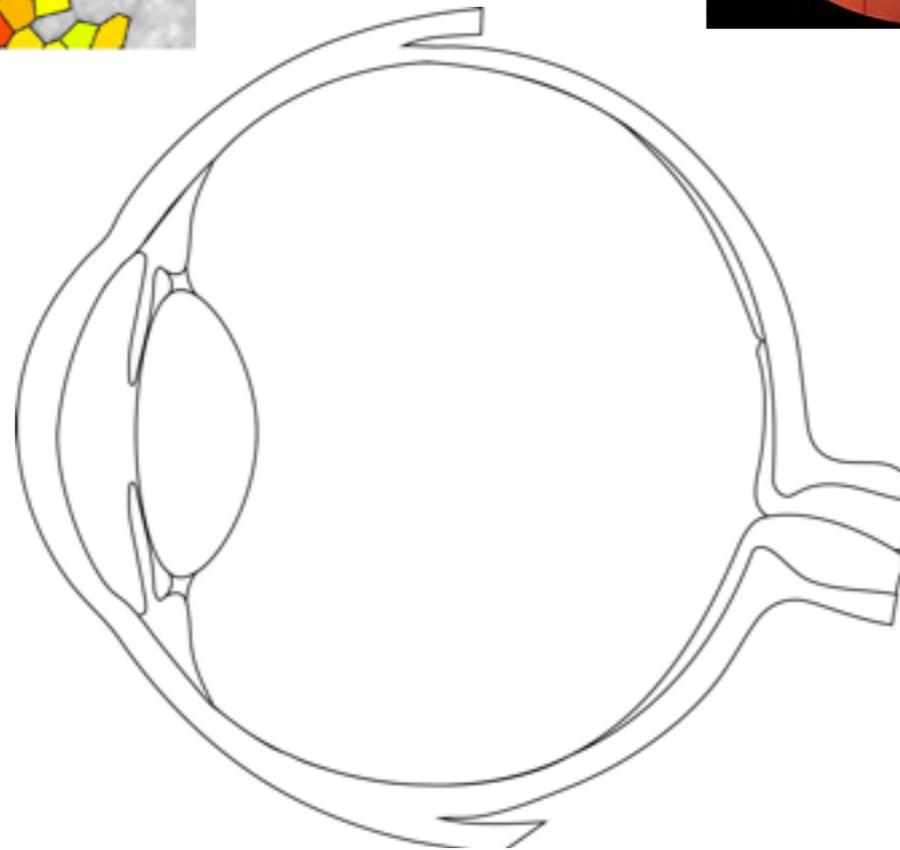
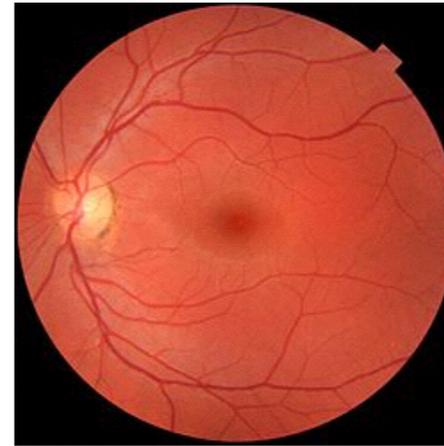
Surgical planning, intraoperative guidance

And many other.

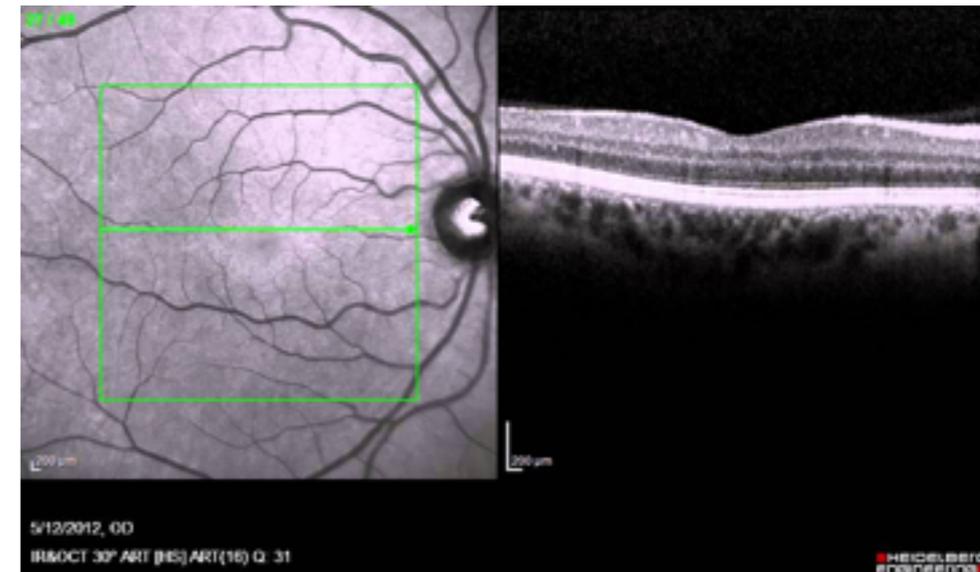
Specular microscope



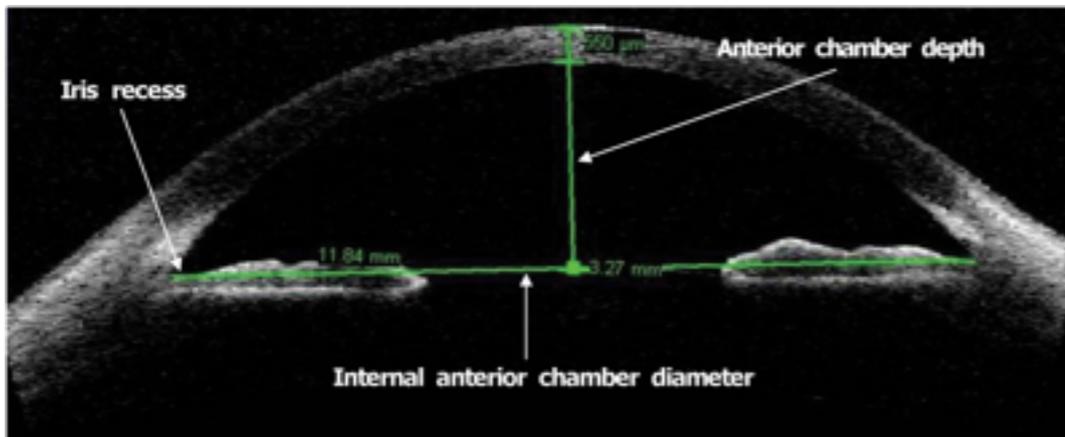
Fundus images



OCT



Anterior OCT



Fluorescein angiography



Until recently:

Technology enabled us to “see” the different parts of the eye **BUT**

- Image interpretation and understanding **relied on expert**
- **Quantitative image analysis** was often not done.

Today:

1. Quantitative analysis is a **must**.
2. Image understanding is **needed**.

Specialist scarcity & Cost-effective screening.

Identifying overlook features.

Improving sensitivity/specificity.

Today:

1. Quantitative analysis is a **must**.
2. Image understanding is **needed**.

Bottom-line: The field **needs help** from **computers**.

Ophthalmic Imaging Timeline

Direct Ophthalmoscope
(Helmholtz)

First in vivo photograph
of retina (Jackman and
Webster)

Fluorescein Angiography
(Indiana University)

1851 1886

1961

Digital Era

Confocal-SLO

Fundus
AutoFluorescence

OCT at MIT

First commercial OCT
Carl Zeiss Meditec OCT3

Wide field retinal
imaging (OPTOS)

Portable fundus
photography

OCT-Angiography

1987 1989 1991

2002 2003 2005 2007

Despite the unprecedented advances of recent years, **considerable deficiencies exist in our retinal imaging capability**. While angiographic techniques provide exquisite detail of vascular structures, our **ability to quantify chorioretinal blood flow and subsequent oxygen saturations – in a noninvasive manner – remains inadequate**. While **OCT** provides cross-sectional images of the neurosensory retina (and more recently the choroid) with high axial resolution, its **transverse resolution is limited**, and our ability to assess many retinal cell types remains poor (e.g., Müller cells, microglia, astrocytes, and individual neuronal elements). Furthermore, many advances in microscopic techniques that permit **“molecular” imaging** in basic science research have yet to make the transition to human clinical studies.



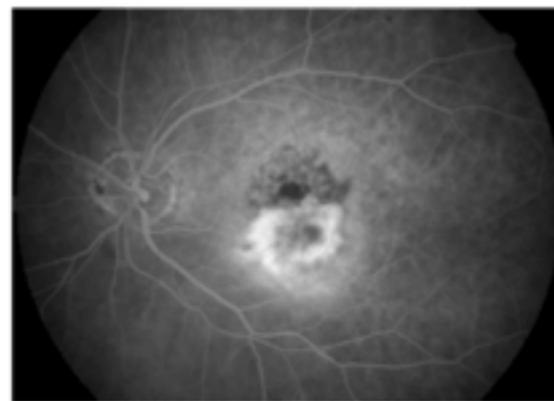
Michael D. Abramoff, MD, PhD Retina specialist and the Robert C. Watzke, MD, Professor of Ophthalmology and Visual Sciences, Electrical and Computer Engineering, and Biomedical Engineering in the Department of Ophthalmology and Visual Sciences at the University of Iowa and the VA Medical Center,

Image Processing (Computer Vision)

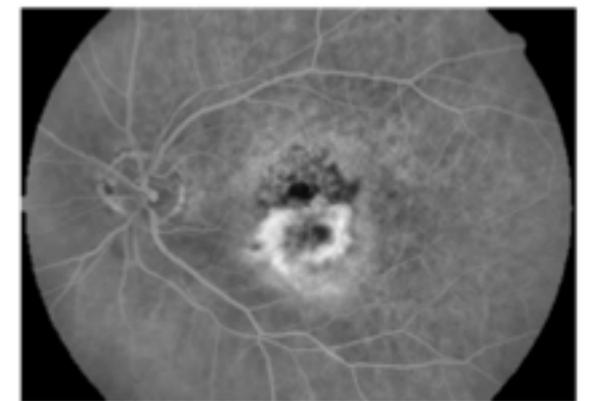
How it typically is.

