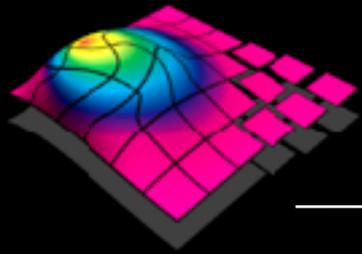


Artificial Intelligence in Ophthalmology

Reinventing the Eye Exam!

Pearse Keane
Moorfields Eye Hospital and
UCL Institute of Ophthalmology



Disclosure

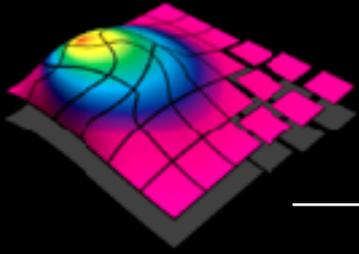
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- Topcon
- Heidelberg
- Haag-Streit
- Allergan
- Bayer
- Novartis
- Zeiss

Consultancy:

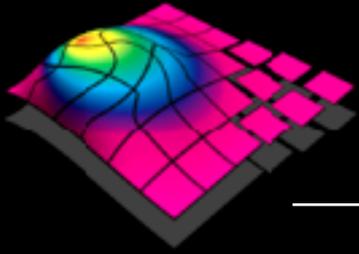
- DeepMind
- Optos





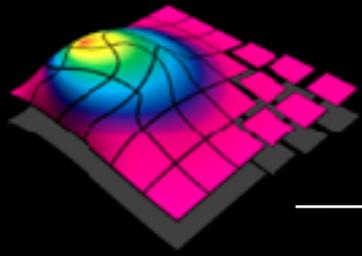
Examining the Eye



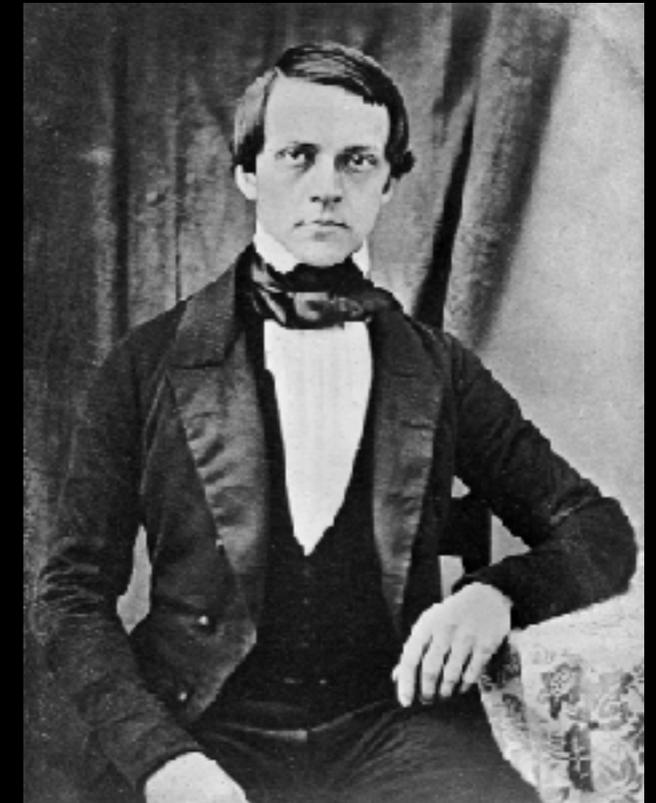


Ophthalmoscopy

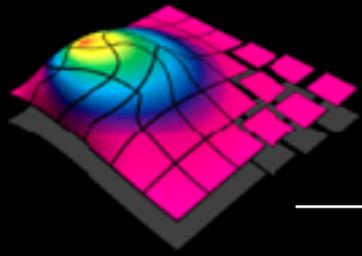




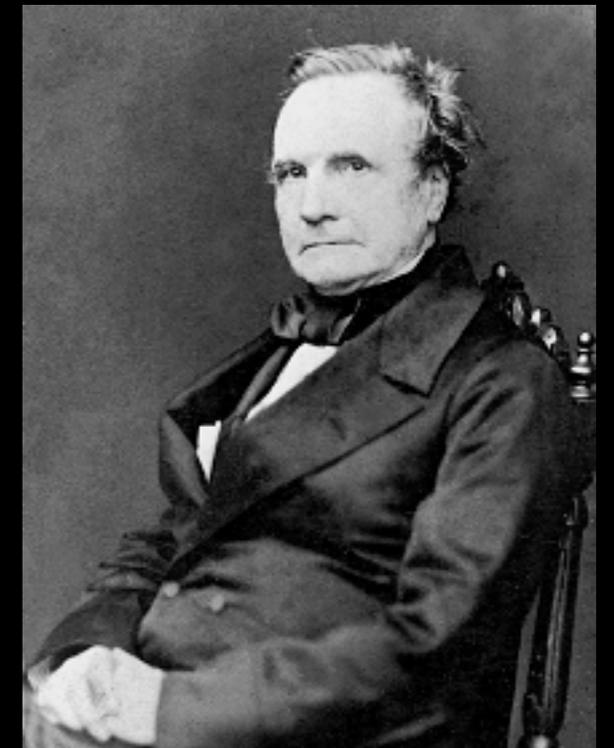
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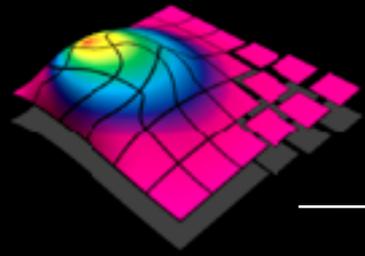
**Herman
von Helmholtz**



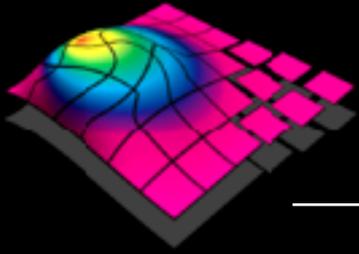
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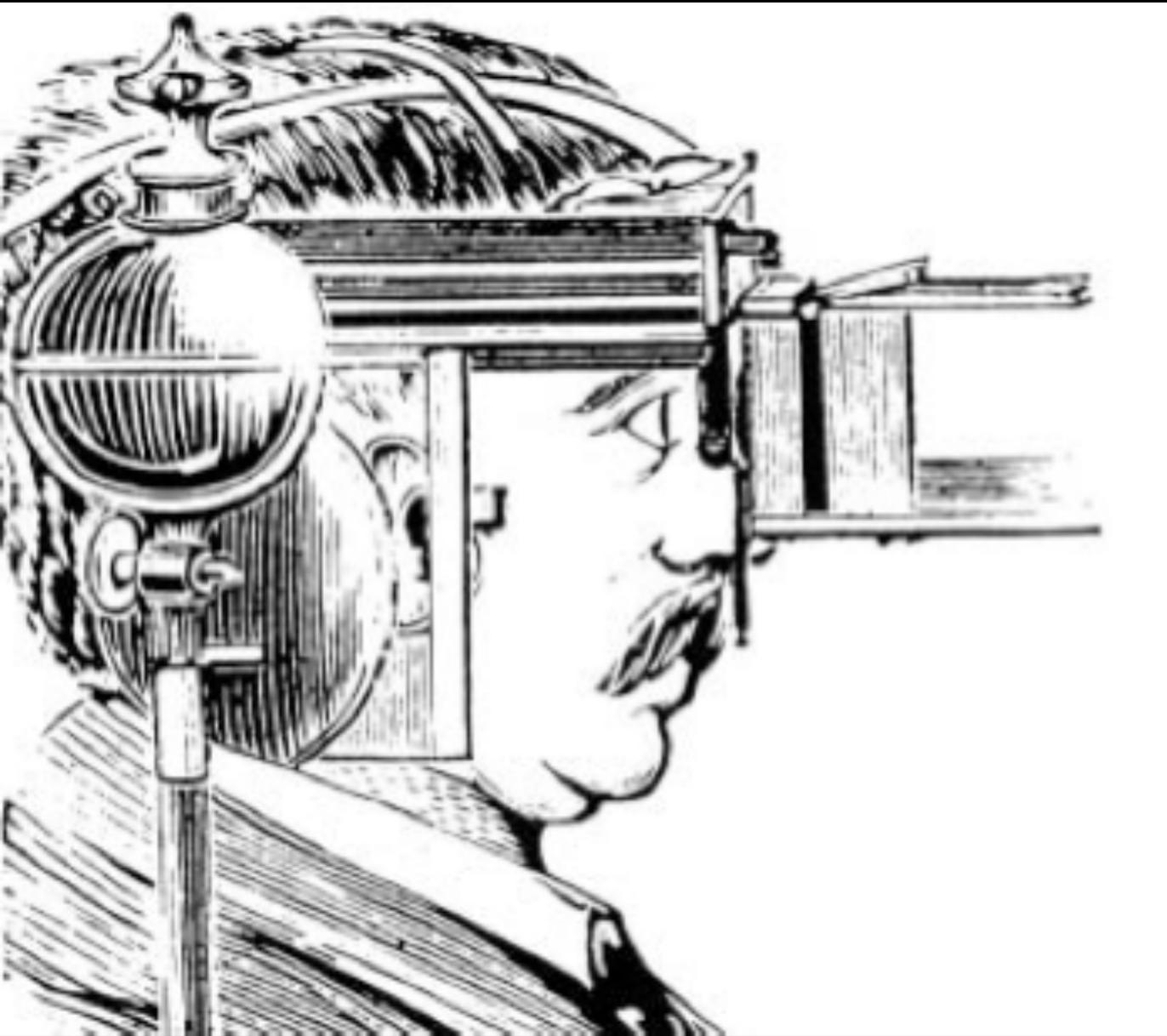
**Charles
Babbage**



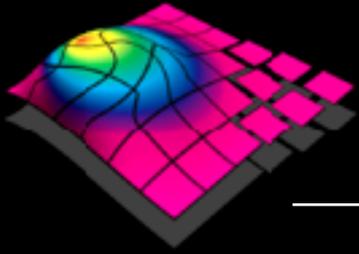
Ophthalmic Imaging



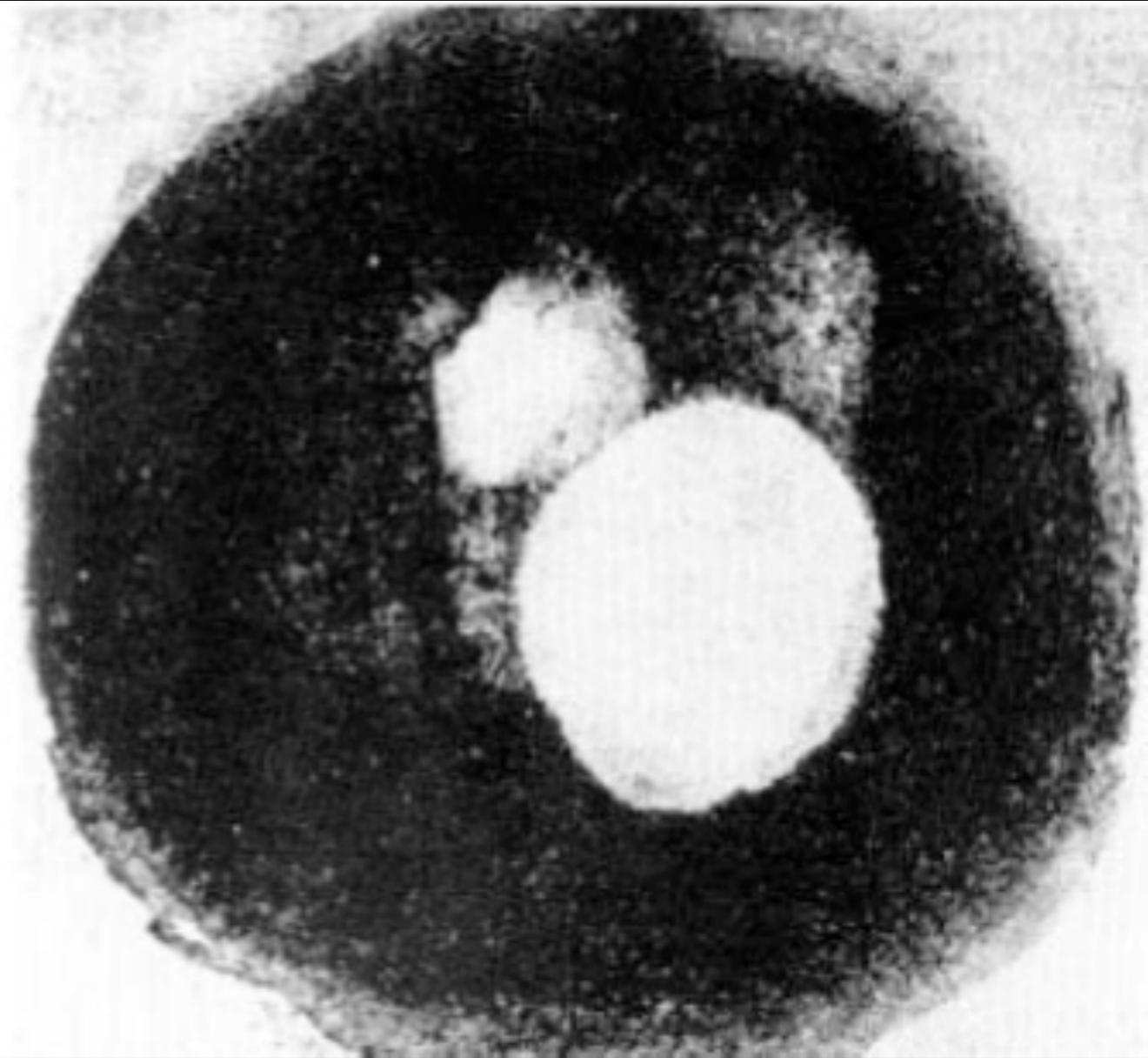
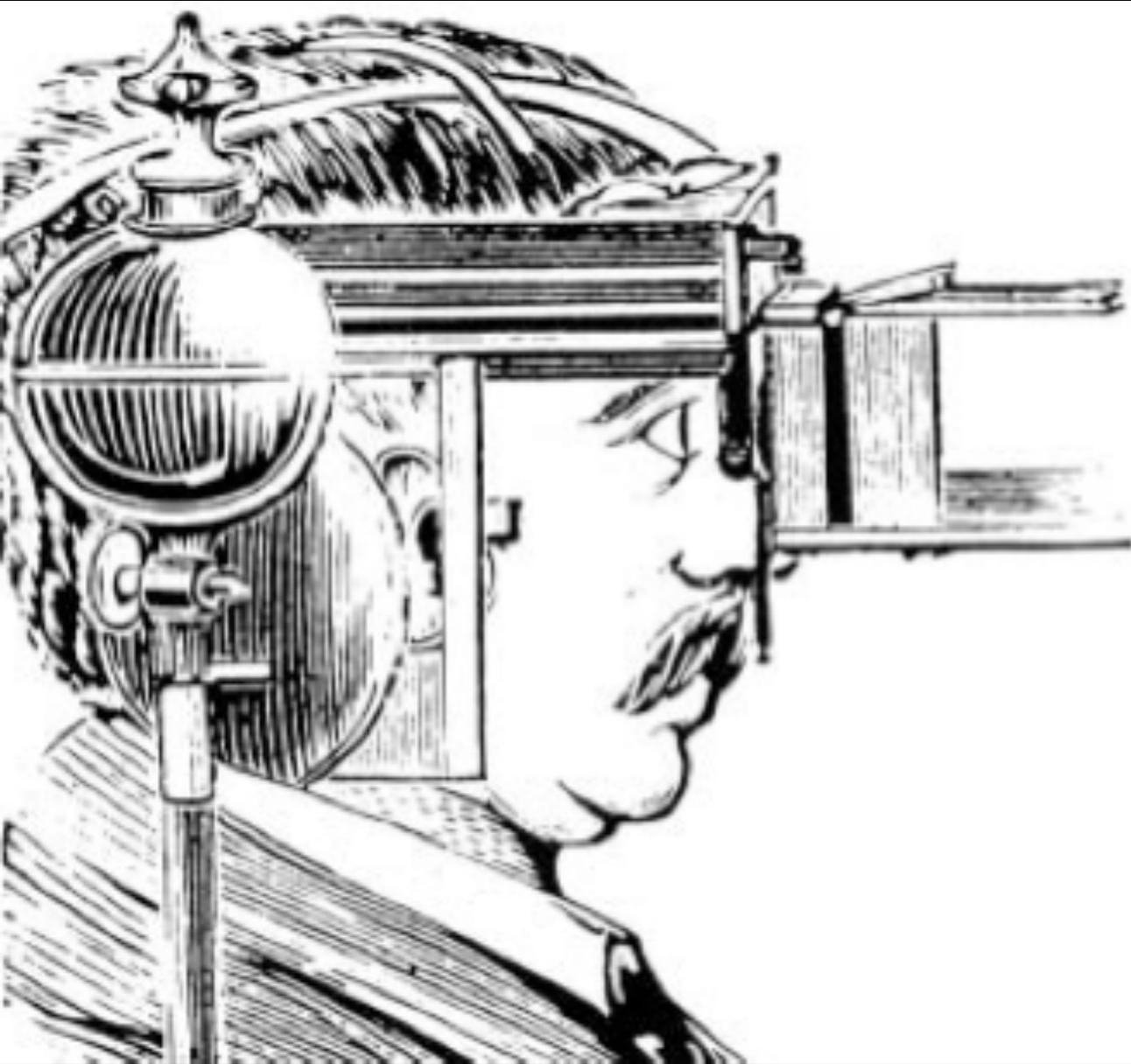
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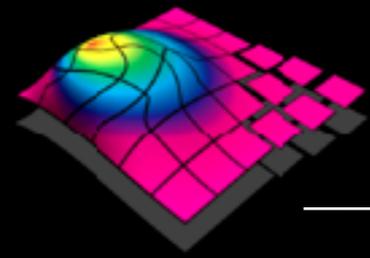
Jackman and Webster



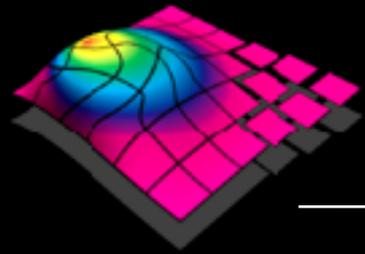
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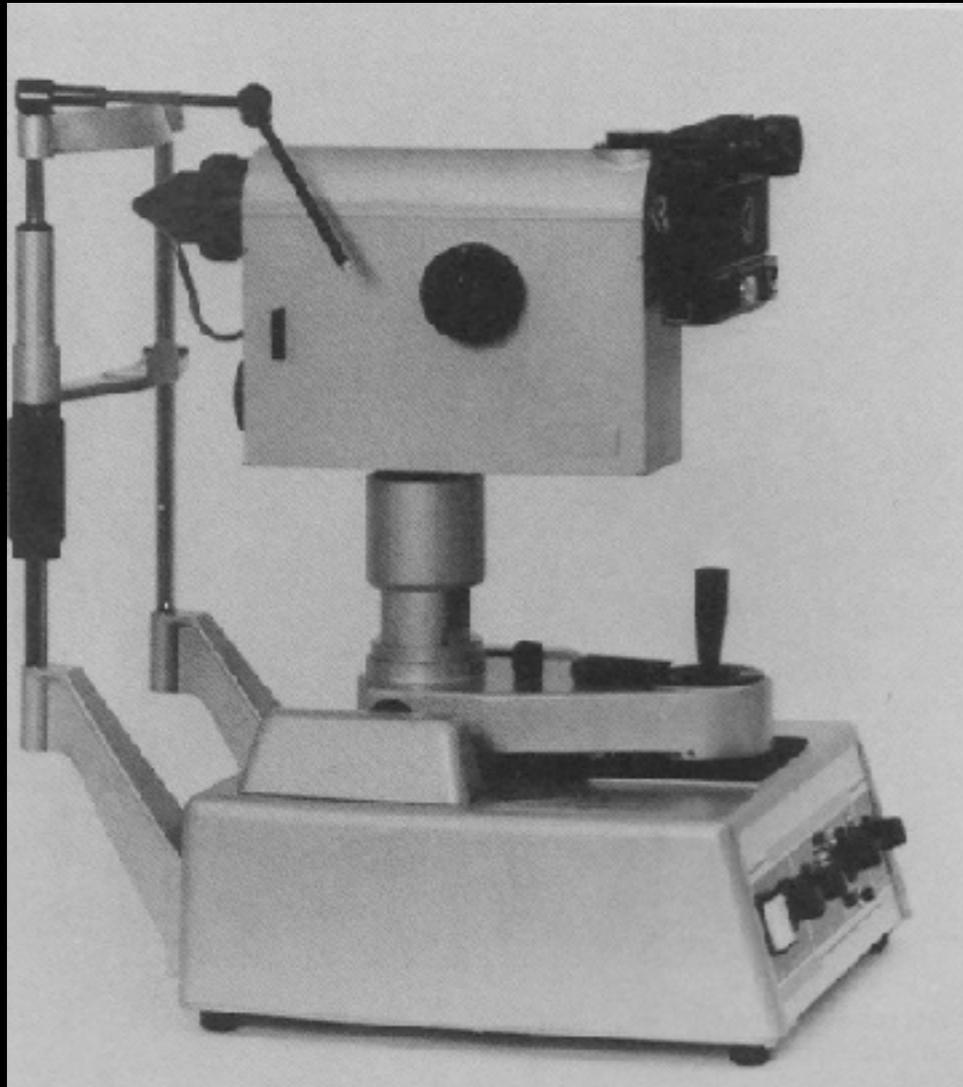
Jackman and Webster



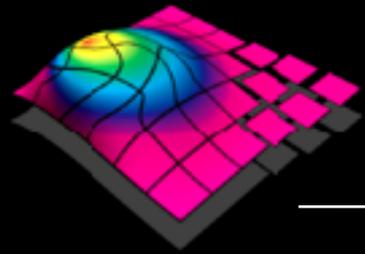
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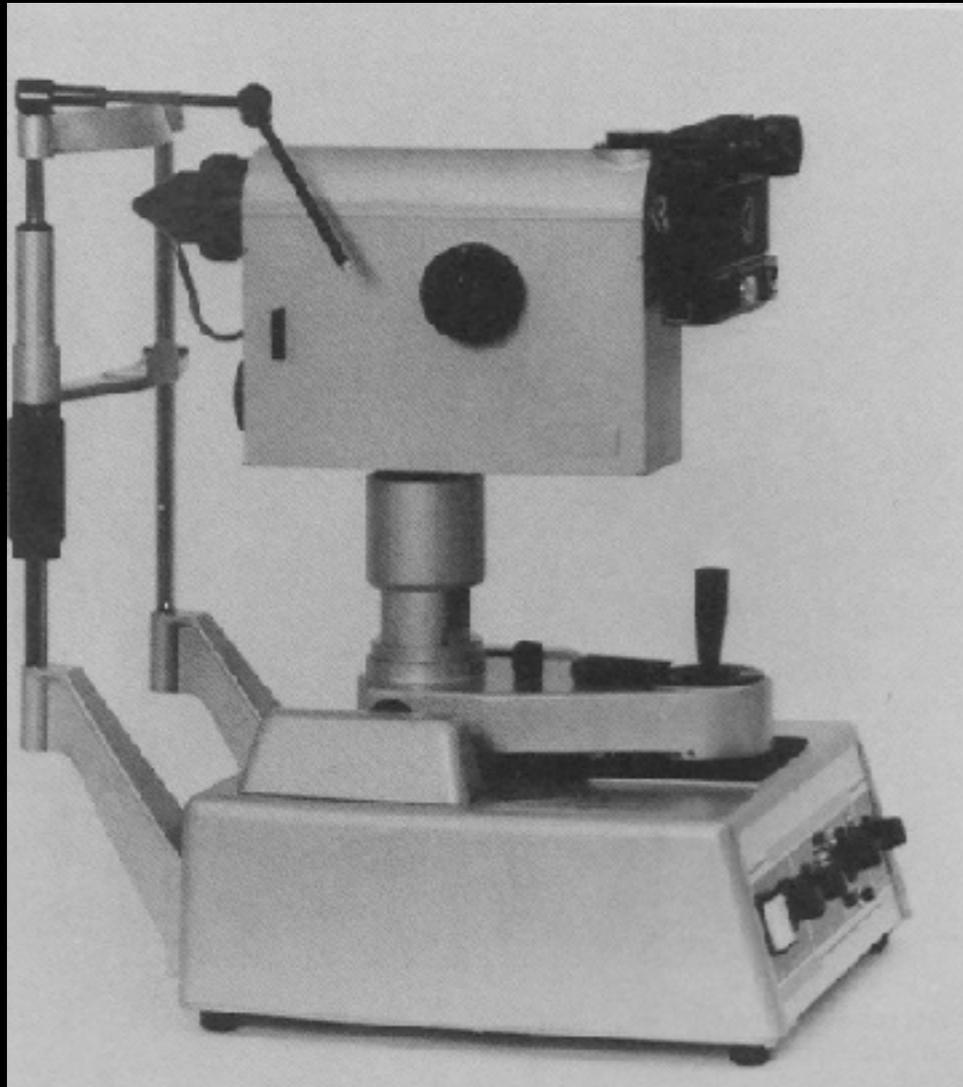
Ophthalmic Photography



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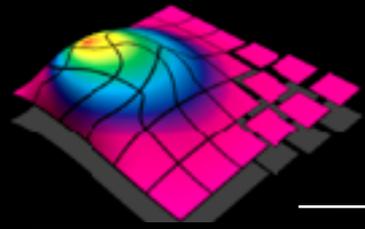
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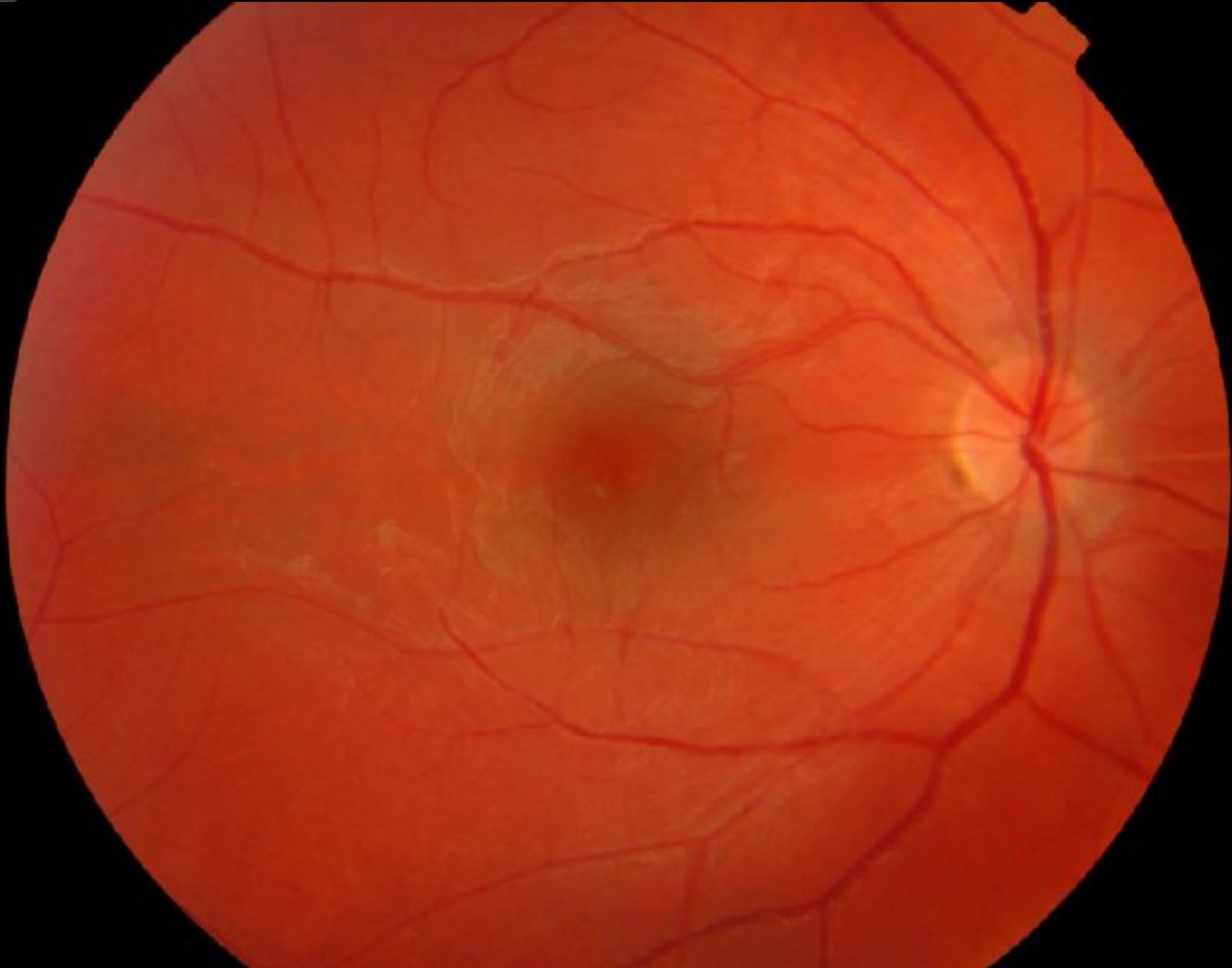
1960s

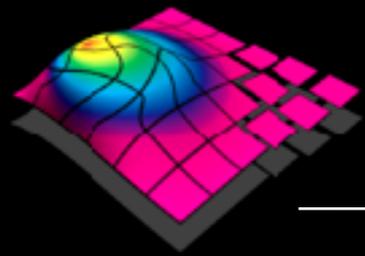


2000s

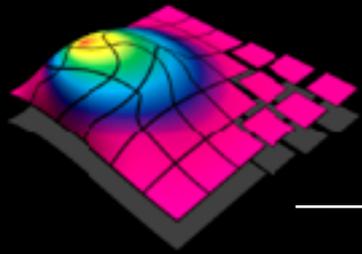


Ophthalmic Photography





Breakthrough



Breakthrough

Science 1991



Reports

Optical Coherence Tomography

DAVID HUANG, ERIC A. SWANSON, CHARLES P. LIN, JOEL S. SCHUMAN, WILLIAM G. STINSON, WARREN CHANG, MICHAEL R. HEE, THOMAS FLOTTE, KENTON GREGORY, CARMEN A. PULIAFITO, JAMES G. FUJIMOTO*

A technique called optical coherence tomography (OCT) has been developed for noninvasive cross-sectional imaging in biological systems. OCT uses low-coherence interferometry to produce a two-dimensional image of optical scattering from internal tissue microstructures in a way that is analogous to ultrasonic pulse-echo imaging. OCT has longitudinal and lateral spatial resolutions of a few micrometers and can detect reflected signals as small as $\sim 10^{-10}$ of the incident optical power. Tomographic imaging is demonstrated in vitro in the peripapillary area of the retina and in the coronary artery, two clinically relevant examples that are representative of transparent and turbid media, respectively.

TOMOGRAPHIC IMAGING TECHNIQUES such as x-ray computed tomography (1), magnetic resonance imaging (2), and ultrasound imaging (3) have found widespread applications in medicine. Each of these techniques measures a different physical property and has a resolution and penetration range that prove advantageous for specific applications. In this report, we discuss OCT. With this technique it is possible to perform noninvasive cross-sectional imaging of internal structures in biological tissues by measuring their optical reflections.

Both low-coherence light and ultrashort laser pulses can be used to measure internal structure in biological systems. An optical signal that is transmitted through or reflected from a biological tissue will contain time-of-flight information, which in turn yields spatial information about tissue microstructure. Time-resolved transmission spectroscopy has been used to measure absorption and scattering properties in tissues and has been demonstrated as a noninvasive diagnostic measure of hemoglobin oxygenation in the brain (4). Optical ranging mea-

surements of microstructure have been performed in the eye and the skin with femtosecond laser pulses (5). Time gating by means of coherent (6) as well as noncoherent (7) techniques has been used to preferentially detect directly transmitted light and obtain transmission images in turbid tissue. Low-coherence reflectometry has been used for ranging measurements in optical components (8), for surface contour mapping in integrated circuits (9), and for ranging measurements in the retina (10) and other eye structures (10, 11).

In contrast to time domain techniques, low-coherence reflectometry can be performed with continuous-wave light without the need for ultrashort pulse laser sources. Furthermore, recent technological advances in low-coherence reflectometry have allowed the construction of compact and modular systems that use diode light sources and fiber optics and have achieved

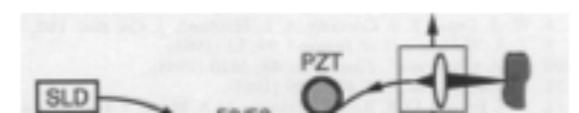
micrometer spatial resolutions and high detection sensitivities (12).

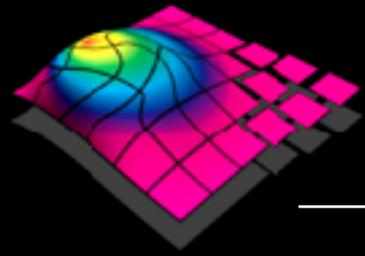
We have extended the technique of low-coherence reflectometry to tomographic imaging in biological systems. In low-coherence reflectometry, the coherence property of light reflected from a sample provides information on the time-of-flight delay from the reflective boundaries and backscattering sites in the sample. The delay information is then used to determine the longitudinal location of the reflection sites. The OCT system performs multiple longitudinal scans at a series of lateral locations to provide a two-dimensional map of reflection sites in the sample. This mode of operation is analogous to ultrasonic pulse-echo imaging (ultrasound B-mode).

The optical sectioning capability of OCT is akin to that of confocal microscopic systems (13, 14). However, although the longitudinal resolution of confocal microscopy depends on the available numerical aperture (15), OCT's resolution is limited only by the coherence length of the light source. Thus, OCT can maintain high depth resolution even when the available aperture is small. This feature will be particularly useful for in vivo measurement of deep tissues, for example, in transpupillary imaging of the posterior eye and in endoscopic imaging.