- Preprocessing
- Detection
- Segmentation
- Registration
- Interpretation

Original



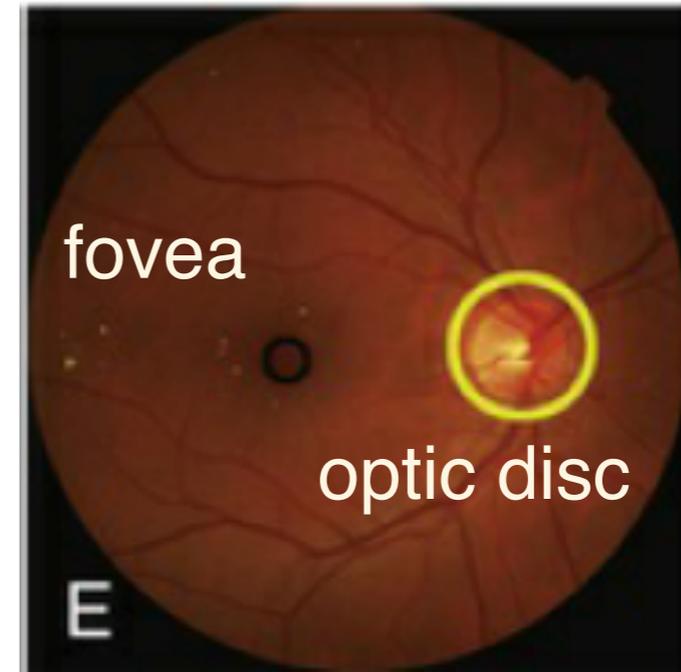
Enhanced



Remove variability without losing essential information.

Image Processing (Computer Vision)

How it typically is.

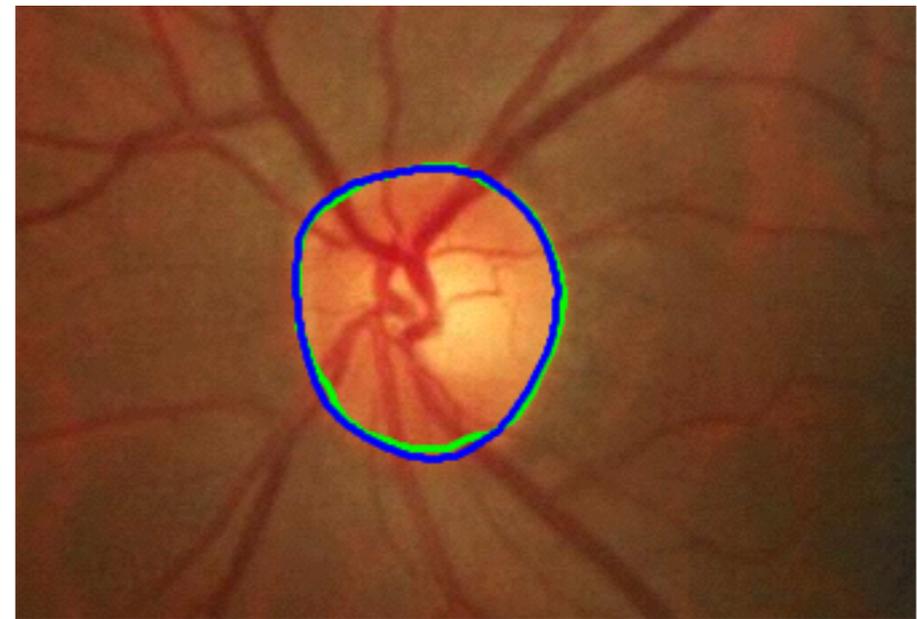


Locate specific structures of interest, or features.

- Preprocessing
- Detection
- Segmentation
- Registration
- Interpretation

Image Processing (Computer Vision)

How it typically is.

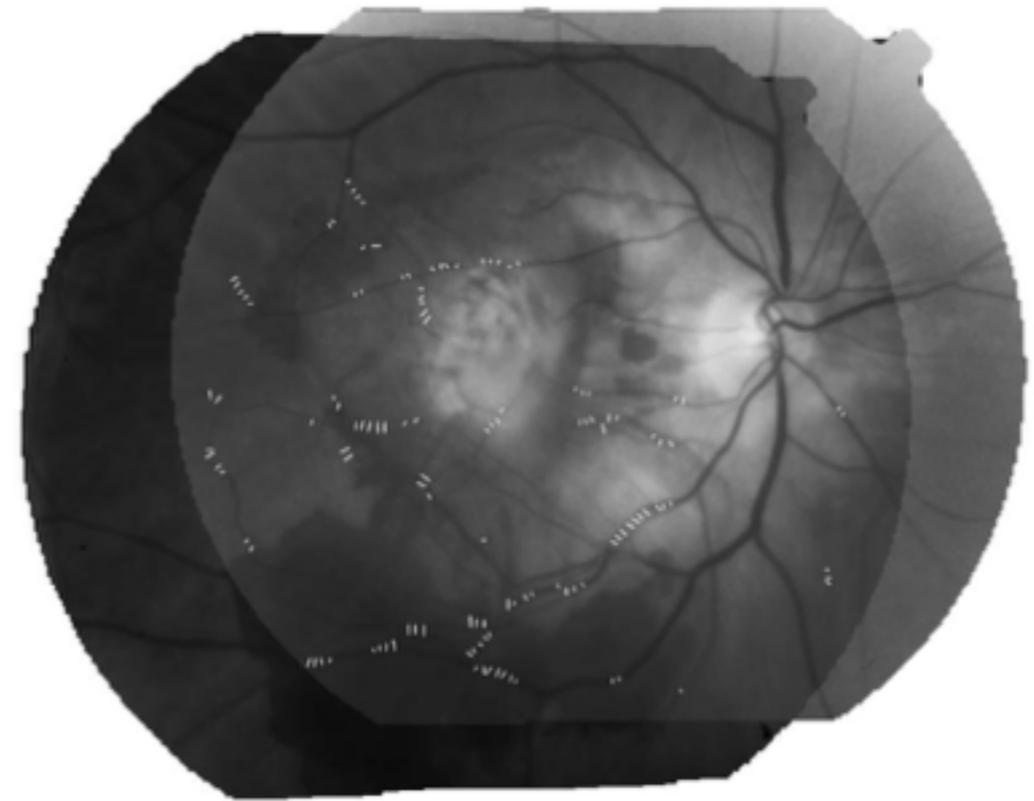


— Algorithm — Ground-truth

To determine precise boundaries of objects.

Image Processing (Computer Vision)

How it typically is.



To find similar regions in two or more images

- Preprocessing
- Detection
- Segmentation
- Registration
- Interpretation

Image Processing (Computer Vision)

How it typically is.



Integration of previous steps, and output clinically relevant information.