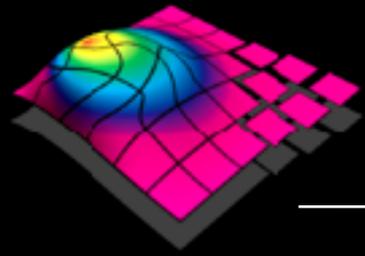
The OCT scanner (Fig. 1) is an extension of previous low-coherence reflectometer systems (12). High-speed, continuous-motion longitudinal scanning is used to increase the data acquisition rate, and a transverse scanning mechanism makes possible two-dimensional imaging. The heart of the system is the fiber optic Michelson interferometer, which is illuminated by low-coherence light (830 nm wavelength) from a superluminescent diode (SLD). The tissue sample is placed in one interferometer arm, and sample reflections are combined with the reflection from the reference mirror. The amplitudes and delays of tissue reflections are measured by scanning the reference mirror

Fig. 1. Schematic of the OCT scanner. The SLD output is coupled into a single mode fiber and split at the 50/50 coupler into sample and reference arms. Reflections from

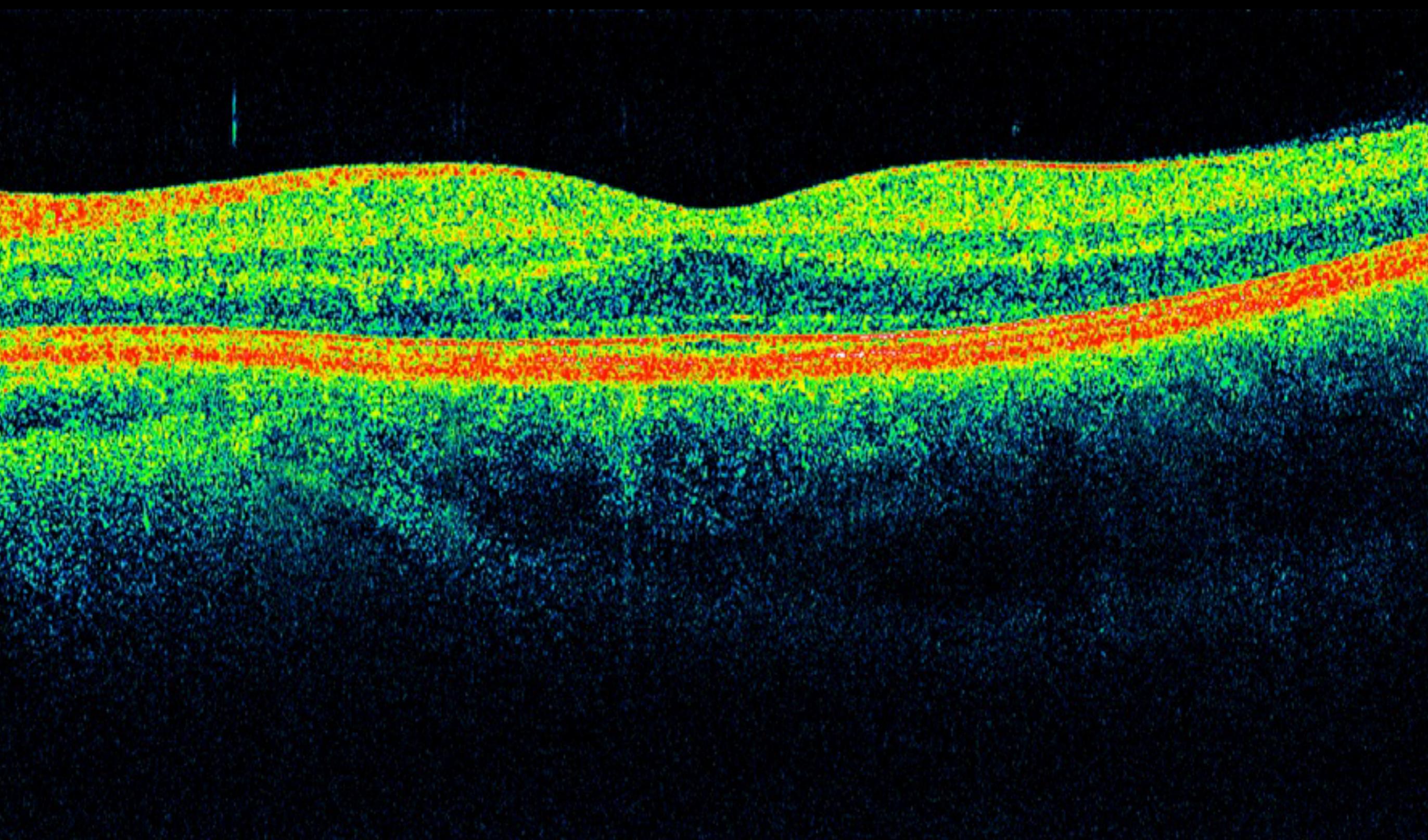


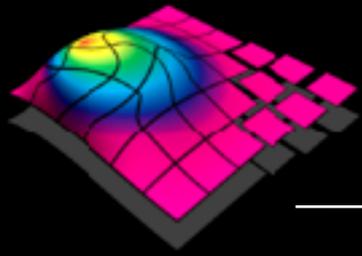


Optical Coherence Tomography



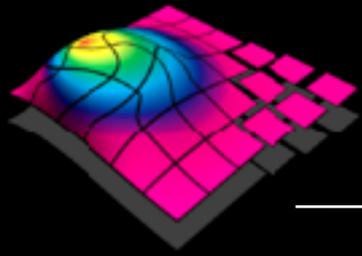
Optical Coherence Tomography





The Problem...

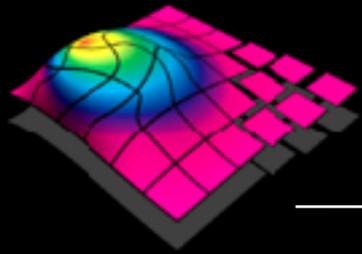




The Problem...



2017

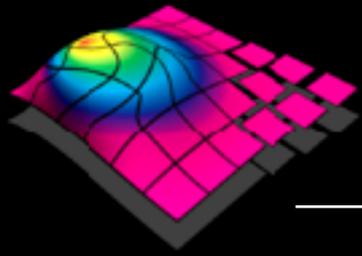


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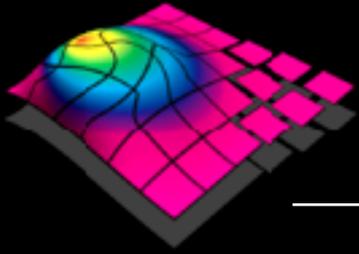


2017

~1000/day!

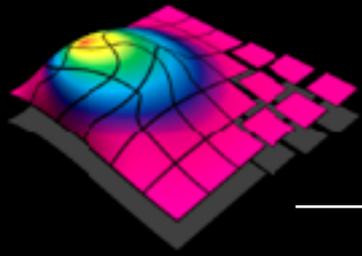


The Problem...



The Problem...

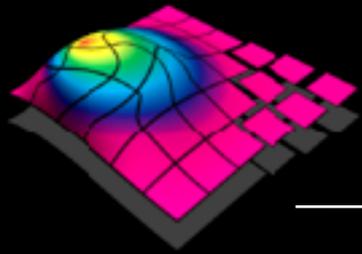




The Problem...

7000

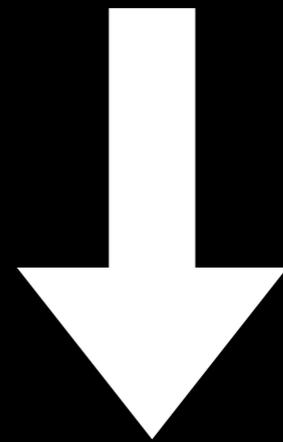




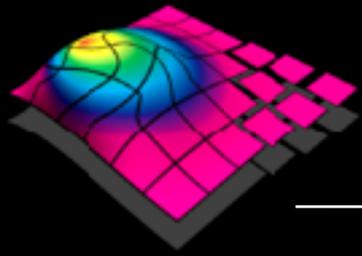
The Problem...



7000



800



The Problem...



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OCT ROLLOUT IN EVERY SPECSAVERS ANNOUNCED

The multiple will ensure all 740 of its UK practices have an OCT device installed within the next two years

22 May 2017 by [Emily McCormick](#)

Category: [Multiple](#), [OCT](#)

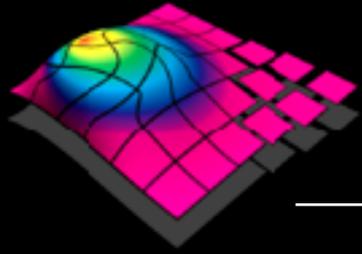


Specsavers has announced a multi-million pound plan to ensure that each of its 740 practices in the UK has an optical coherence tomography (OCT) device installed within the next two years.

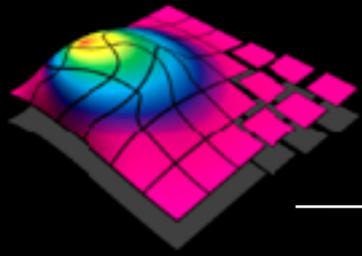
The nationwide rollout will begin in June, the multiple said, confirming that 35 of its practices already have the machine in store.



May 2017



July 2016

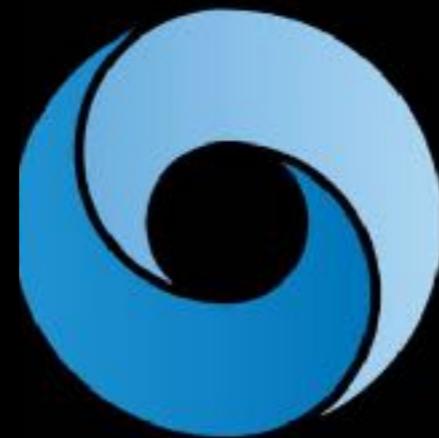


July 2016

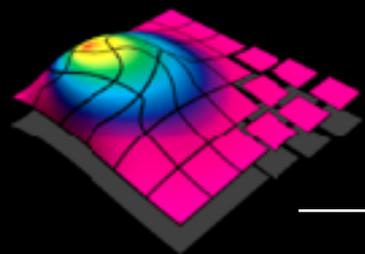
Moorfields Eye Hospital



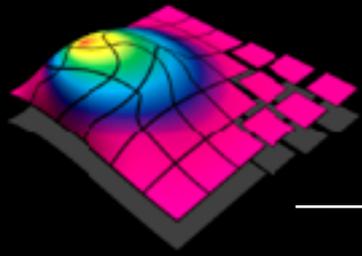
NHS Foundation Trust



DeepMind



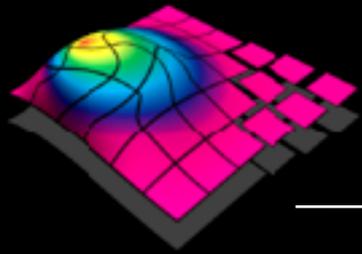
DeepMind



DeepMind



King's Cross, London

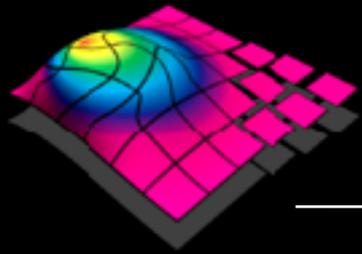


DeepMind



**>800 of the best AI
researchers**

King's Cross, London



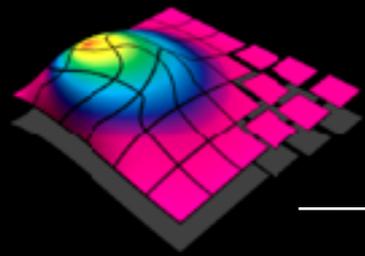
DeepMind



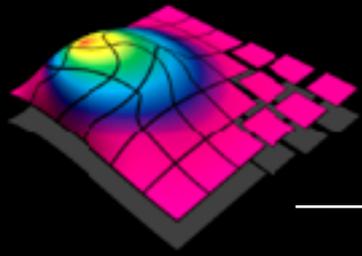
**>800 of the best AI
researchers**

**200+ peer-reviewed
publications**

King's Cross, London



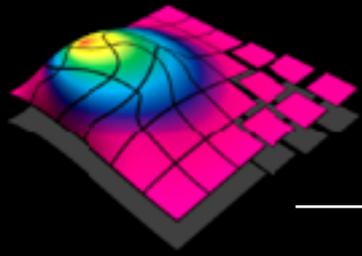
Breakthrough



Breakthrough

ATARI® **2600**™

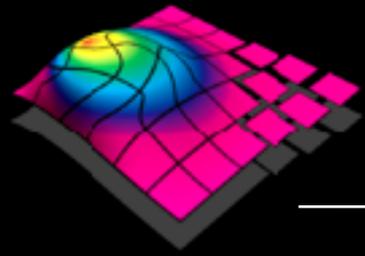




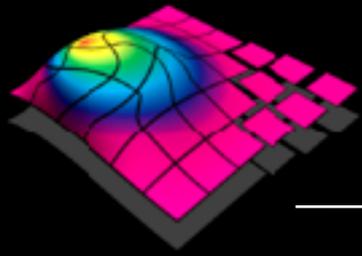
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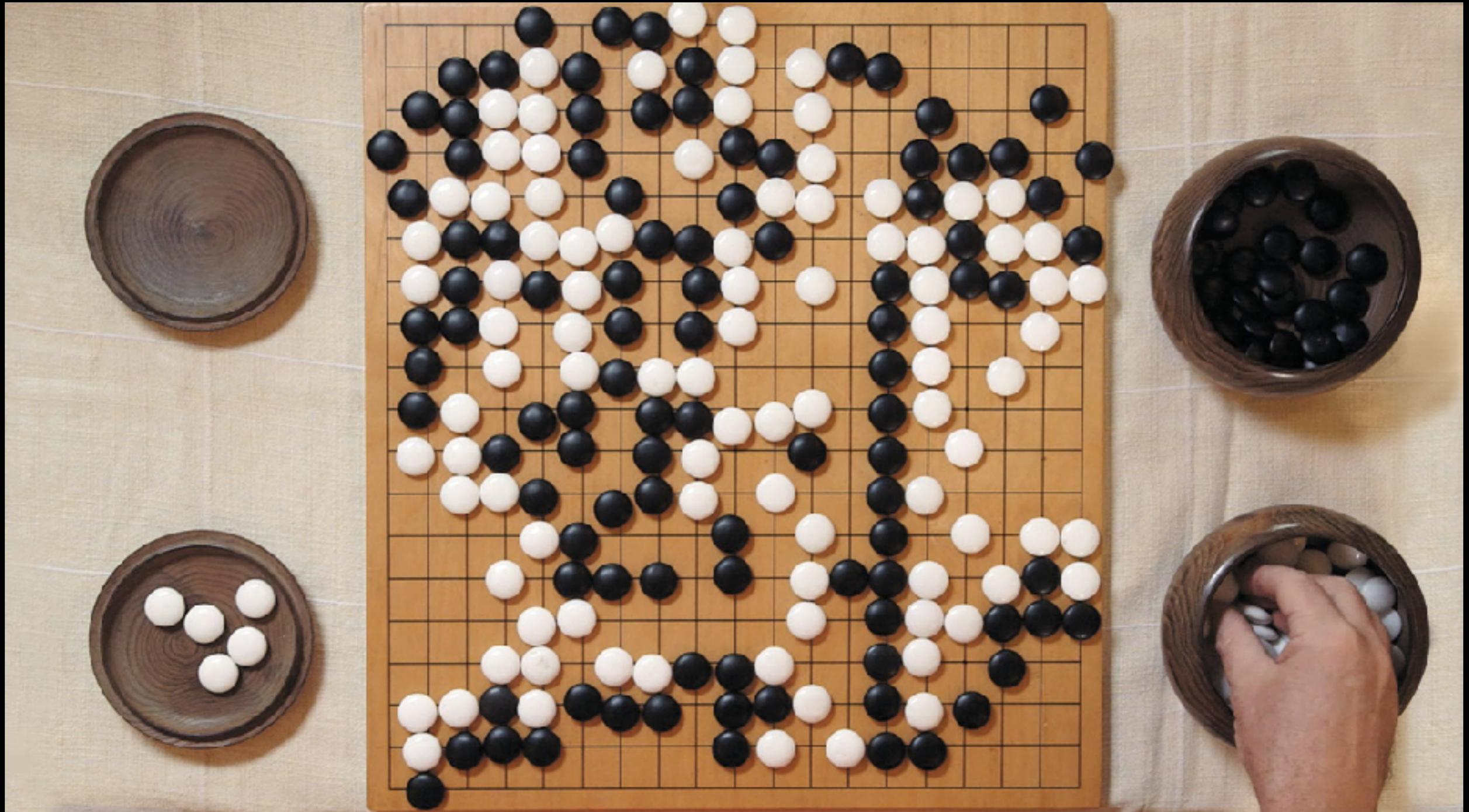
2015

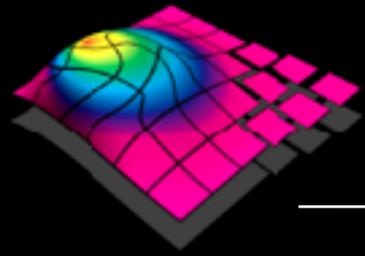


Landmark Work

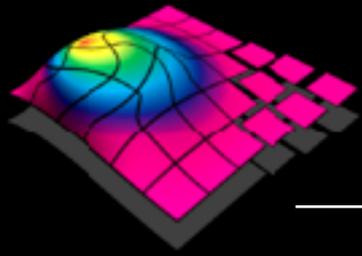


Landmark Work





Landmark Work



Landmark Work

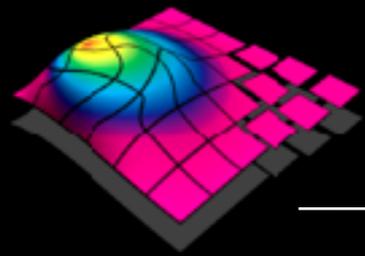
nature

THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

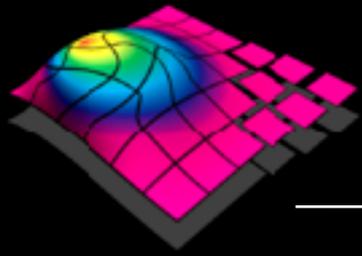
At last — a computer program that
can beat a champion Go player **PAGE 484**

ALL SYSTEMS GO

2016

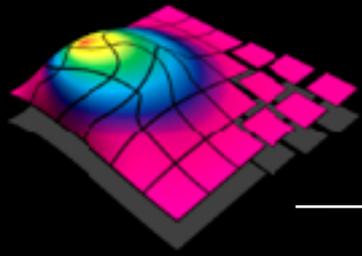


March 2016



March 2016

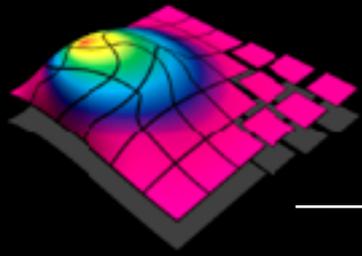




March 2016



AlphaGo wins... 4-1 !!!