Typical Pipeline

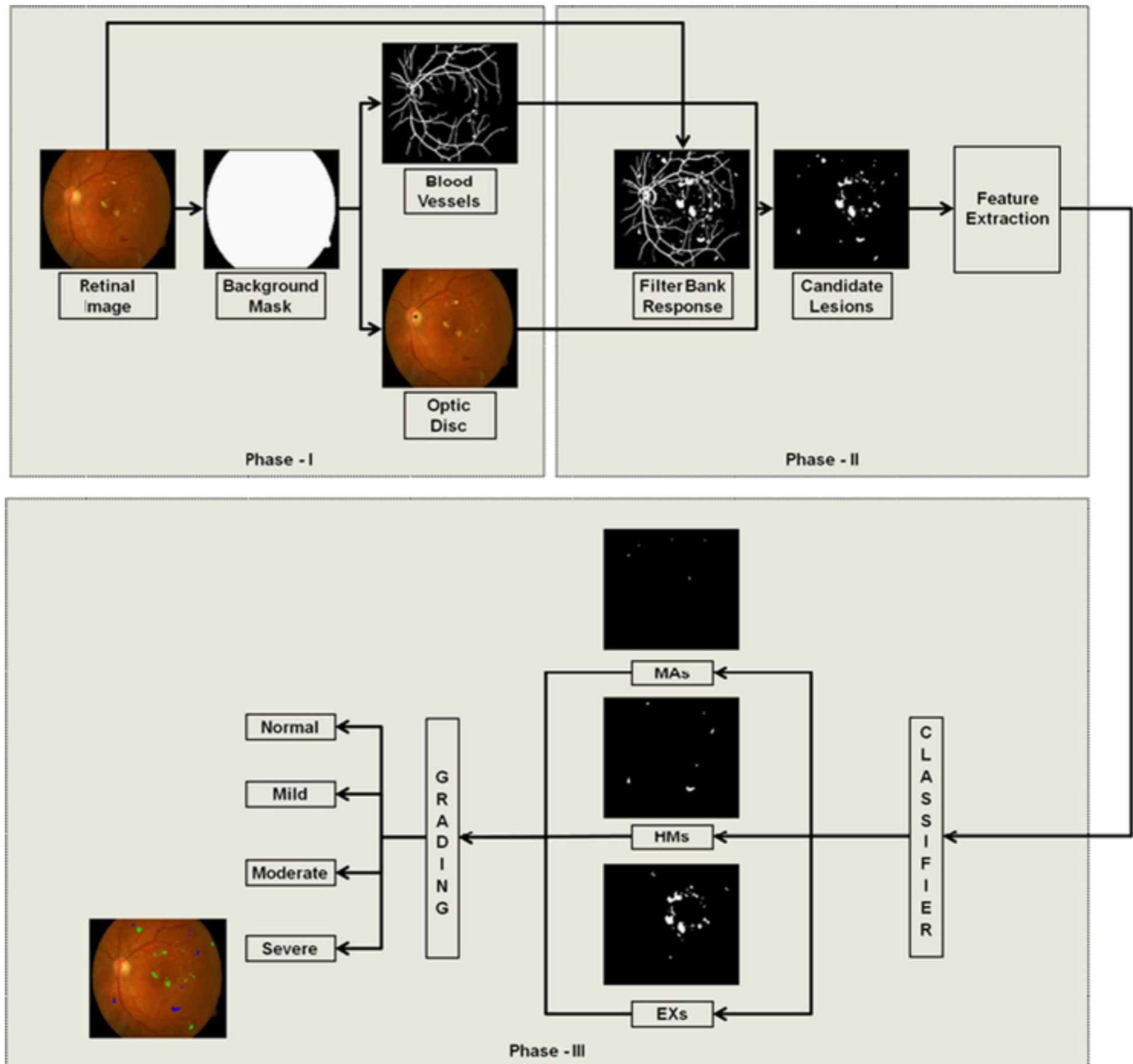
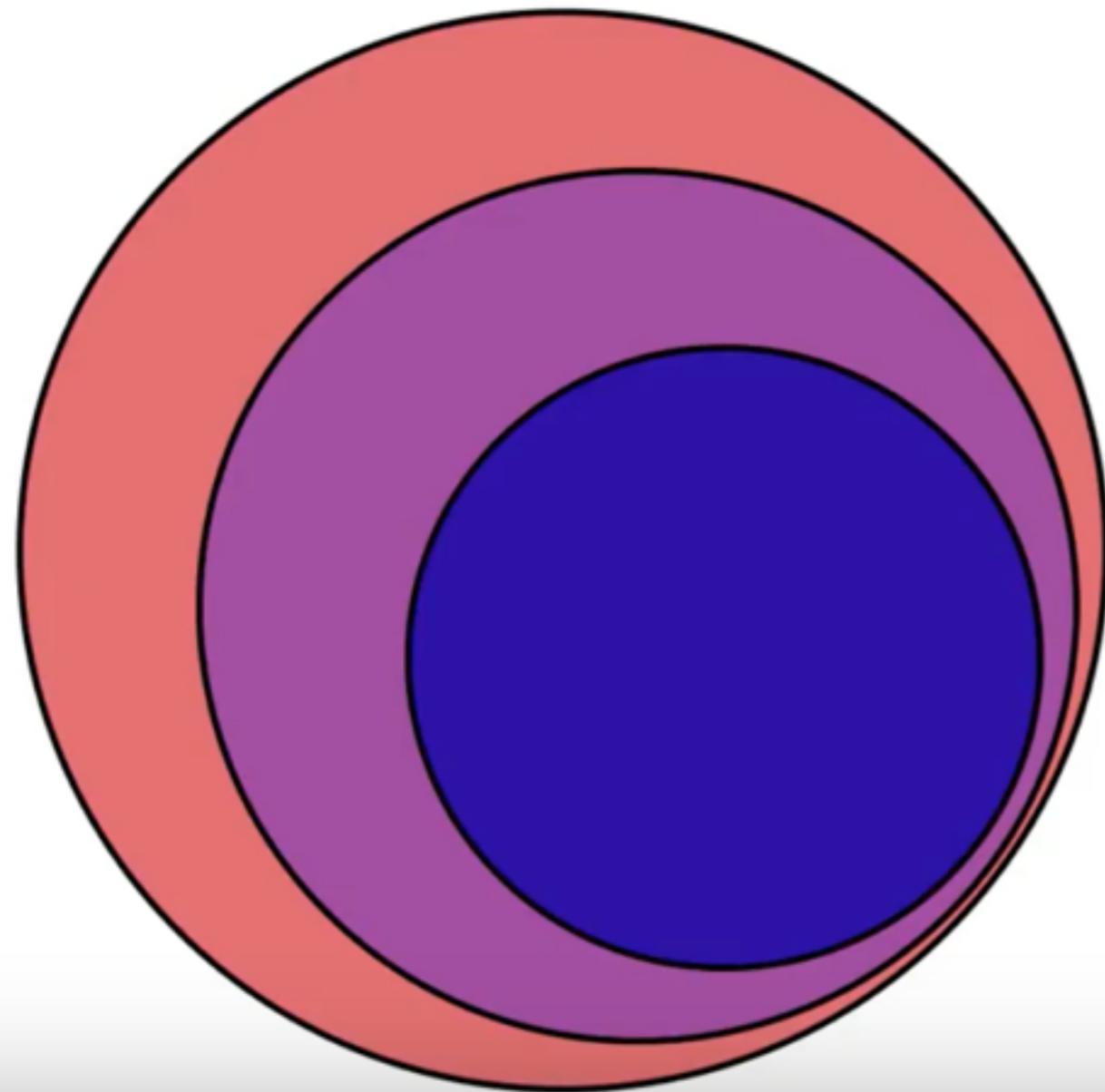


Image Processing (Computer Vision)

How it is becoming.

- Previous processing steps are typically explicitly created by the image analysis developers.
- The so called deep-learning approaches do not have these explicit steps, instead having learned these implicitly.

Image Processing (Computer Vision)



artificial intelligence

grand project to build non-human intelligence

machine learning

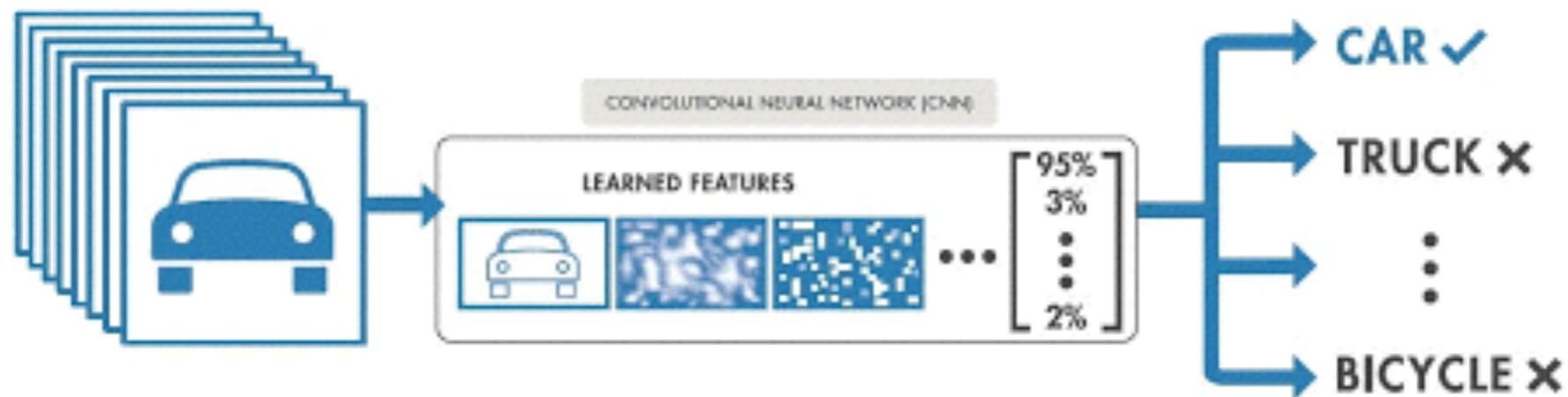
machines that learn to be smarter

deep learning

particular kind of machine learning

Image Processing (Computer Vision)

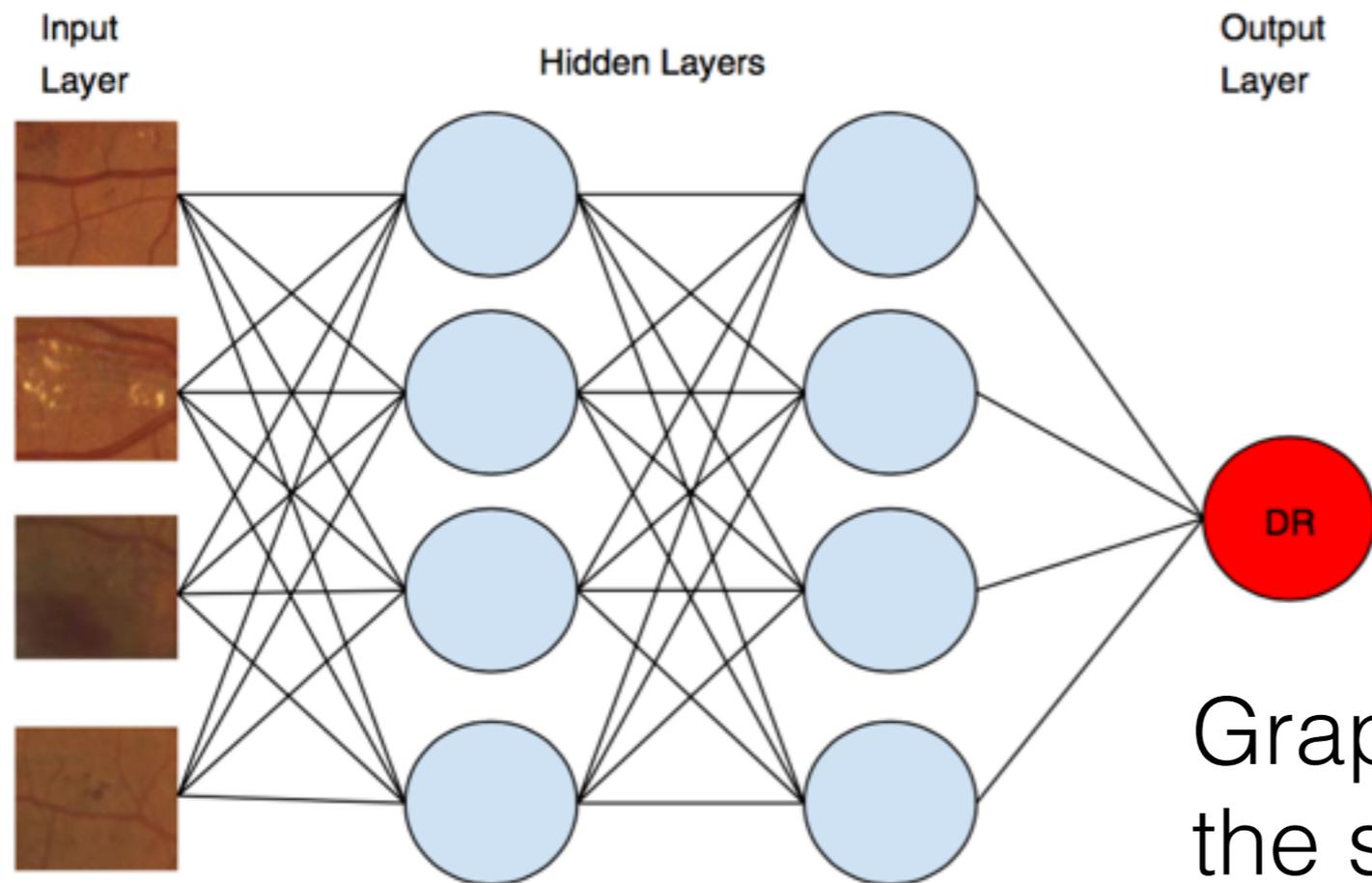
How it is becoming.



Research in Artificial Intelligence (AI) shifts from a knowledge-driven approach to a data-driven approach.

Image Processing (Computer Vision)

How it is becoming.



Graphical representation of the structure of an artificial neural network (ANN).

Image Processing (Computer Vision)

A comparison between a conventional approach and a black-box approach.

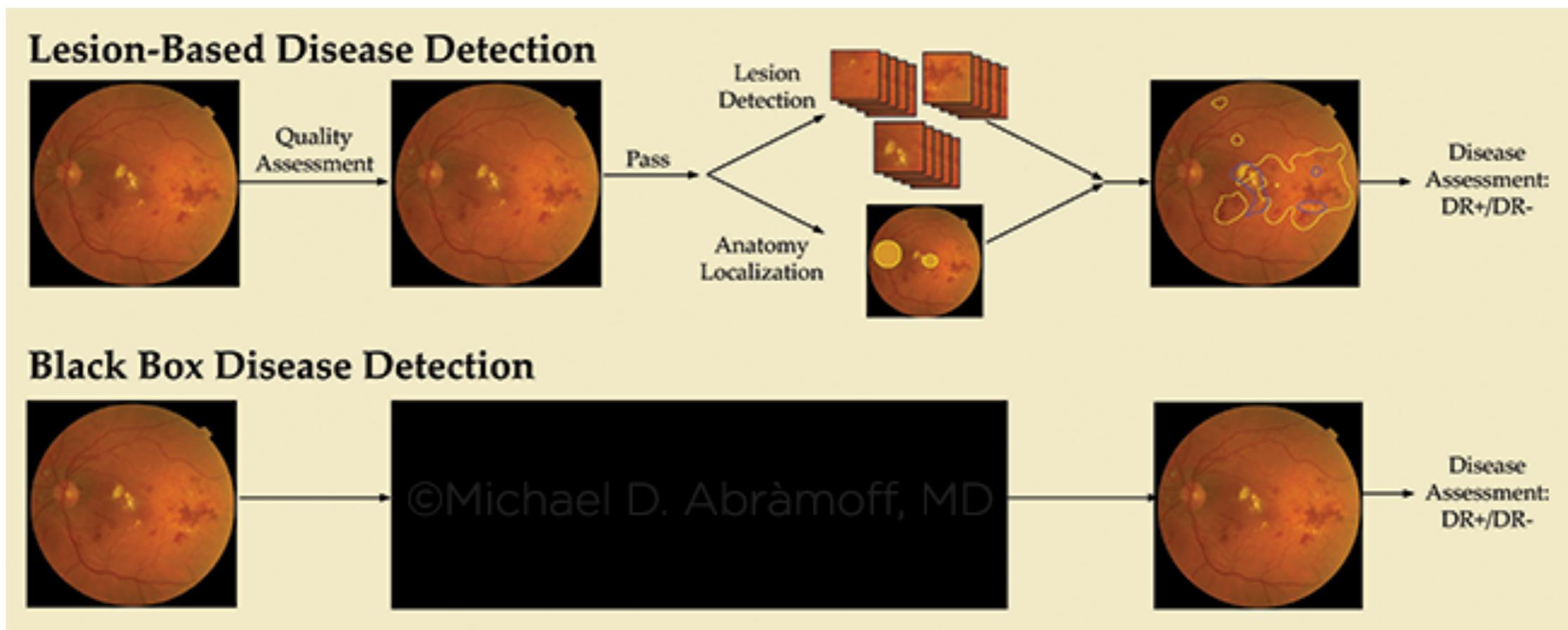


Image Processing (Computer Vision)

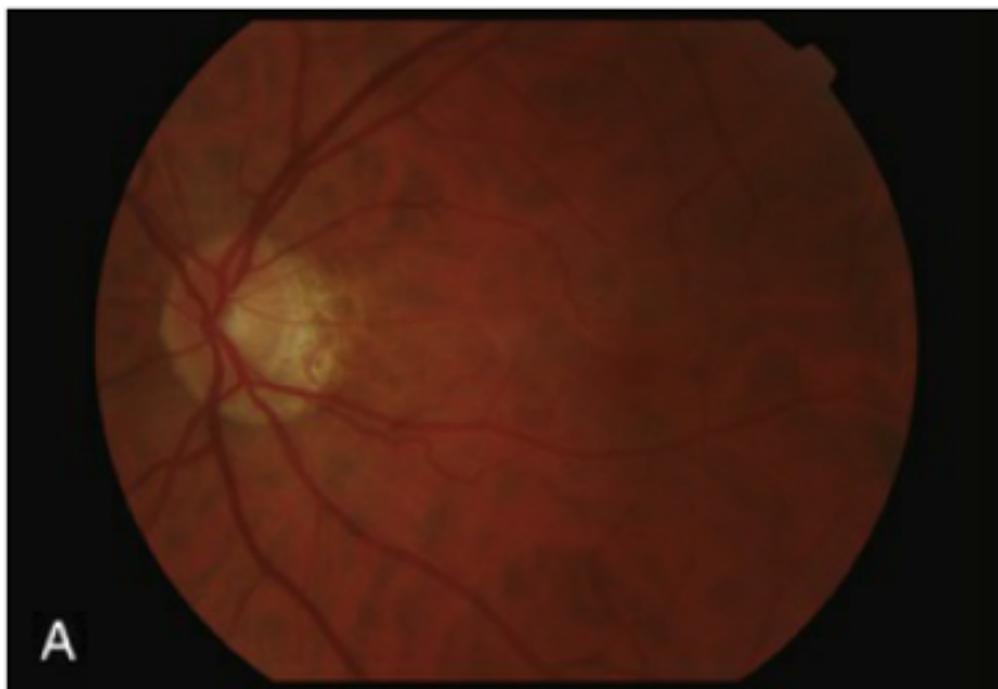
Image analysis has mostly operated reactively.

We expect more integration in device development and image analysis.

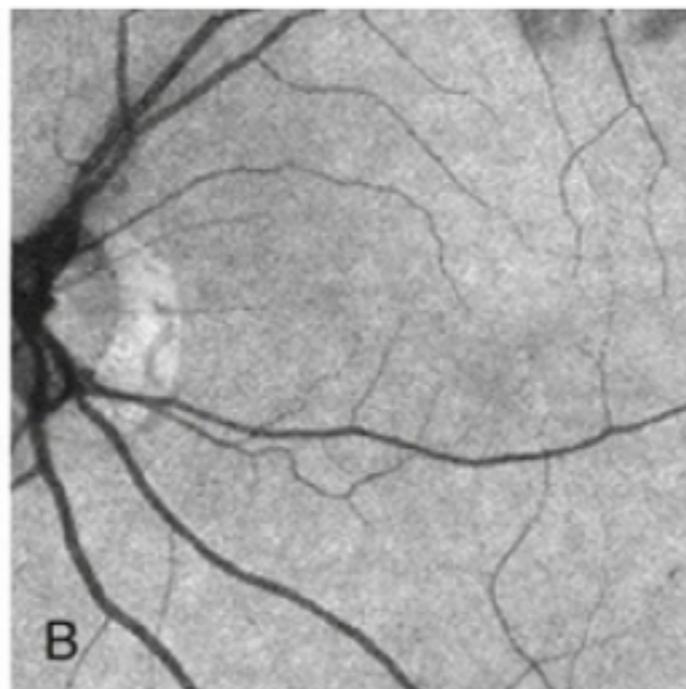
2. Enabling new technologies ...