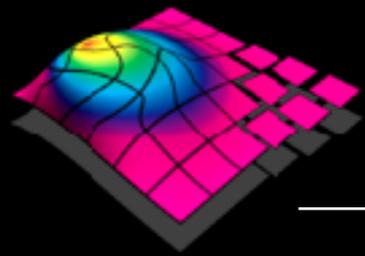


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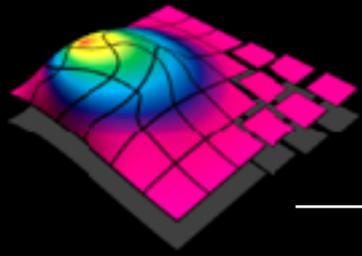
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ALPHAGO



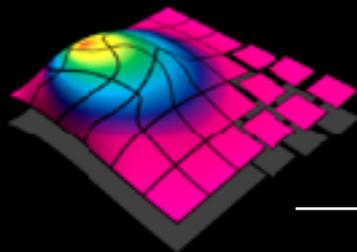


December 2018



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How research funders profit from hidden investments p. 1130 | New books for budding scientists p. 1134 | Drug leads for malaria pp. 1122 & 1129

Science

315
7 DECEMBER 2018
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AAAS

A DIGITAL PRODIGY

AlphaZero teaches itself chess, shogi, and Go
pp. 1087, 1118, & 1140

RESEARCH

COMPUTER SCIENCE

A general reinforcement learning algorithm that masters chess, shogi, and Go through self-play

David Silver^{1,2*}, Thomas Hubert^{1*}, Julian Schrittwieser^{1*}, Ioannis Antonoglou¹, Matthew Lai¹, Arthur Guez¹, Marc Lanctot¹, Laurent Sifre¹, Dhruv Kumaran¹, Thore Graepel¹, Timothy Lillicrap¹, Karen Simonyan¹, Demis Hassabis¹

The game of chess is the longest studied domain in the history of artificial intelligence. The strongest programs are based on a combination of sophisticated search techniques, domain-specific adaptations, and handcrafted evaluation functions that have been refined by human experts over several decades. By contrast, the AlphaGo Zero program recently achieved superhuman performance in the game of Go by reinforcement learning from self-play. In this paper, we generalize this approach into a single AlphaZero algorithm that can achieve superhuman performance in many challenging games. Starting from random play and given no domain knowledge except the game rules, AlphaZero convincingly defeated a world champion program in the games of chess and shogi (Japanese chess), as well as Go.

The study of computer chess is as old as computer science itself. Charles Babbage, Alan Turing, Claude Shannon, and John von Neumann devised hardware, algorithms, and theory to analyze and play the game of chess. Chess subsequently became a grand challenge task for a generation of artificial intelligence researchers, motivating its high-performance computer chess programs that play at a superhuman level (1, 2). However, these systems are highly tuned to their domain and cannot be generalized to other games without substantial human effort, whereas general game-playing systems (3, 4) remain comparatively weak.

A long-standing ambition of artificial intelligence has been to create programs that can instead learn for themselves from first principles (5, 6). Recently, the AlphaGo Zero algorithm achieved superhuman performance in the game

of Go by representing Go knowledge with the use of deep convolutional neural networks (7, 8), trained solely by reinforcement learning from games of self-play (9). In this paper, we introduce AlphaZero, an end-to-end generalization of the AlphaGo Zero algorithm that accommodates, without special casing, a broader class of game rules. We apply AlphaZero to the games of chess and shogi, as well as Go, by using the same algorithm and network architecture for all three games. Our results demonstrate that a general-purpose reinforcement learning algorithm can learn, *tabula rasa*—without domain-specific human knowledge or data, as evidenced by the same algorithm succeeding in multiple domains—superhuman performance across multiple challenging games.

A landmark for artificial intelligence was achieved in 1997 when Deep Blue defeated the human world chess champion (1). Computer chess programs continued to progress steadily beyond human level in the following two decades. These programs evaluate positions by using handcrafted features and carefully tuned weights constructed by strong human players and

programmers, combined with a high-performance alpha-beta search that expands a vast search tree by using a large number of clever heuristics and domain-specific adaptations. In (10) we describe these augmentations, focusing on the 2015 Top Chess Engine Championship (TCEC) season 9 world champion Stockfish (11) and other strong chess programs. Including Deep Blue, we use very similar architectures (1, 12).

In terms of game tree complexity, shogi is a substantially harder game than chess (13, 14). It is played on a larger board with a wider variety of pieces; any captured opponent piece can be eaten and may subsequently be dropped anywhere on the board. The strongest shogi programs, such as the 2017 Computer Shogi Association (CSA) world champion Elmo, have only recently defeated human champions (15). These programs use an algorithm similar to those used by computer chess programs again based on a highly optimized alpha-beta search engine with many domain-specific adaptations.

AlphaZero replaces the handcrafted knowledge and domain-specific augmentations used in traditional game-playing programs with deep neural networks, a general-purpose reinforcement learning algorithm, and a general-purpose tree search algorithm.

Instead of a handcrafted evaluation function and move-ordering heuristic, AlphaZero uses a deep neural network $(\mathbf{g}, \mathbf{v}) = f_{\theta}(\mathbf{s})$ with parameter θ . This neural network f_{θ} takes the board position \mathbf{s} as an input and outputs a vector of move probabilities with components $p_a = P(\mathbf{s}|a)$ for each action a and a scalar value estimating the expected outcome v of the game from position \mathbf{s} , $v = v(\mathbf{s})$. AlphaZero learns these move probabilities and value estimates entirely from self-play; these are then used to guide its search in future games.

Instead of a handcrafted search with domain-specific enhancements, AlphaZero uses a general-purpose Monte-Carlo tree search (MCTS) algorithm. Each search consists of a series of simulated games of self-play that traverse a tree from root state \mathbf{s}_{root} until a leaf state is reached. Each simulation proceeds by selecting in each state \mathbf{s} a move a with low visit count (not previously frequently explored), high move probability, and high value (averaged over the leaf states of

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*These authors contributed equally to this work
CORRESPONDENCE: DAVID SILVER (dsilver@deepmind.com) OR THOMAS HUBERT (thubert@deepmind.com) (UK)

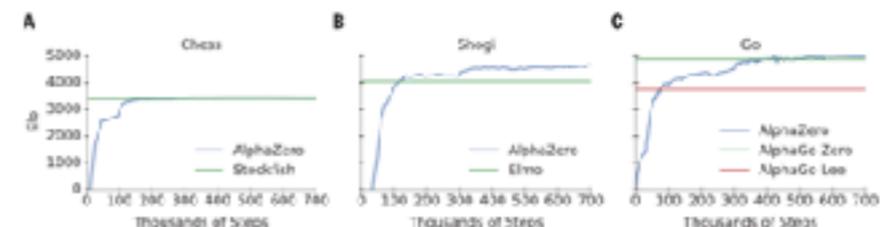
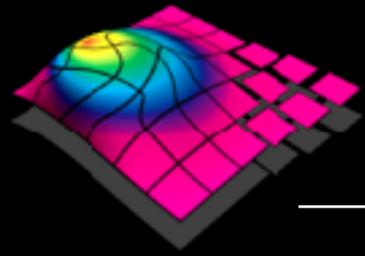
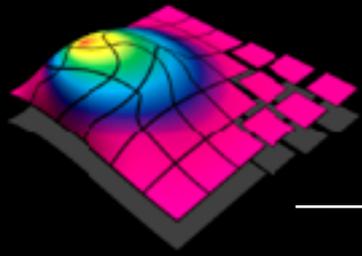


Fig. 1. Training AlphaZero for 700,000 chess. Elo ratings were computed from games between different players where each player was given 1 vs. 1000. (A) The performance of AlphaZero in chess compared with the 2015 TCEC world champion program Stockfish.

(B) Performance of AlphaZero in shogi compared with the 2017 CSA world champion program Elmo. (C) Performance of AlphaZero in Go compared with AlphaGo Lee and AlphaGo Zero (20 blocks over 2 days).

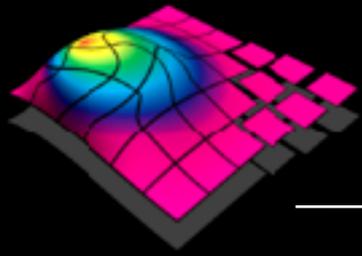


A New Artificial Intelligence “Spring”?



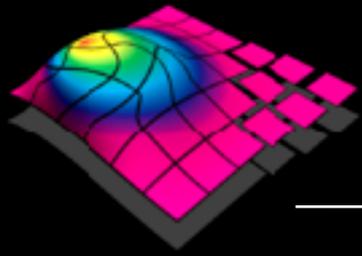
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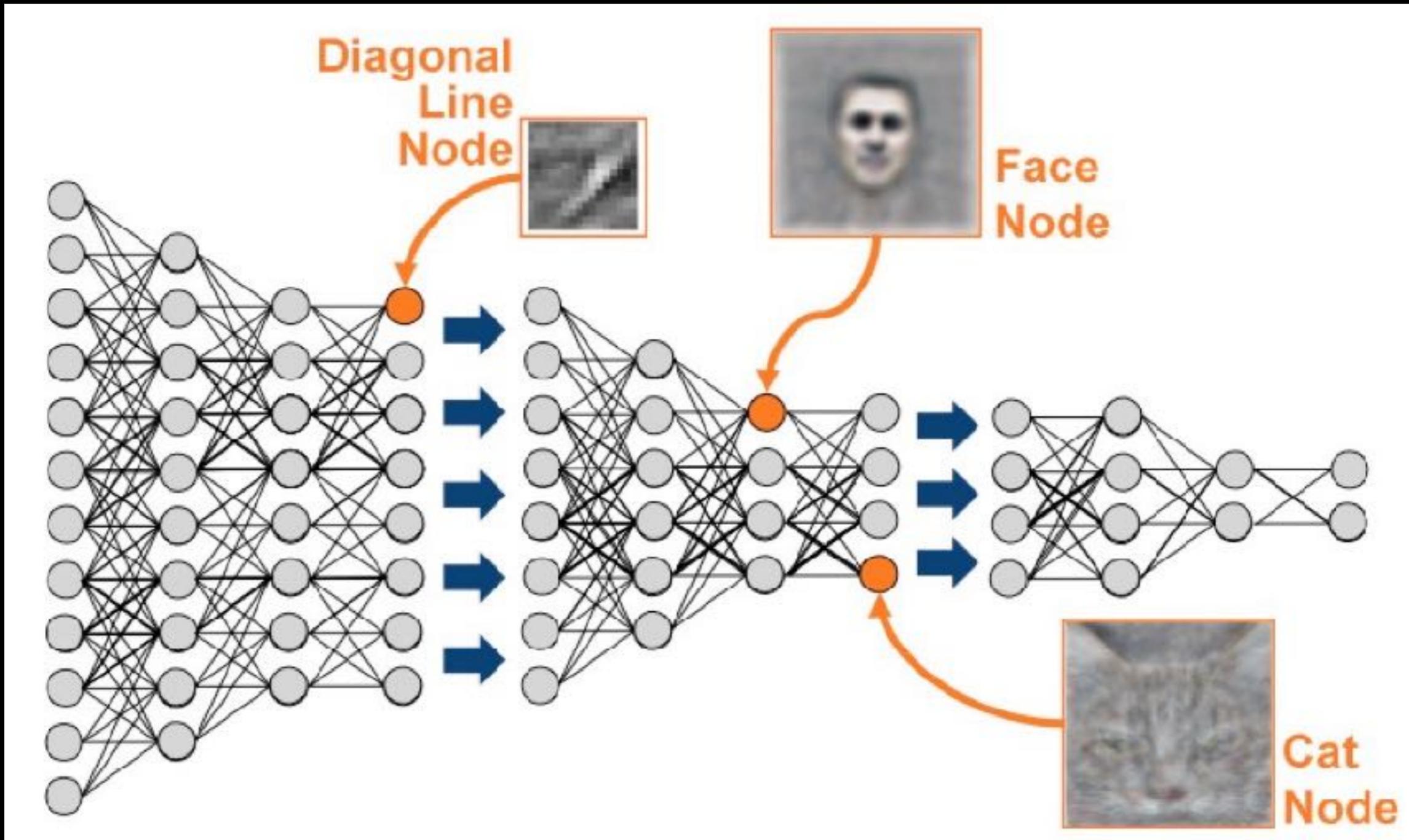


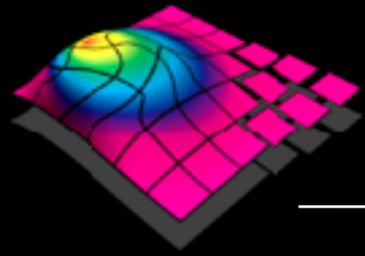
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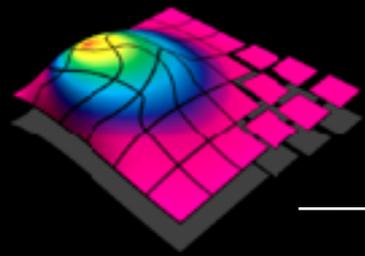
Artificial Neural Networks





Artificial Neural Networks

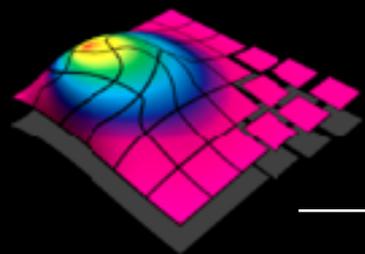
Learns from Experience



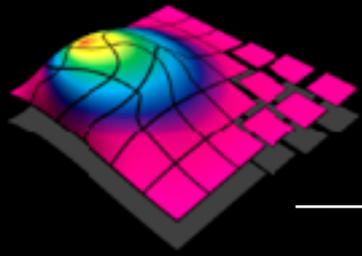
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Learns from Experience

Not Pre-designed or Pre-Specified



“Deep Learning”



“Deep Learning”

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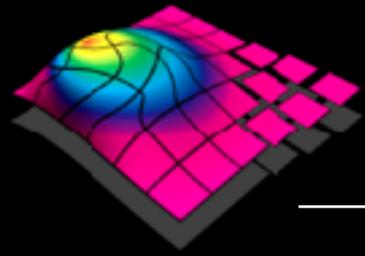
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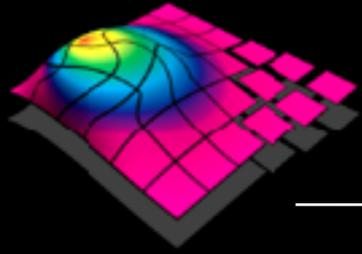
World Changing Ideas 2015

10 big advances that will improve life, transform computing and maybe even save the planet

By THE EDITORS on December 1, 2015



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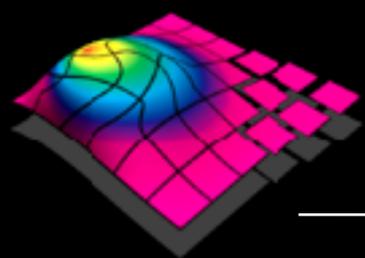


Digging a Little Bit Deeper...