Successes to date

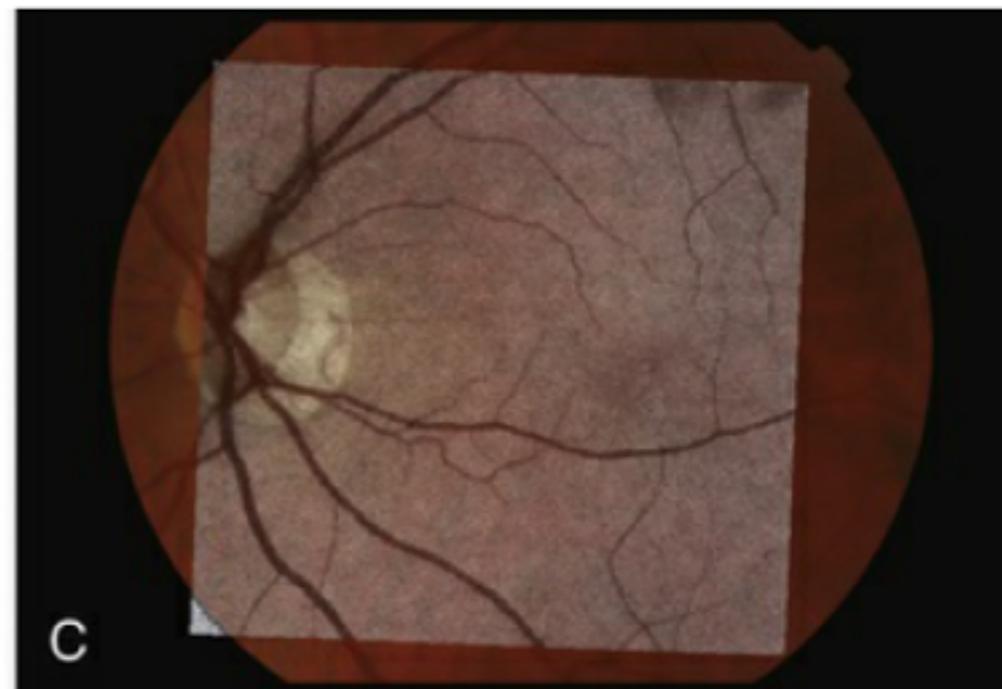
Multimodal registration



Fundus image



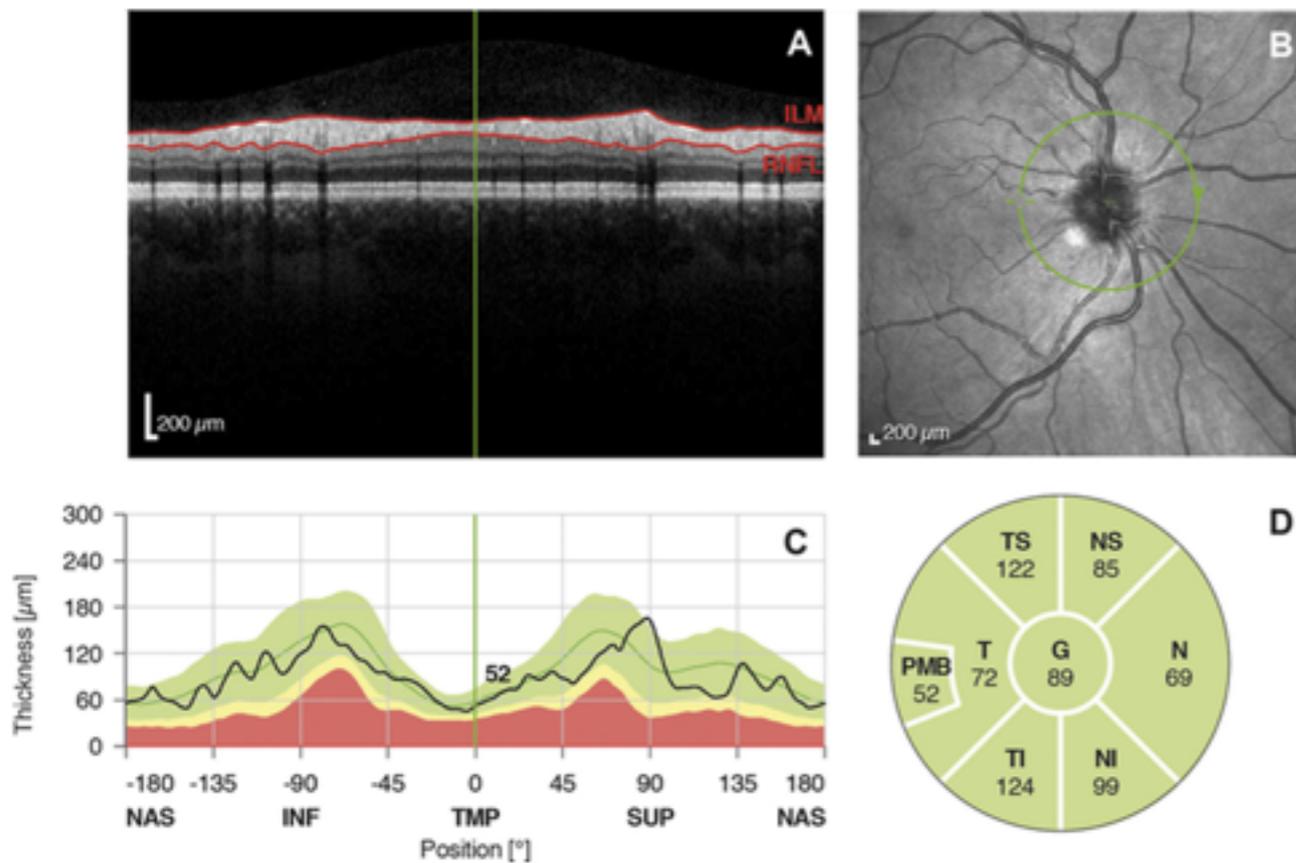
3D OCT



Registration

Successes to date

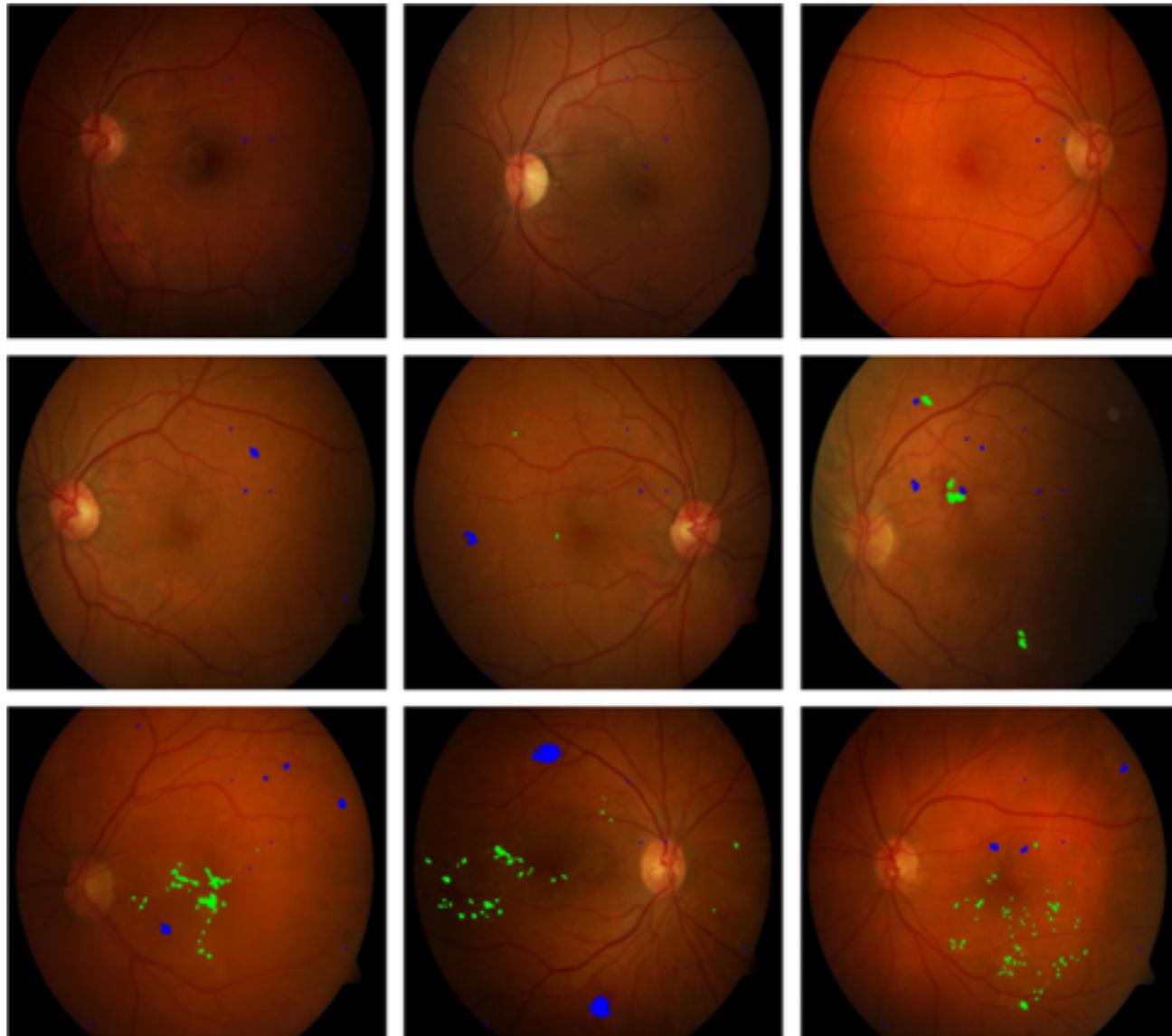
Eye-tracking technology and reproducibility in OCT



The reproducibility of RNFL measurements with Spectralis SD-OCT is excellent in both normal and glaucomatous eyes and can be significantly improved by using the eye tracker and retest software.

Successes to date

Retinal Lesion Detection



Conventional step-by-step algorithms have achieved high lesion detection rates.