Classical Statistics	Artificial Intelligence
Low dimensional data	High dimensional data (e.g., more than 1000 dimensions)
Lots of noise in the data	Noise is not sufficient to obscure the structure in the data if processed right
Not much structure in the data and what structure there is can be represented by a fairly simple model	A huge amount of structure in the data, but the structure is too complicated to be represented by a single model (e.g., the mapping of an OCT volume scan to a specific disease diagnosis)
Main problem is distinguishing true structure from noise	Main problem is figuring out how to represent the complicated structure in a way that allows it to be learned

Source: adapted from lecture by Professor Geoff Hinton, FRS, to the Royal Society, 2016

YouTube link: https://www.youtube.com/watch?v=VhmE_UXDOGs

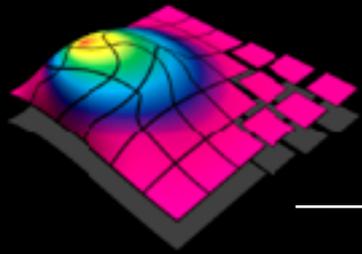


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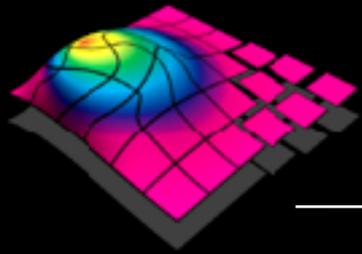


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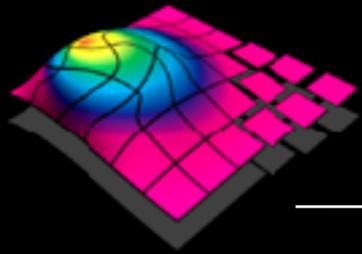


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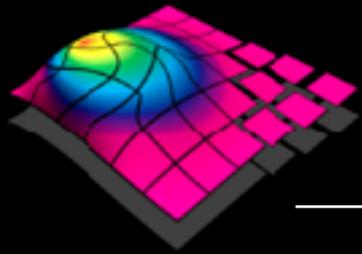


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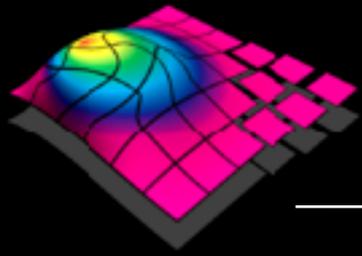


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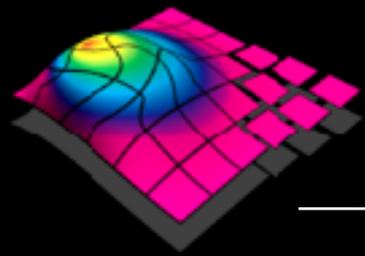


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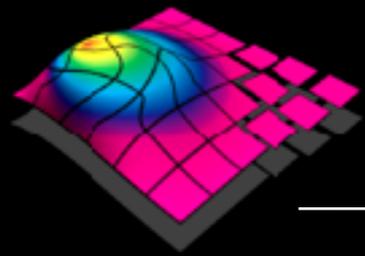
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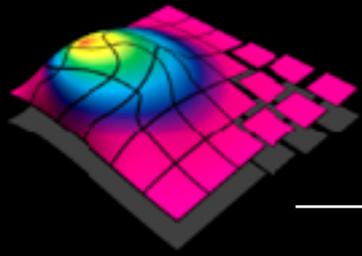
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High Dimensional Data

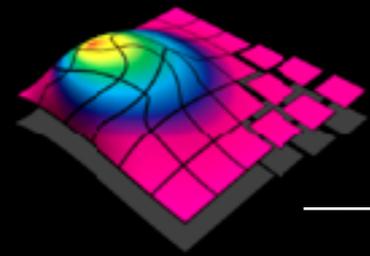


High Dimensional Data

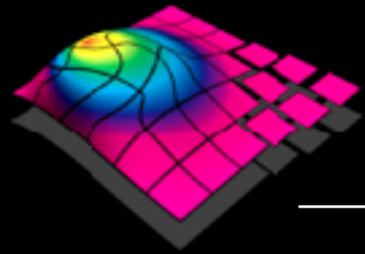


High Dimensional Data

***~65 million
datapoints!!!***



Example from Google Brain



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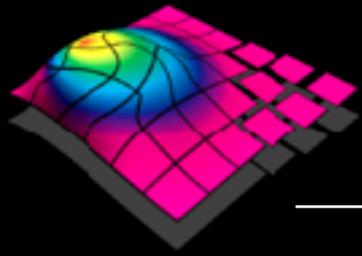
<https://doi.org/10.1038/s41551-018-0195-0>

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}

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.

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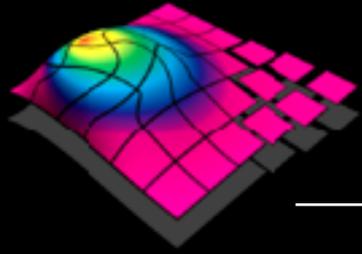
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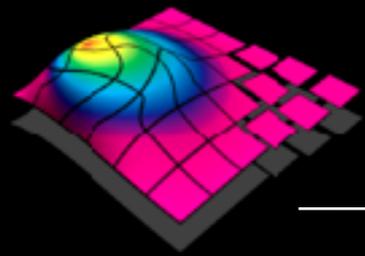
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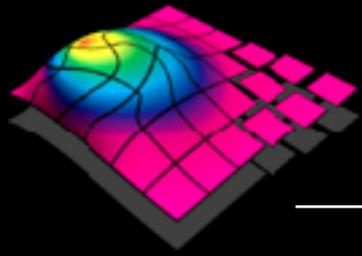
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NATURE | LETTER

日本語要約

Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteva, Brett Kuprel, Roberto A. Novoa, Justin Ko, Susan M. Swetter, Helen M. Blau & Sebastian Thrun

[Affiliations](#) | [Contributions](#) | [Corresponding authors](#)

Nature 542, 115–118 (02 February 2017) | doi:10.1038/nature21056
Received 26 June 2016 | Accepted 14 December 2016 | Published online 25 January 2017

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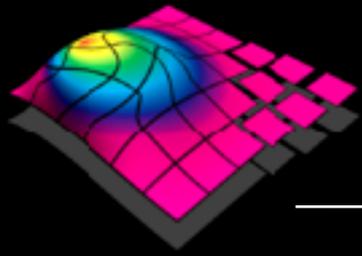
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CheXNet: Radiologist-Level Pneumonia Detection on Chest X-Rays with Deep Learning

Pranav Rajpurkar, Jeremy Irvin, Kaylie Zhu, Brandon Yang, Hershel Mehta, Tony Duan, Daisy Ding, Aarti Bagul, Curtis Langlotz, Katie Shpanskaya, Matthew P. Lungren, Andrew Y. Ng

(Submitted on 14 Nov 2017)

We develop an algorithm that can detect pneumonia from chest X-rays at a level exceeding practicing radiologists. Our algorithm, CheXNet, is a 121-layer convolutional neural network trained on ChestX-ray14, currently the largest publicly available chest X-ray dataset, containing over 100,000 frontal-view X-ray images with 14 diseases. Four practicing academic radiologists annotate a test set, on which we compare the performance of CheXNet to that of radiologists. We find that CheXNet exceeds average radiologist performance on pneumonia detection on both sensitivity and specificity. We extend CheXNet to detect all 14 diseases in ChestX-ray14 and achieve state of the art results on all 14 diseases.

Subjects: Computer Vision and Pattern Recognition (cs.CV), Learning (cs.LG), Machine Learning (stat.ML)

Cite as: arXiv:1711.05225 [cs.CV]

(or arXiv:1711.05225v1 [cs.CV] for this version)

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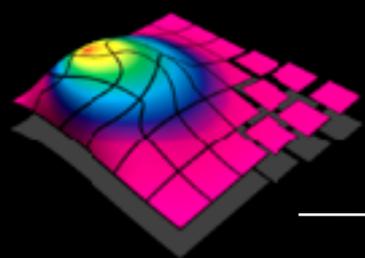
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November 2017



Clinical and Scientific Applications?

CheXNet: Radiologist-Level Pneumonia Detection on Chest X-Rays with Deep Learning

Pranav Rajpurkar^{*1} Jeremy Irvin^{*1} Kaylic Zhu¹ Brandon Yang¹ Hershel Mehta¹
Tony Duan¹ Daisy Ding¹ Aarti Bagul¹ Curtis Langlotz² Katie Shpankaya²
Matthew P. Lungren² Andrew Y. Ng¹

Abstract

We develop an algorithm that can detect pneumonia from chest X-rays at a level exceeding practicing radiologists. Our algorithm, CheXNet, is a 121-layer convolutional neural network trained on ChestX-ray14, currently the largest publicly available chest X-ray dataset, containing over 100,000 frontal-view X-ray images with 14 diseases. Four practicing academic radiologists annotate a test set, on which we compare the performance of CheXNet to that of radiologists. We find that CheXNet exceeds average radiologist performance on pneumonia detection on both sensitivity and specificity. We extend CheXNet to detect all 14 diseases in ChestX-ray14 and achieve state of the art results on all 14 diseases.

1. Introduction

More than 1 million adults are hospitalized with pneumonia and around 50,000 die from the disease every year in the US alone (CDC, 2017). Chest X-rays are currently the best available method for diagnosing pneumonia (WHO, 2001), playing a crucial role in clin-

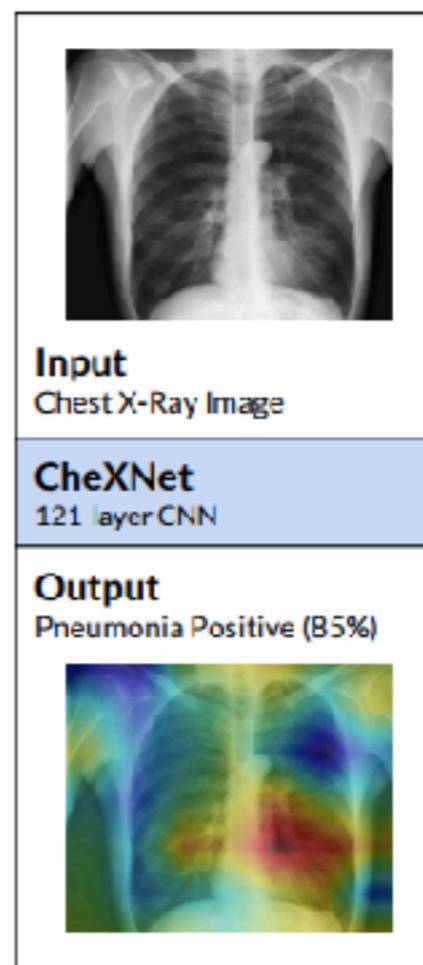
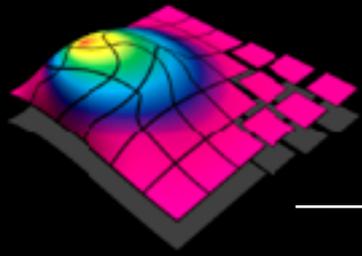
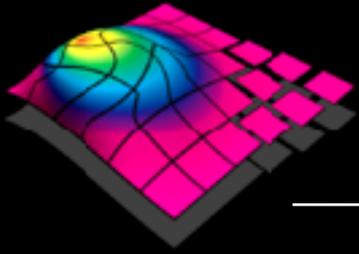


Figure 1. CheXNet is a 121-layer convolutional neural network that takes a chest X-ray image as input, and outputs a heatmap showing pneumonia detection.



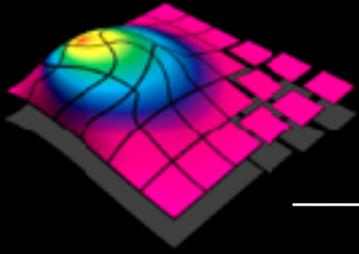
Claim... and a Pushback!



Claim... and a Pushback!

"If a typical person can do a mental task with less than one second of thought, we can probably automate it using AI either now or in the near future."

Andrew Ng



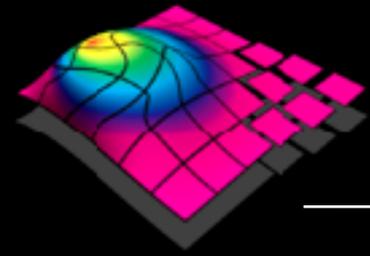
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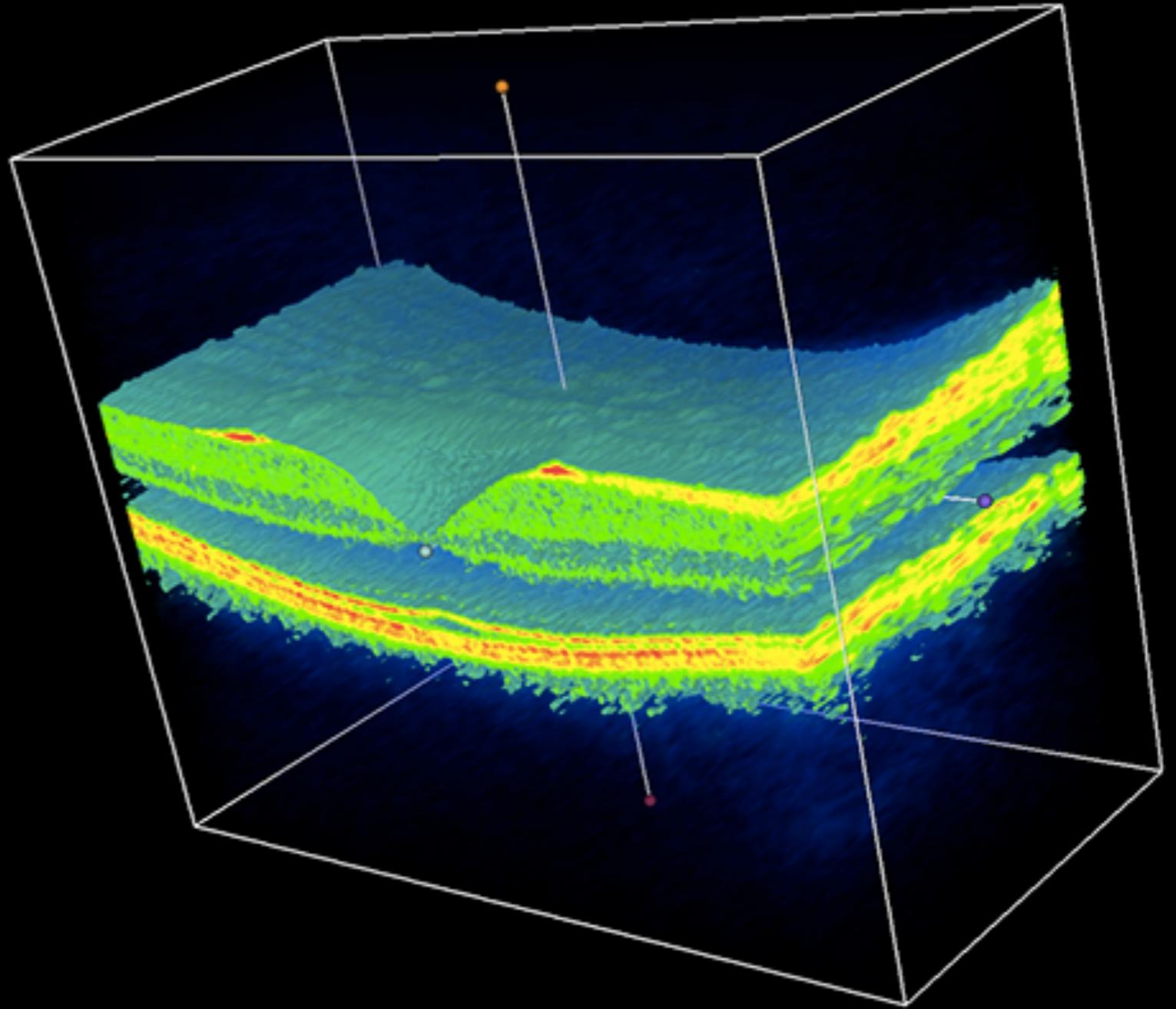
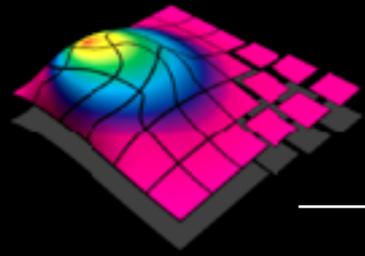
"If a typical person can do a mental task with less than one second of thought, and we can gather an enormous amount of directly relevant data, we have a fighting chance — so long as the test data aren't too terribly different from the training data, and the domain doesn't change too much over time"

Gary Marcus

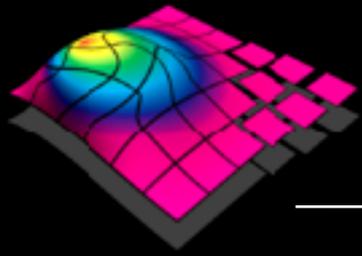


Applications in Ophthalmology?

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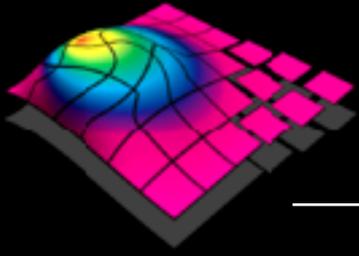


OCT



July 2015

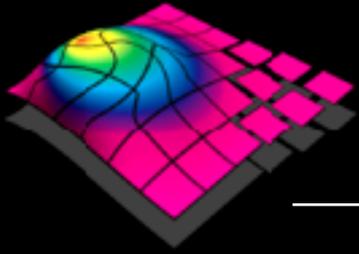




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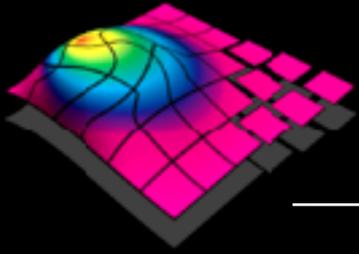
1. Datasets Quantity and Quality



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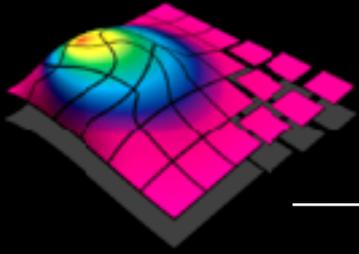
1. **Datasets Quantity and Quality**
2. **Technical Feasibility**



July 2015



- 1. Datasets Quantity and Quality**
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- 3. Ethical / Governance Requirements**

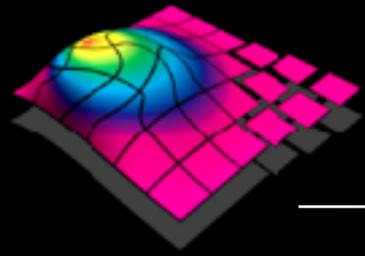


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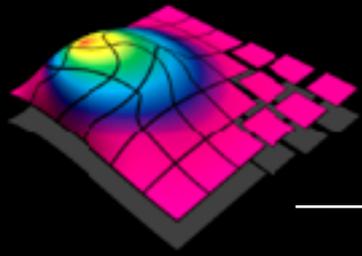


1. **Datasets Quantity and Quality**
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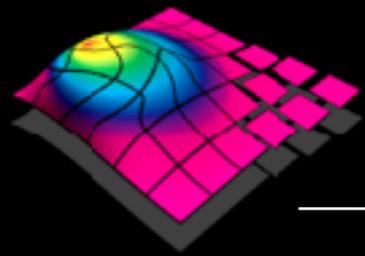
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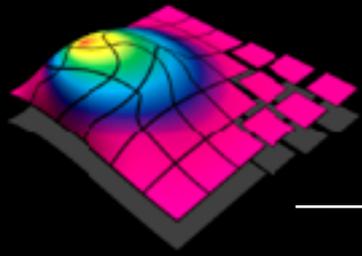
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*Research
Collaboration
Agreement*



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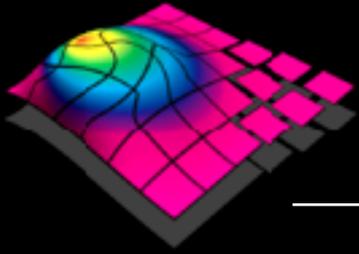
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[Looking after your eyes](#)

[Yes EYE Can](#)

[Yes Eye Did](#)

[Anatomy of the eye](#)

DeepMind Health Q&A

[How did the partnership come about?](#)



[What will the project involve?](#)



[What is the project trying to achieve?](#)



[How long will the project last?](#)



[How much data has DeepMind been given access to?](#)



[Do patients have to give their consent for their data to be used?](#)



[What are the data protection measures in place for this project?](#)



[Will any further patient information be shared between Moorfields and DeepMind in future?](#)



[How can patients be sure that no identifiable data is being shared with DeepMind?](#)

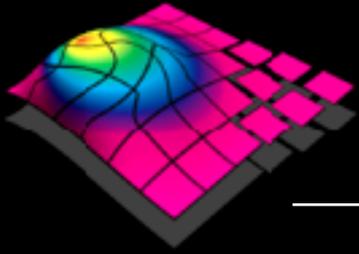


[What processes are in place to ensure the data transferred to DeepMind is only ever seen by the research team?](#)



[What approvals has DeepMind been given for this research project?](#)





Research Protocol

F1000Research

F1000Research 2016, null:null Last updated: 10 JUN 2016



STUDY PROTOCOL

Automated analysis of retinal imaging using machine learning techniques for computer vision

Jeffrey De Fauw¹, Pearse Keane¹, Nenad Tomasev¹, Daniel Visentin¹,
George van den Driessche¹, Mike Johnson¹, Cian O Hughes¹, Carlton Chu¹,
Joseph Ledsam¹, Trevor Back¹, Tunde Peto², Geraint Rees³, Hugh Montgomery⁵,
Rosalind Raine⁴, Olaf Ronneberger¹, Julien Cornebise¹

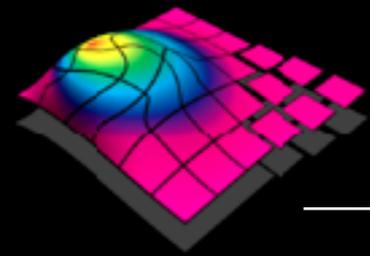
¹Google DeepMind, London, EC4A 3TW, UK

²Moorfields Eye Hospital NHS Foundation Trust, London, EC1V 2PD, UK

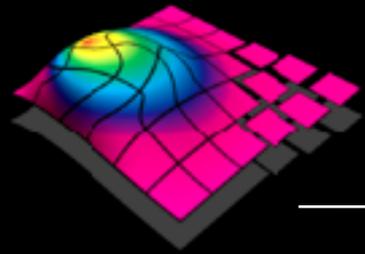
³Alexandra House University College London, Bloomsbury Campus, London, WC1N 3AR, UK

⁴Department of Applied Health Research, University College London, London, WC1E 7HB, UK

⁵Institute of Sport, Exercise and Health, London, W1T 7HA, UK



Patient-Centred Research



Patient-Centred Research

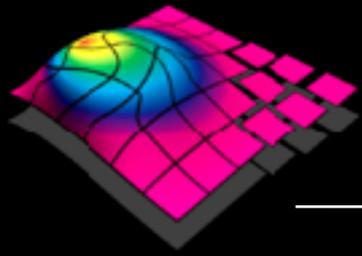


Macular Society

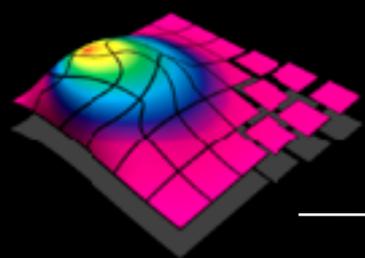
*Royal National
Institute for the Blind*

Fight For Sight UK

Patient Engagement Event, Sept 2016



August 2018



August 2018

nature
medicine

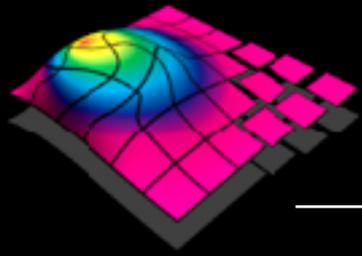
ARTICLES

<https://doi.org/10.1038/s41591-018-0107-6>

Clinically applicable deep learning for diagnosis and referral in retinal disease

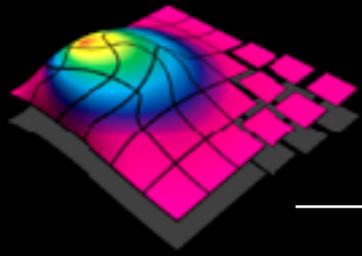
Jeffrey De Fauw¹, Joseph R. Ledsam¹, Bernardino Romera-Paredes¹, Stanislav Nikolov¹, Nenad Tomasev¹, Sam Blackwell¹, Harry Askham¹, Xavier Glorot¹, Brendan O'Donoghue¹, Daniel Visentin¹, George van den Driessche¹, Balaji Lakshminarayanan¹, Clemens Meyer¹, Faith Mackinder¹, Simon Bouton¹, Kareem Ayoub¹, Reena Chopra², Dominic King¹, Alan Karthikesalingam¹, Cian O. Hughes^{1,3}, Rosalind Raine³, Julian Hughes², Dawn A. Sim², Catherine Egan², Adnan Tufail², Hugh Montgomery³, Demis Hassabis¹, Geraint Rees³, Trevor Back¹, Peng T. Khaw², Mustafa Suleyman¹, Julien Cornebise^{1,3,4}, Pearse A. Keane^{2,4*} and Olaf Ronneberger^{1,4*}

The volume and complexity of diagnostic imaging is increasing at a pace faster than the availability of human expertise to interpret it. Artificial intelligence has shown great promise in classifying two-dimensional photographs of some common diseases and typically relies on databases of millions of annotated images. Until now, the challenge of reaching the performance of expert clinicians in a real-world clinical pathway with three-dimensional diagnostic scans has remained unsolved. Here, we apply a novel deep learning architecture to a clinically heterogeneous set of three-dimensional optical coherence tomography scans from patients referred to a major eye hospital. We demonstrate performance in making a referral recommendation that reaches or exceeds that of experts on a range of sight-threatening retinal diseases after training on only 14,884 scans. Moreover, we demonstrate that the tissue segmentations produced by our architecture act as a device-independent representation; referral accuracy is maintained when using tissue segmentations from a different type of device. Our work removes previous barriers to wider clinical use without prohibitive training data requirements across multiple pathologies in a real-world setting.



August 2018





August 2018

nature
medicine

SEPTEMBER 2018 VOL 24 NO 9
www.nature.com/naturemedicine

AI accelerates diagnosis
NAD⁺ biosynthesis and high-risk hospitalizations
Targeted microbiome therapy for thrombosis

FREE LONDON MONDAY 13 AUGUST 2018

Evening Standard

DIER: WE'RE READY TO SILENCE OUR CRITICS
SPURS MIDFIELDER SAYS TEAM WILL SHINE DESPITE NO SIGNINGS 3 SPORT PAGE 52

FLEX APPEAL - GET STRONG WITH YOGA
DYNAMIC SEQUENCE TO WORK EVERY MUSCLE 7 FITNESS & BEAUTY STARTS ON PAGE 29

COMPUTER DIAGNOSIS COULD SAVE SIGHT OF MILLIONS
PIONEERING TECH TRIALLED AT MOOKFIELDS RIVALS WORLD-LEADING EXPERTS FOR SPOTTING EYE DISEASE

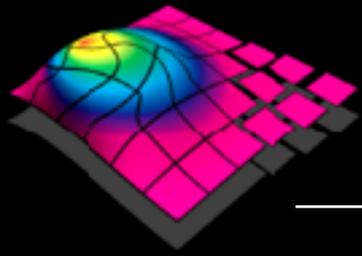
KATIE PIPER REVEALED AS FIRST STRICTLY ST...

INSIDE TODAY
Boris should focus on Sadiq, say PM's allies

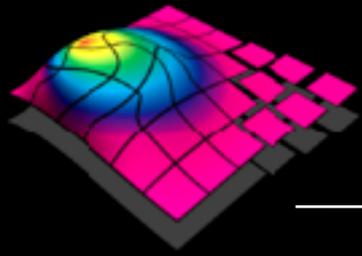
Pray for Aretha: singer is 'gravely ill with cancer'

No new cash for rough sleepers, minister admits

Back with mother in Dubai

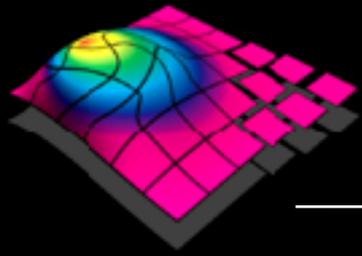


High Level Support!

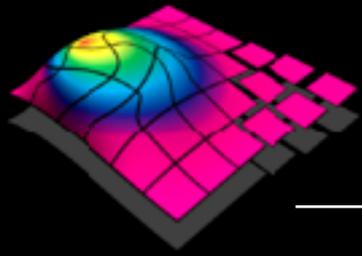


High Level Support!