Successes to date

Data-driven approach

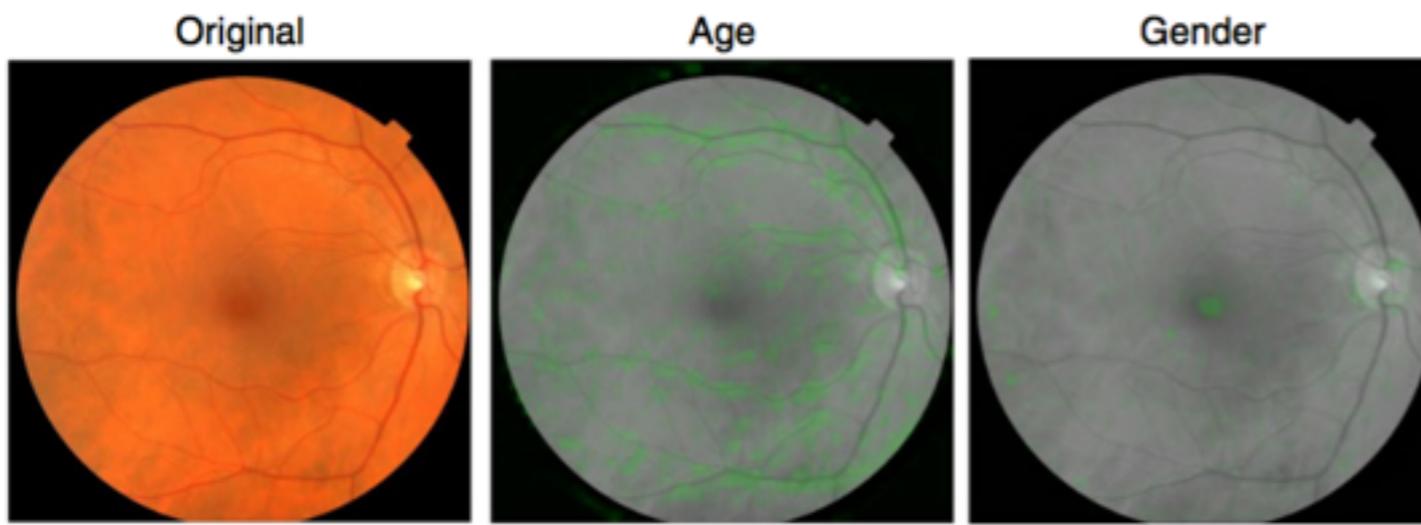
nature
biomedical engineering

ARTICLES

<https://doi.org/10.1038/s41551-018-0195-0>

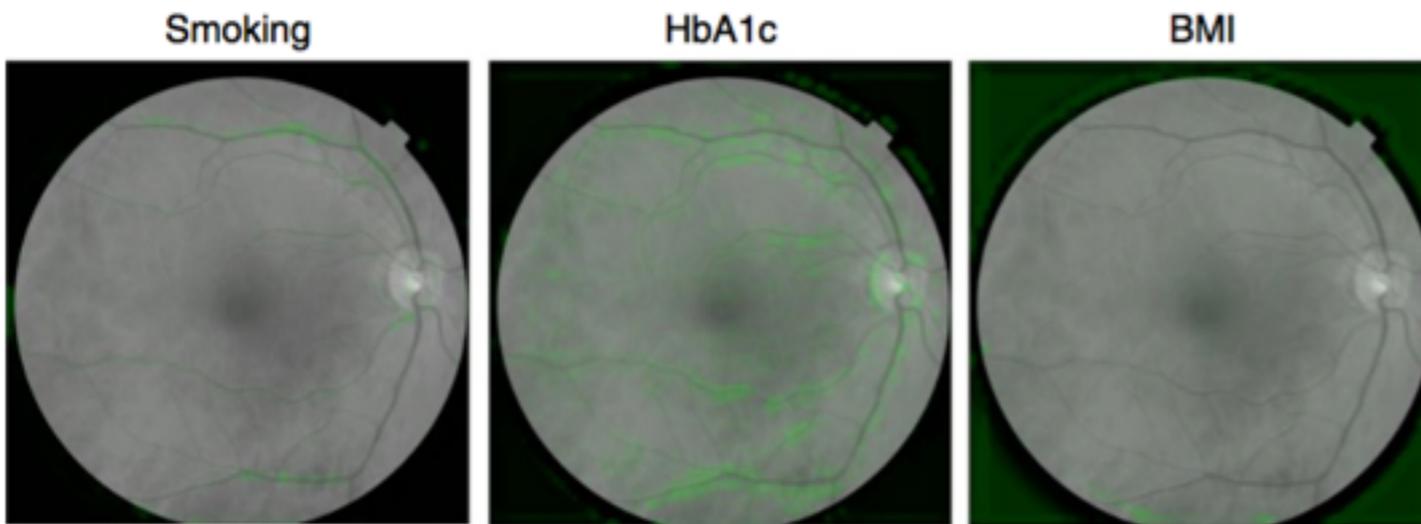
Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning

Ryan Poplin^{1,4}, Avinash V. Varadarajan^{1,4}, Katy Blumer¹, Yun Liu¹, Michael V. McConnell^{2,3},
Greg S. Corrado¹, Lily Peng^{1,4*} and Dale R. Webster^{1,4}



Actual: 57.6 years
Predicted: 59.1 years

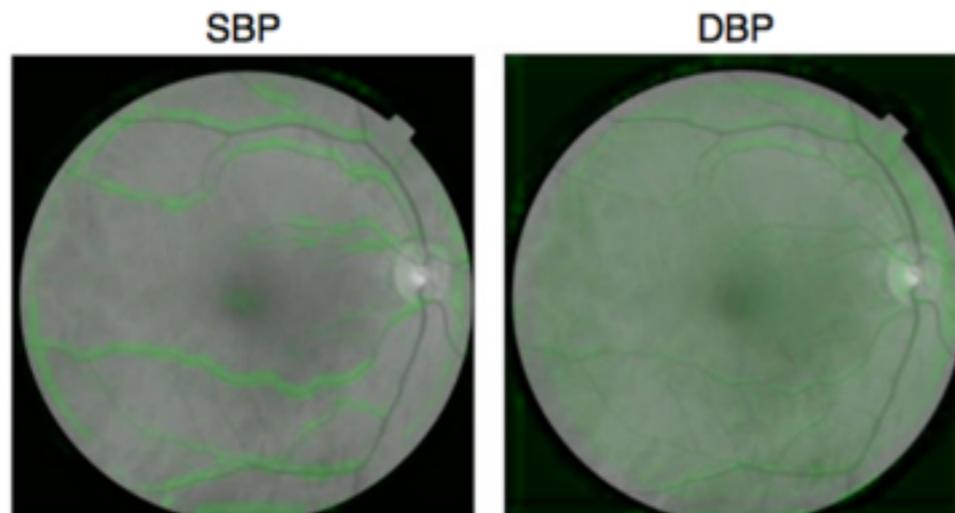
Actual: female
Predicted: female



Actual: non-smoker
Predicted: non-smoker

Actual: non-diabetic
Predicted: 6.7%

Actual: 26.3 kg m⁻²
Predicted: 24.1 kg m⁻²



Actual: 148.5 mmHg
Predicted: 148.0 mmHg

Actual: 78.5 mmHg
Predicted: 86.6 mmHg

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

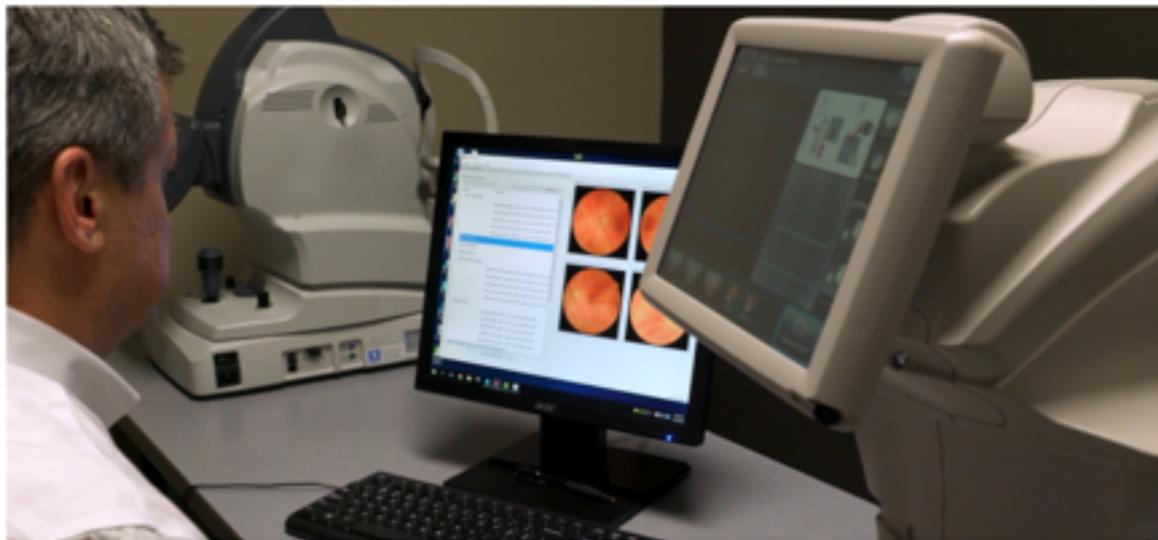
Ryan Poplin^{1,4}, Avinash V. Varadarajan^{1,4}, Katy Blumer¹, Yun Liu¹, Michael V. McConnell^{2,3}, Greg S. Corrado¹, Lily Peng^{1,4*} and Dale R. Webster^{1,4}

They predicted cardiovascular risk factors not previously thought to be present or quantifiable in retinal images.

Successes to date



IDx-DR first AI system approved by FDA



IDx-DR

The first ever autonomous AI system cleared by the FDA to provide a diagnostic decision

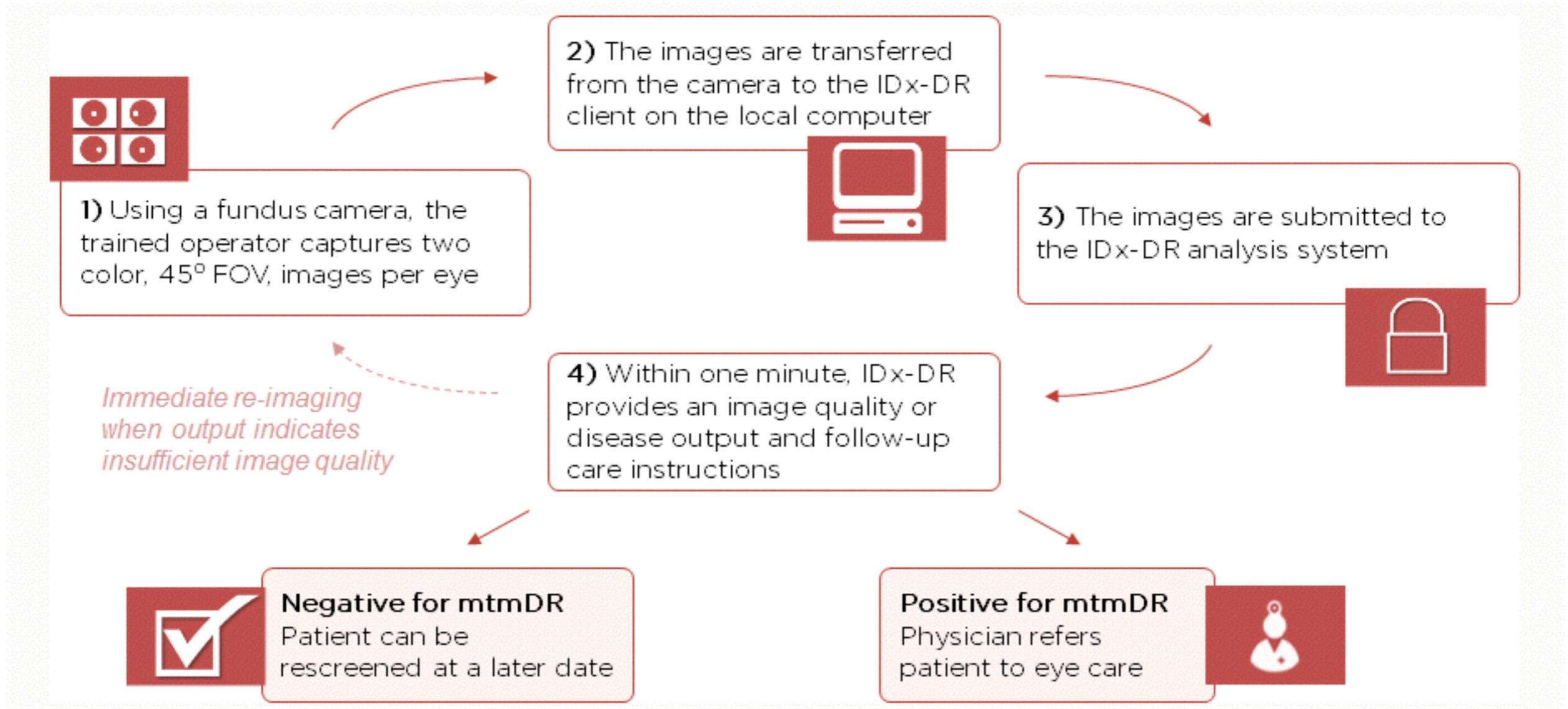
87% Sensitivity
90% Specificity
96% Imageability

Endpoints Exceeded By A Wide Margin

Successes to date

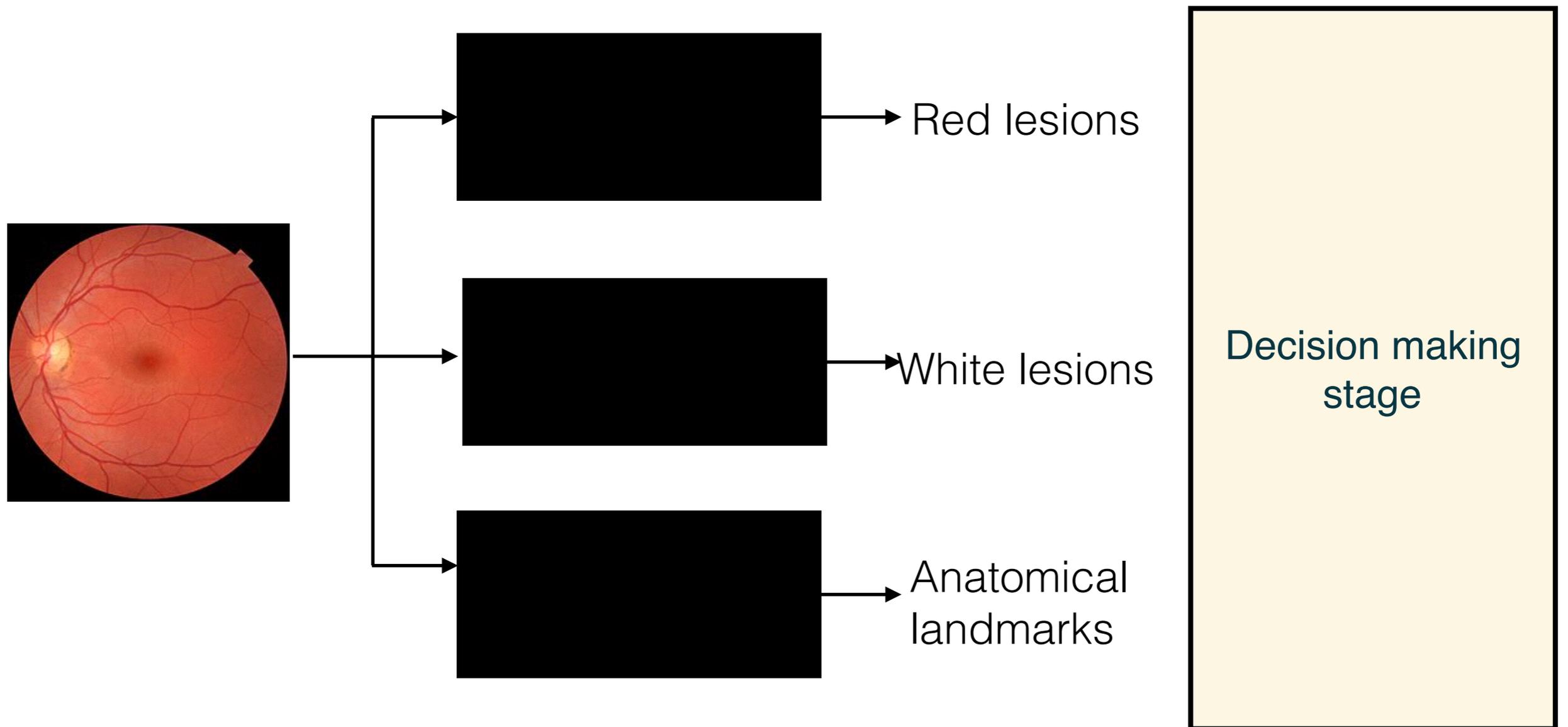


IDx-DR first AI system approved by FDA



Successes to date

Hybrid approach in DR automated detection



3. Challenges ahead...

Challenges

1. Due to imaging technology (**hardware**).
2. Due to image processing (**software**).

Challenges

Black-box systems detecting DR

OPEN ACCESS

ARVO Annual Meeting Abstract | June 2017

Catastrophic Failure in Image-Based Convolutional Neural Network Algorithms for Detecting Diabetic Retinopathy

Stephanie Klein Lynch; Abhay Shah; James C Folk; Xiaodong Wu; Michael David Abramoff

Challenges

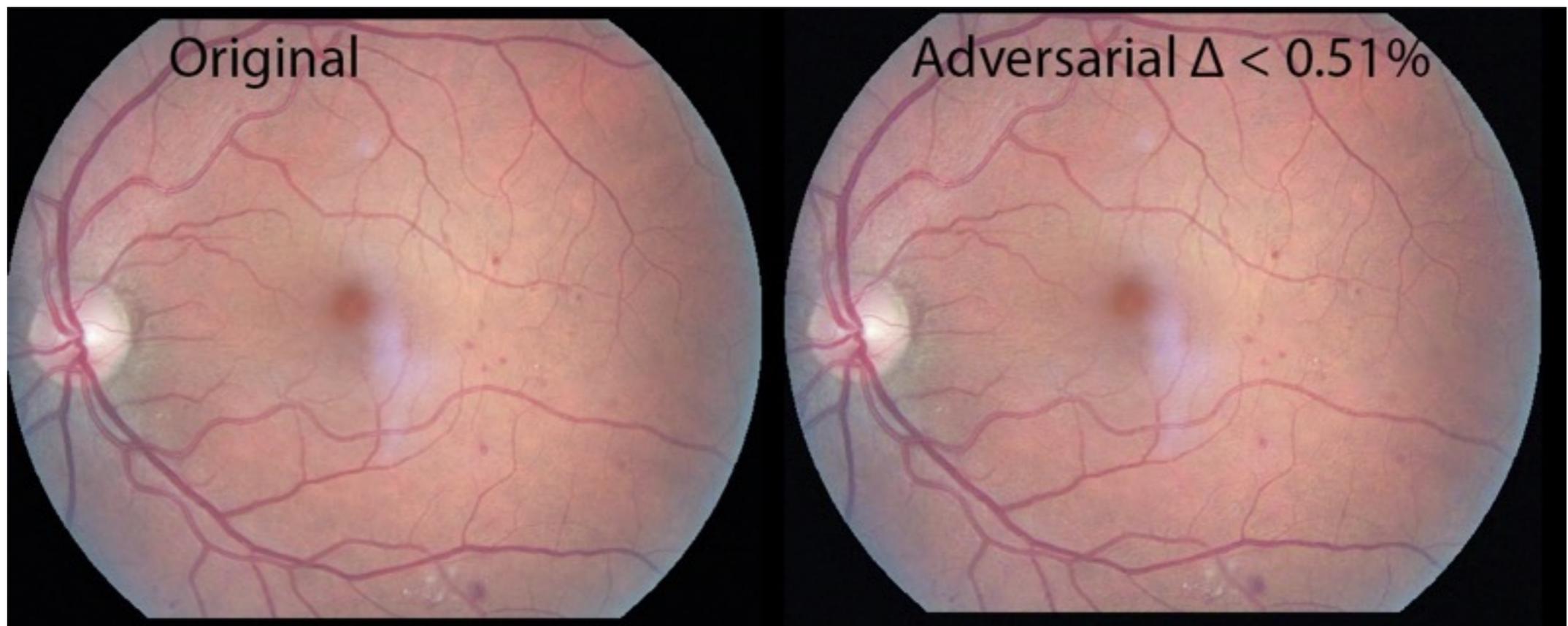
OPEN ACCESS

ARVO Annual Meeting Abstract | June 2017

Catastrophic Failure in Image-Based Convolutional Neural Network Algorithms for Detecting Diabetic Retinopathy

Stephanie Klein Lynch; Abhay Shah; James C Folk; Xiaodong Wu; Michael David Abramoff

Black-box systems detecting DR



Specialist ✓

Hybrid algorithm ✓

Image-based algorithm ✗

Challenges

Different generation devices & different results

	Topcon 3DOCT1000	Topcon 3D OCT2000
Ganglion layer	$32.5 \pm 5.8 \mu\text{m}$	$36.2 \pm 5.3 \mu\text{m}$
Outer Nuclear layer	$87.2 \pm 8.8 \mu\text{m}$	$90.5 \pm 8.2 \mu\text{m}$
RPE	$19.5 \pm 1.6 \mu\text{m}$	$16.9 \pm 0.9 \mu\text{m}$

Results using the same robust algorithm.

Challenges

Different generation devices & different results

Probably due to difference in image quality between OCT devices.

Comparing pixel intensity distributions indeed showed qualitative differences, with the second generation OCT system having less variance in dark region intensities and fatter high intensity tails. ””

Challenges

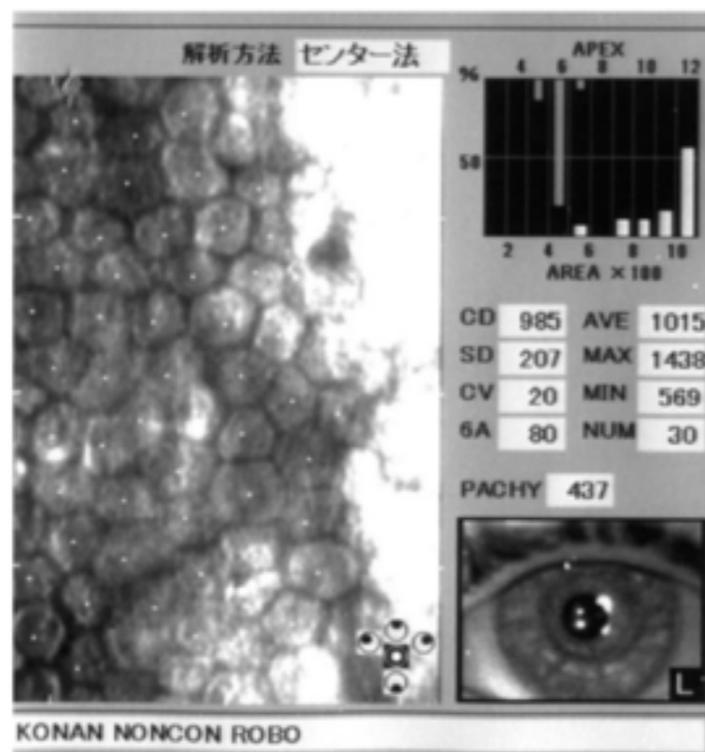
Different generation devices & different results

Bottom-line: Automated parameters should be **interpreted with caution** when comparing data from different devices.