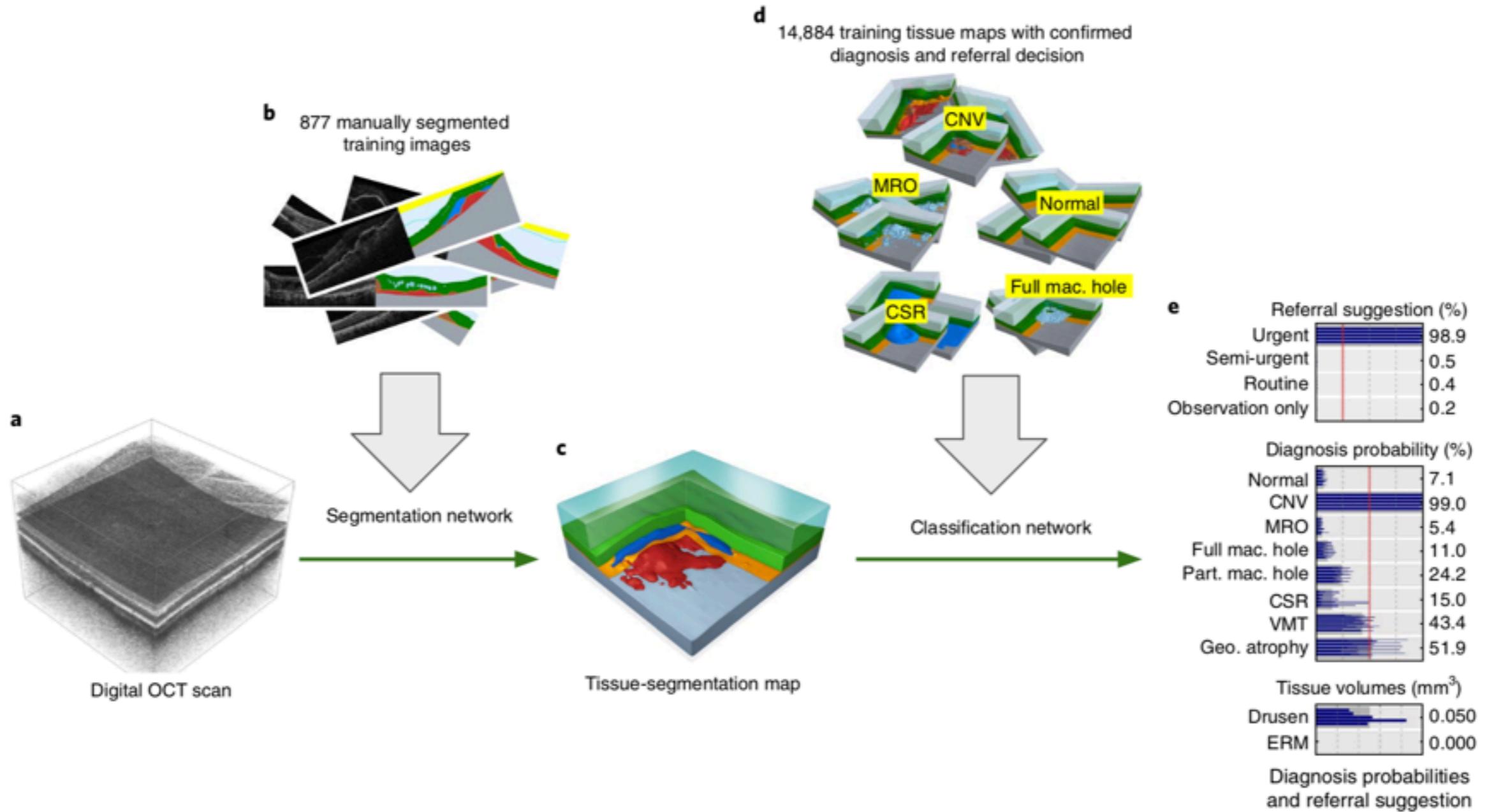


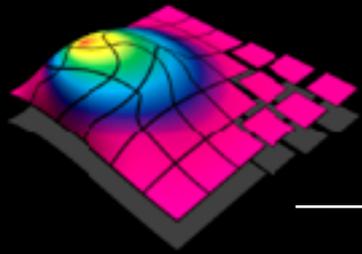


Novel Framework

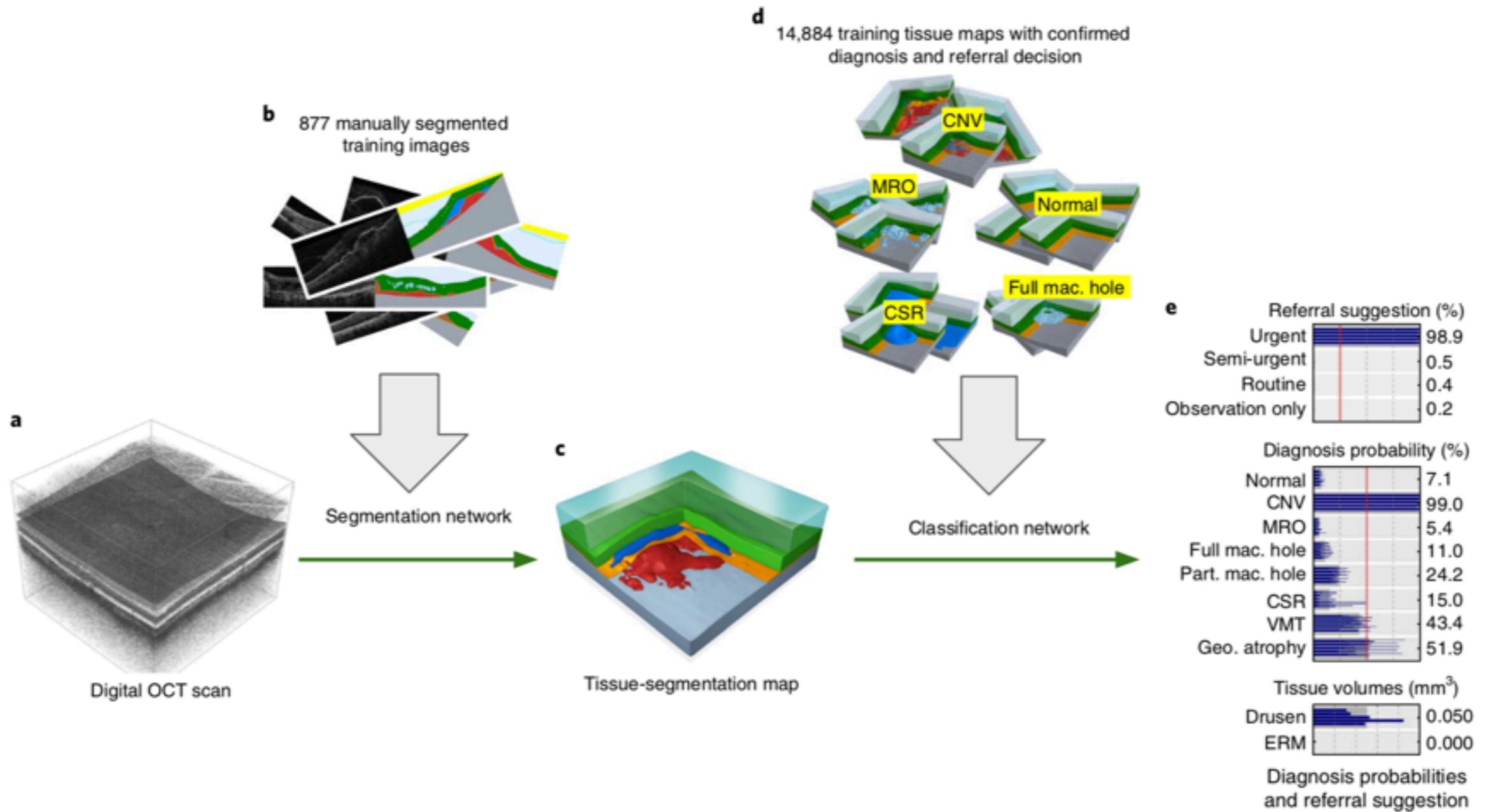


Novel Framework

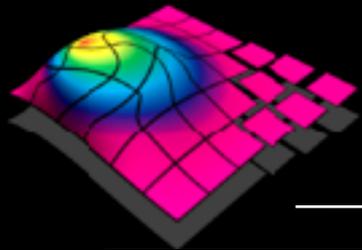




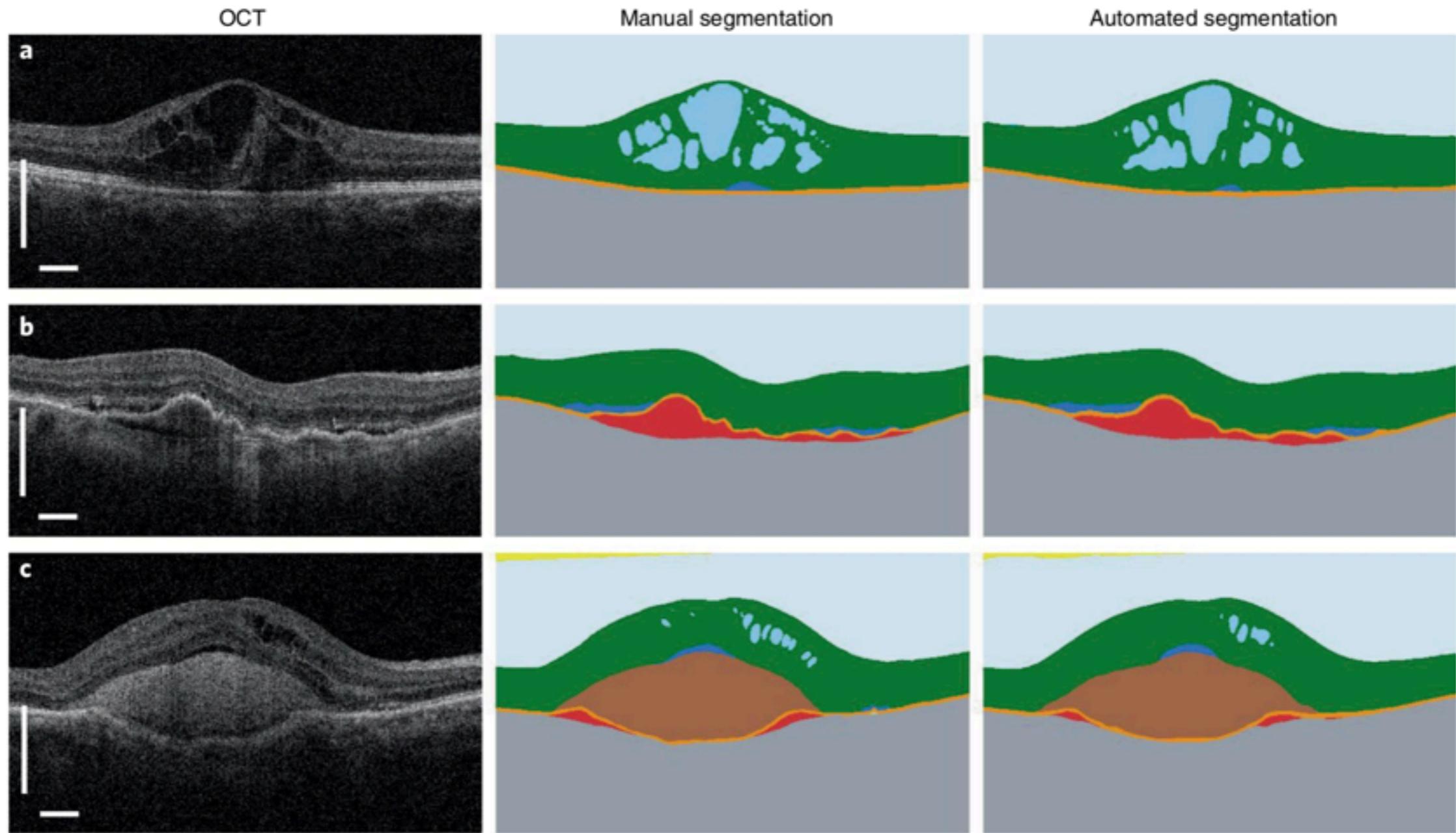
Novel Framework



3D Model



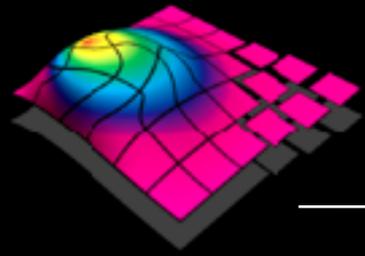
Segmentation Outputs



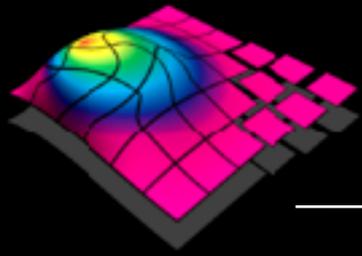
- Vitreous or subhyaloid space
- Posterior hyaloid
- Epiretinal membrane
- Neurosensory retina
- Intraretinal fluid

- Subretinal fluid
- Subretinal hyper reflect. mat.
- Retinal pigment epithelium
- Drusenoid PED
- Serous PED

- Fibrovascular PED
- Choroid and outer layers
- Padding artefact
- Blink artefact
- Foldover artefact

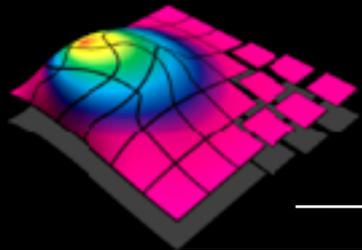


Referral Categories

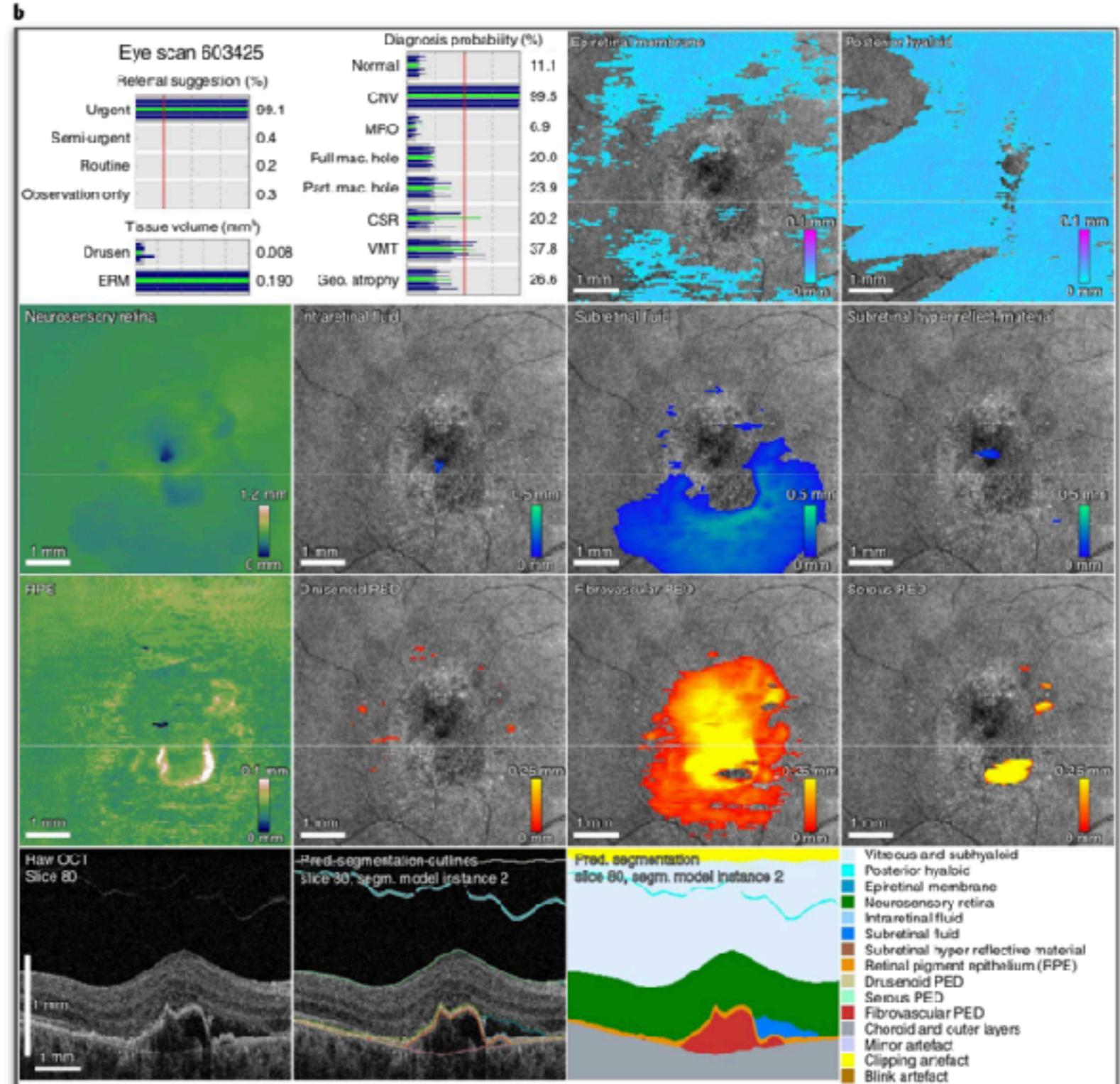
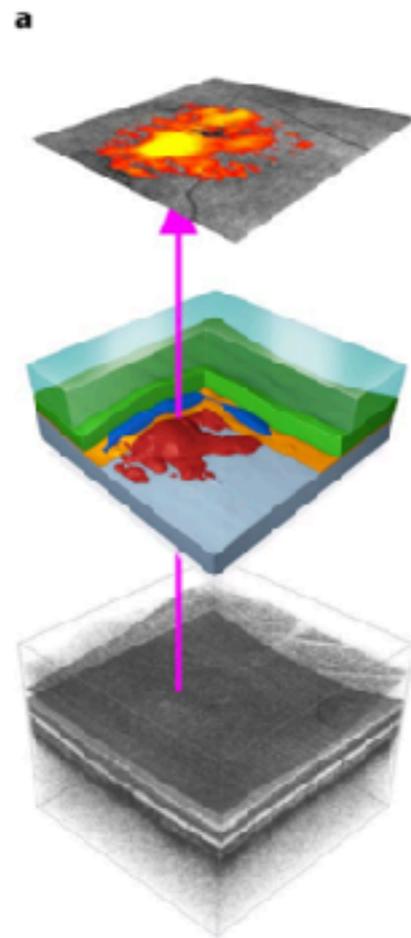


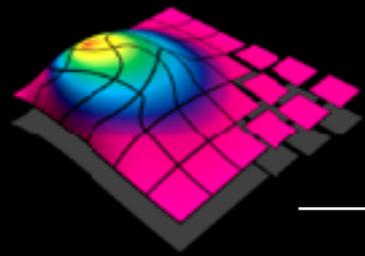
Referral Categories

Referral Category	Definition
Urgent	All causes of choroidal neovascularization, including age related macular degeneration, high myopia, central serous retinopathy, inherited retinal dystrophies (e.g., angioid streaks), posterior uveitis (e.g., multiple choroiditis), and post traumatic choroidal rupture.
Semi-urgent	Referable edema classed as semi-urgent included diabetic maculopathy, retinal vein occlusion, postoperative (Irvine-Gass syndrome), uveitis, Coat's disease, radiation and miscellaneous other cases.
Routine	All other non-urgent cases with a large variety, from uncomplicated central serous retinopathy to more rare conditions such as Macular Telangiectasia (MacTel) type 2.
Observation only	The absence of pathology classes described above.