Challenges

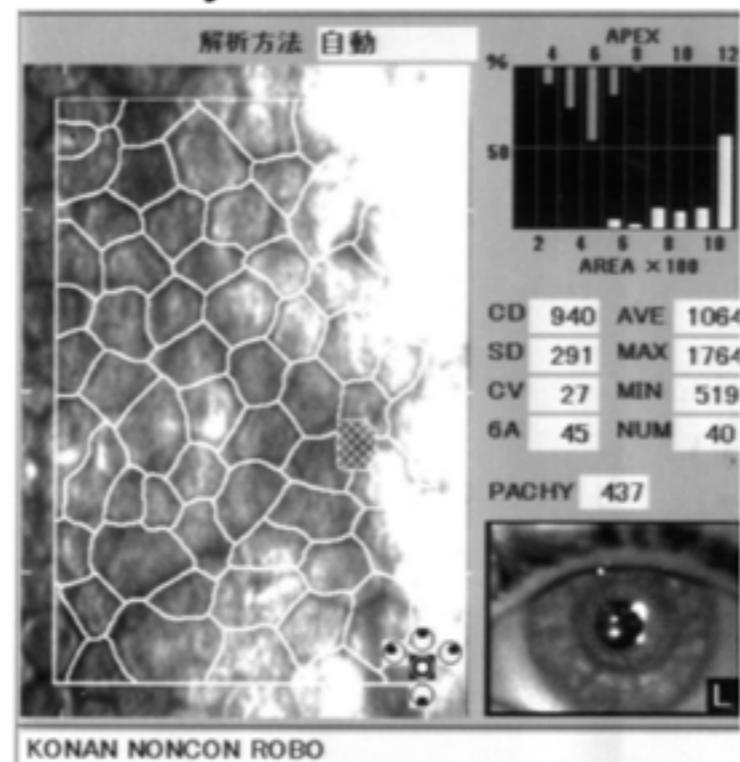
Cell counting in optical specular microscope

Semi-automated



Labor intensive
Time consuming

Fully automated



No intervention

Challenges

Cell counting in optical specular microscope

Low precision in fully automated method vs semi-automated.

Larger error in patients with low ECD.

Challenges

Screening with portable/low cost devices

There is clearly excellent potential in smartphone-based DR screening.

Questionable ability to provide fundus images through undilated pupils poses a problem for screening programs.



References

- [1] “FTC hearing: Not all AI is created equal, so safety and validation are critical,” Nov. 2018.
- [2] M. U. Akram, S. Khalid, A. Tariq, S. A. Khan, and F. Azam, “Detection and classification of retinal lesions for grading of diabetic retinopathy,” *Computers in Biology and Medicine*, vol. 45, no. C, pp. 161–171, Feb. 2014.
- [3] S. J. Langenegger, J. Funk, and M. Töteberg-Harms, “Reproducibility of Retinal Nerve Fiber Layer Thickness Measurements Using the Eye Tracker and the Retest Function of Spectralis SD-OCT in Glaucomatous and Healthy Control Eyes,” *Invest Ophth Vis Sci*, vol. 52, no. 6, pp. 3338–7, May 2011.
- [4] A. Zhang, Q. Zhang, C.-L. Chen, and R. K. Wang, “Methods and algorithms for optical coherence tomography-based angiography: a review and comparison,” *J. Biomed. Opt.*, vol. 20, no. 10, pp. 100901–14, Oct. 2015.
- [5] T. E. de Carlo, “A review of optical coherence tomography angiography (OCTA),” pp. 1–15, Apr. 2015.
- [6] S. Schmitz-Valckenberg, F. G. Holz, A. C. Bird, and R. F. Spaide, “Fundus autofluorescence imaging: review and perspectives,” *Retina*, vol. 28, no. 3, pp. 385–409, Mar. 2008.
- [7] R. H. Webb, G. W. Hughes, and F. C. Delori, “Confocal scanning laser ophthalmoscope,” *Appl Opt*, vol. 26, no. 8, pp. 1492–1499, Apr. 1987.
- [8] D. T. Hogarty, D. A. Mackey, and A. W. Hewitt, “Current state and future prospects of artificial intelligence in ophthalmology: a review,” *Clinical & Experimental Ophthalmology*, vol. 29, pp. 254–12, Sep. 2018.

References

- [9] S. S. Shoughy, J. F. Arevalo, and I. Kozak, “Update on wide- and ultra-widfield retinal imaging.,” *Indian J Ophthalmol*, vol. 63, no. 7, pp. 575–581, Jul. 2015.
- [10] J. W. Kitchens, “Retinal Imaging: Just the Tip of the Iceberg....”
- [11] “Ophthalmic Imaging,” pp. 1–19, Dec. 2016.
- [12] M. Sonka and M. D. Abramoff, “Quantitative analysis of retinal OCT,” *Medical Image Analysis*, vol. 33, no. C, pp. 165–169, Oct. 2016.
- [13] V. Mazlin, P. Xiao, E. Dalimier, K. Grieve, K. Irsch, J.-A. Sahel, M. Fink, and A. C. Boccara, “In vivo high resolution human corneal imaging using full-field optical coherence tomography.,” *Biomedical Optics Express*, vol. 9, no. 2, pp. 557–568, Feb. 2018.
- [14] D. V. P. P. MRCOphth and C. N. M. P. FRCOphth, “Quantitative analysis of in vivo confocal microscopy images: A review,” *Survey of Ophthalmology*, vol. 58, no. 5, pp. 466–475, Sep. 2013.
- [15] B. Winkelman, J. M. Colijn, P. W. M. Bonnemaier, F. Fujihara, M. D. Abramoff, K. E. Lee, A. S. Fairbanks, S. M. Meuer, B. E. K. Klein, R. Klein, and C. Klaver, “Retinal layer segmentation results differ between two generations of OCT devices,” *Invest Ophth Vis Sci*, vol. 58, no. 8, pp. 672–672, Jun. 2017.
- [16] Z. Hu, Z. C. Wang, and S. R. Sadda, “Automated 3D Choroidal Segmentation Using Multimodal Complementary Information,” *Invest Ophth Vis Sci*, vol. 58, no. 8, pp. 19–19, Jun. 2017.
- [17] S. K. Lynch, A. Shah, J. C. Folk, X. Wu, and M. D. Abramoff, “Catastrophic Failure in Image-Based Convolutional Neural Network Algorithms for Detecting Diabetic Retinopathy,” *Invest Ophth Vis Sci*, vol. 58, no. 8, pp. 3776–3776, Jun. 2017.

References

- [18] L. Roach, “Artificial Intelligence,” *Eyenet Magazine*, pp. 77–83, 20-Oct-2017.
- [19] R. Rajalakshmi, R. Subashini, R. M. Anjana, and V. Mohan, “Automated diabetic retinopathy detection in smartphone-based fundus photography using artificial intelligence,” *Eye*, pp. 1–7, Jun. 2018.
- [20] M. D. Abramoff, M. Niemeijer, X. Xu, M. Sonka, J. M. Reinhardt, University of Iowa Research Foundation (UIRF), and U. D. O. V. Affairs, “Automated determination of arteriovenous ratio in images of blood vessels,” US2012/0236259A1, 27-Mar-2018.
- [21] R. A. O'Halloran and A. W. Turner, “Evaluating the impact of optical coherence tomography in diabetic retinopathy screening for an Aboriginal population,” *Clinical & Experimental Ophthalmology*, vol. 46, no. 2, pp. 116–121, Aug. 2017.
- [22] S. S. Johnson, J.-K. Wang, M. S. Islam, M. J. Thurtell, R. H. Kardon, and M. K. Garvin, *Local Estimation of the Degree of Optic Disc Swelling from Color Fundus Photography*. Springer International Publishing, 2018, pp. 1–8.
- [23] P. Costa, A. Galdran, M. I. Meyer, M. Niemeijer, M. D. Abramoff, A. M. Mendonca, and A. Campilho, “End-to-End Adversarial Retinal Image Synthesis,” *IEEE Transactions on Medical Imaging*, vol. 37, no. 3, pp. 781–791, Mar. 2018.
- [24] A. Shah, L. Zhou, M. D. Abramoff, and X. Wu, “Multiple surface segmentation using convolution neural nets: application to retinal layer segmentation in OCT images,” pp. 1–18, Aug. 2018.
- [25] B. J. Fenner, R. L. M. Wong, W.-C. Lam, G. S. W. Tan, and G. C. M. Cheung, “Advances in Retinal Imaging and Applications in Diabetic Retinopathy Screening: A Review,” *Ophthalmology and Therapy*, vol. 7, no. 2, pp. 333–346, Nov. 2018.

References

- [26] R. Poplin, A. V. Varadarajan, K. Blumer, Y. Liu, M. V. McConnell, G. S. Corrado, L. Peng, and D. R. Webster, “Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning,” *Nature Biomedical Engineering*, vol. 2, no. 3, pp. 1–9, Feb. 2018.
- [27] S. Maruoka, S. Nakakura, N. Matsuo, K. Yoshitomi, C. Katakami, H. Tabuchi, T. Chikama, and Y. Kiuchi, “Comparison of semi-automated center-dot and fully automated endothelial cell analyses from specular microscopy images,” *International Ophthalmology*, vol. 35, pp. 1–13, Oct. 2017.
- [28] C. Stewart, Chia-Ling Tsai, and B. Roysam, “The dual-bootstrap iterative closest point algorithm with application to retinal image registration,” *Medical Imaging, IEEE Transactions on*, vol. 22, no. 11, pp. 1379–1394, 2003.
- [29] M. D. Abramoff, M. Garvin, and M. Sonka, “Retinal Imaging and Image Analysis,” *Biomedical Engineering, IEEE Reviews in*, vol. 3, pp. 169–208, 2010.



UNIVERSITAT POLITÈCNICA
DE CATALUNYA



Universidad
Tecnológica
de Bolívar

CARTAGENA DE INDIAS

Thank you.



Centre de Cooperació per al
Desenvolupament de la UPC