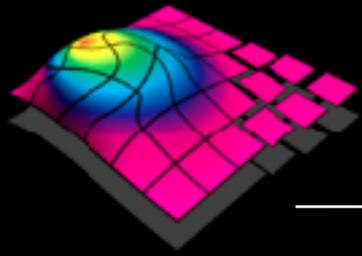


Prototype OCT Viewer

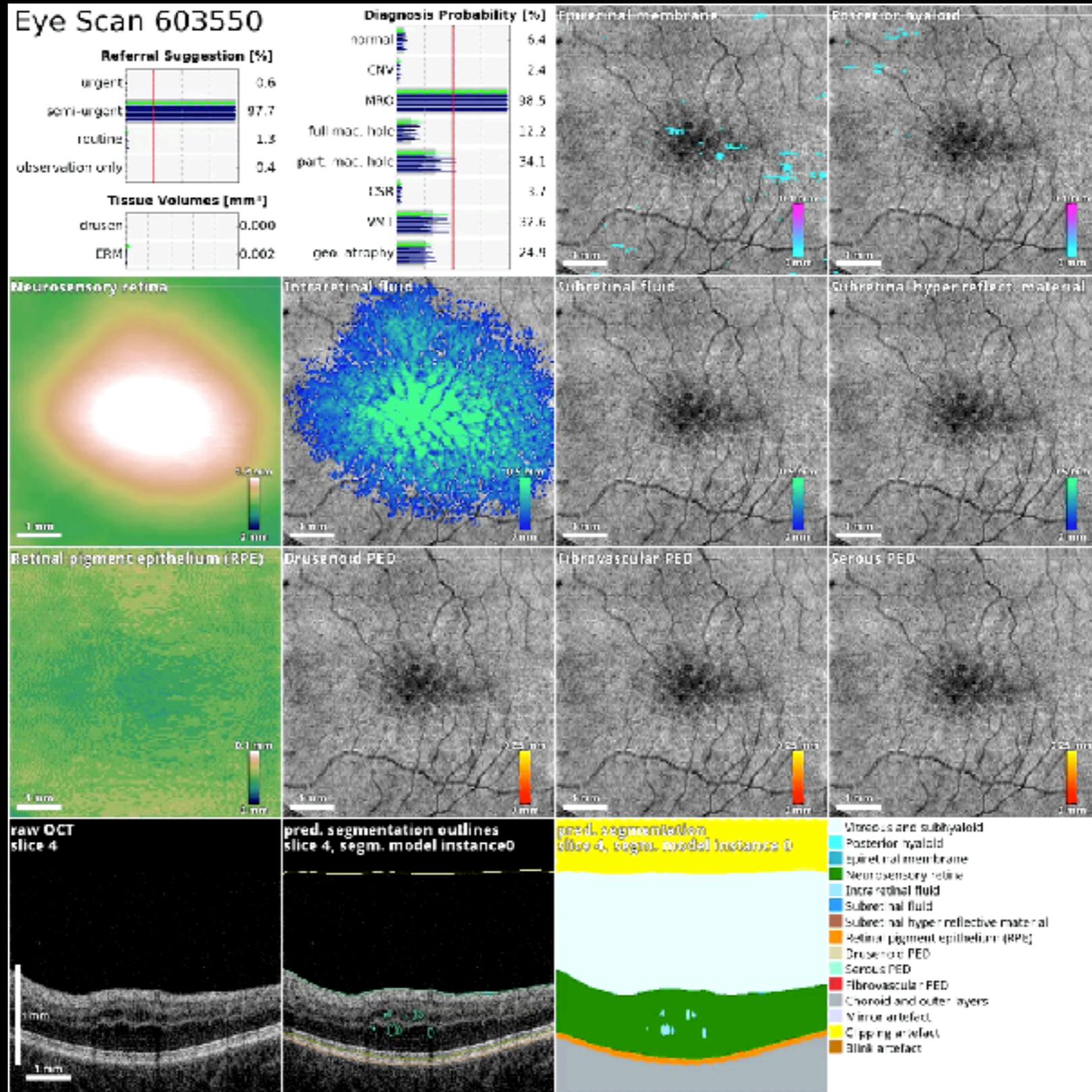


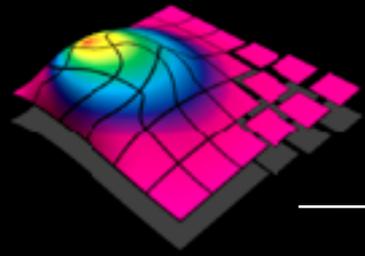


Examples - CMO

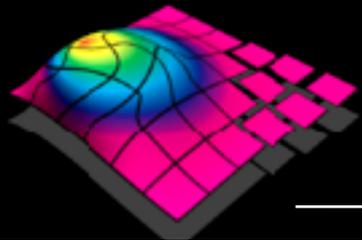


Examples - CMO

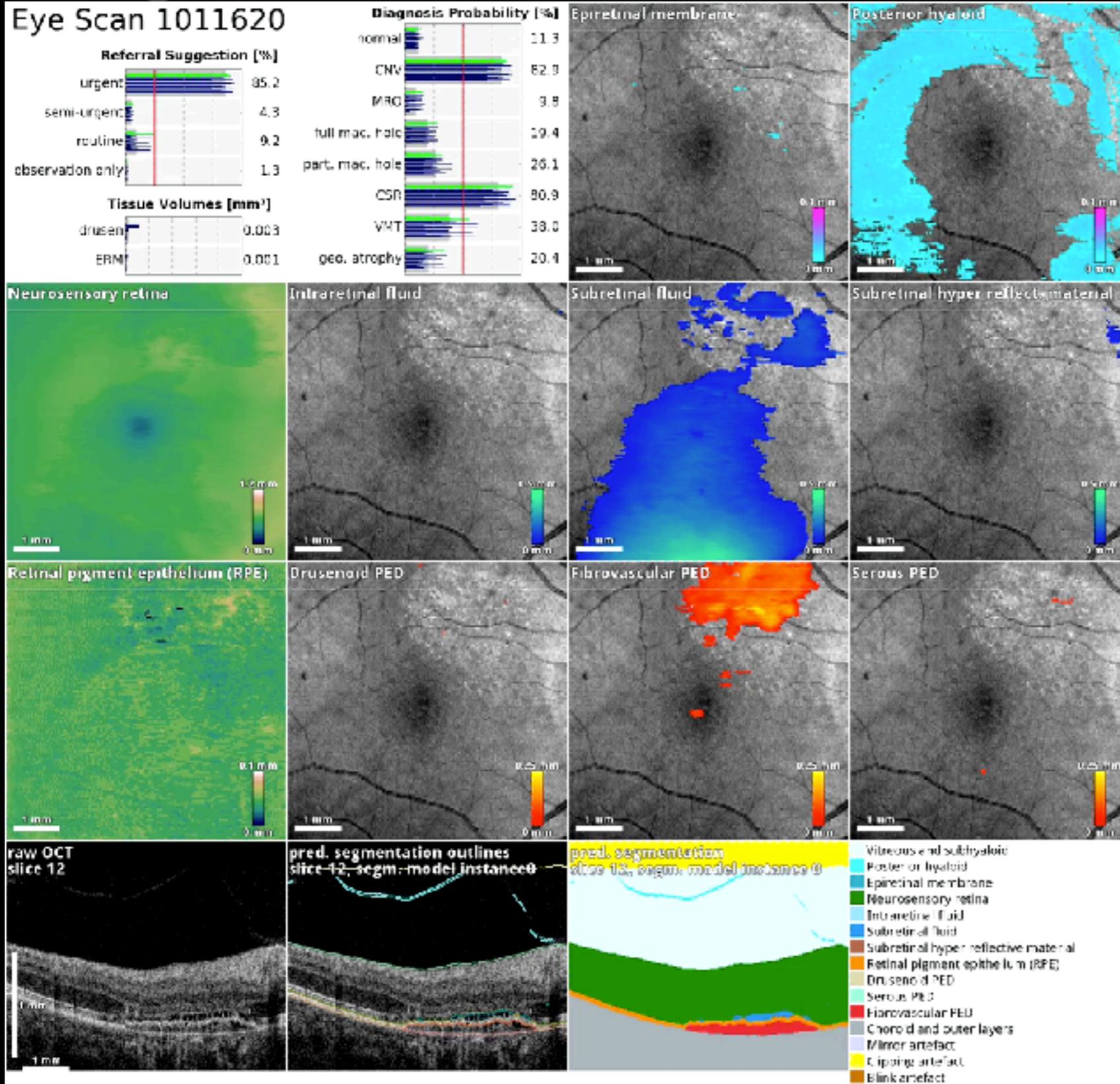


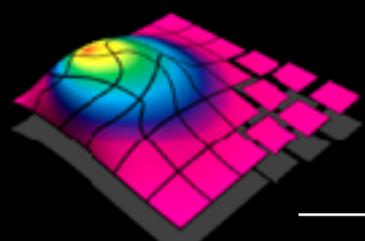


Examples - CSCR/CNV

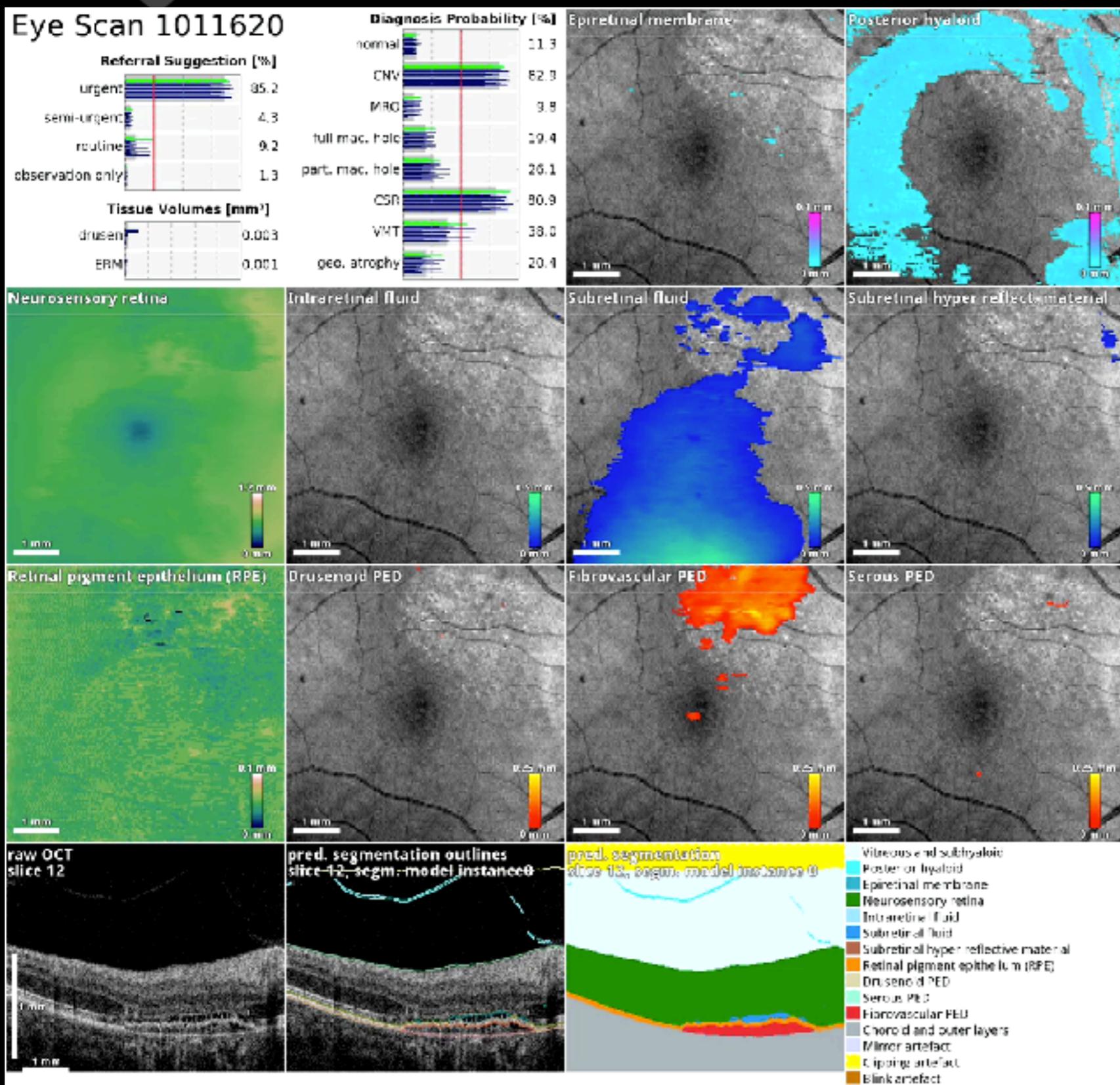


Examples - CSCR/CNV

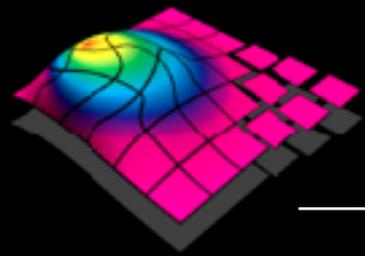




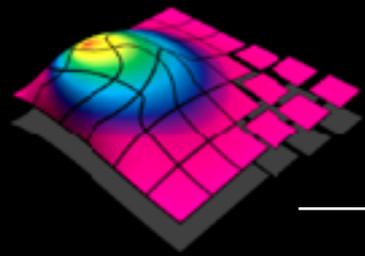
Examples - CSCR/CNV



Multi-class classification

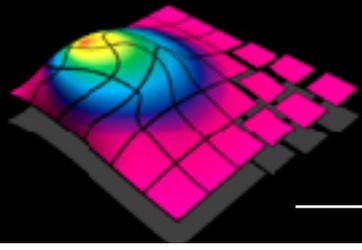


Examples - GA

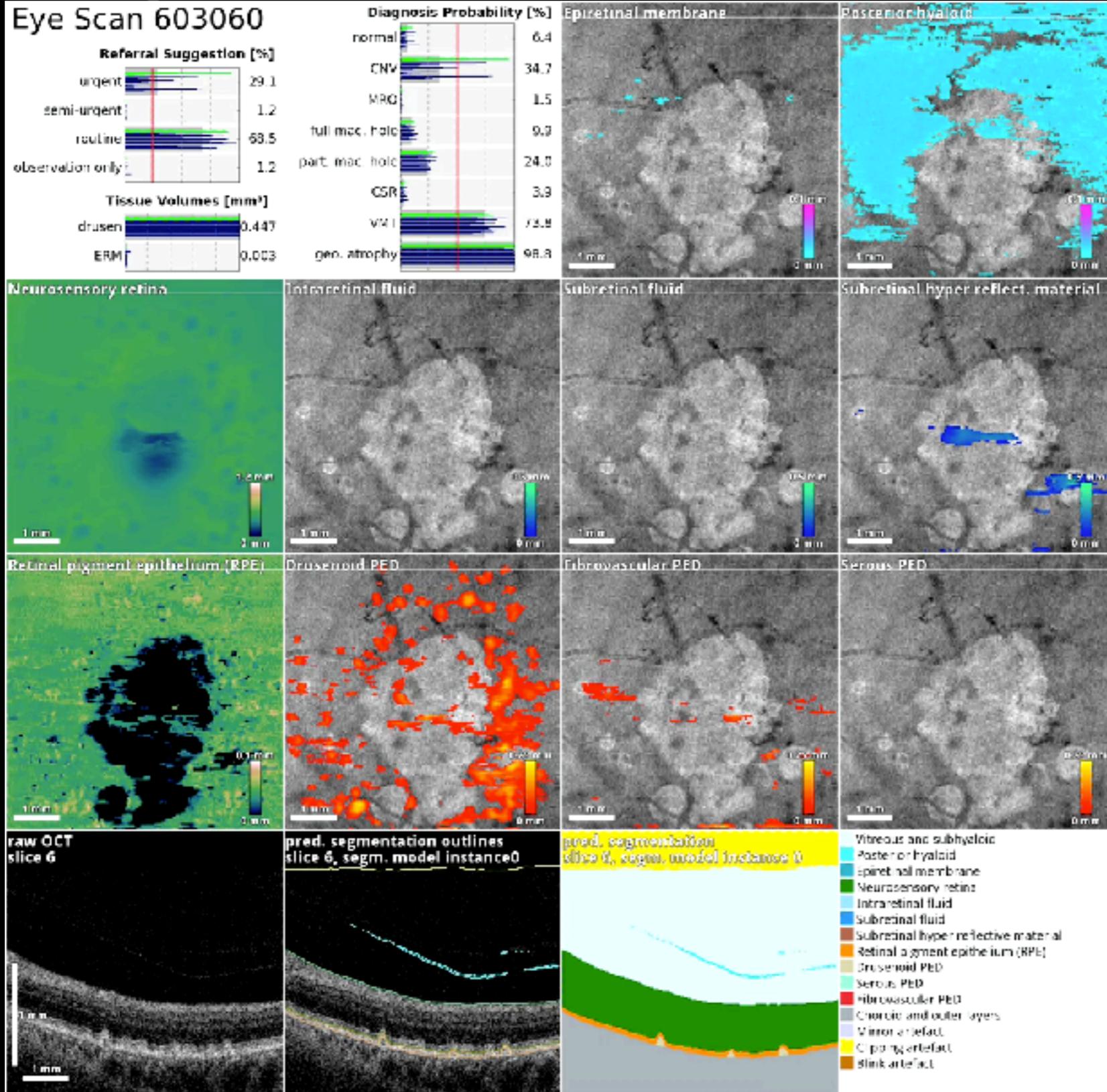


Examples - GA

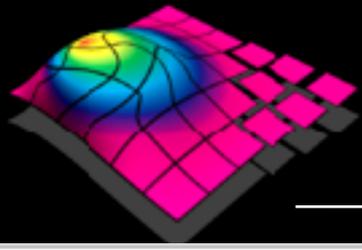
**Ambiguous
Cases**



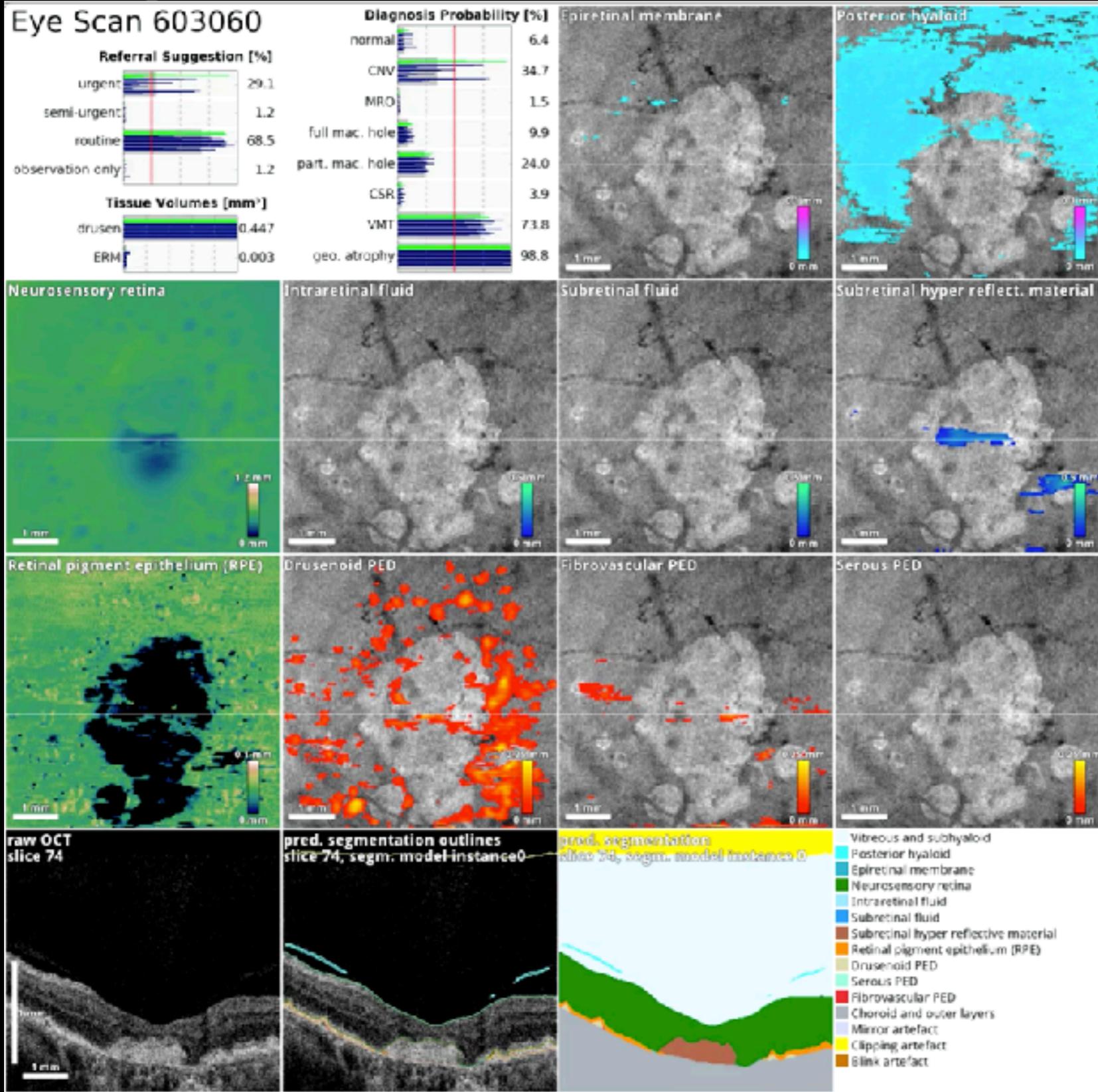
Examples - GA



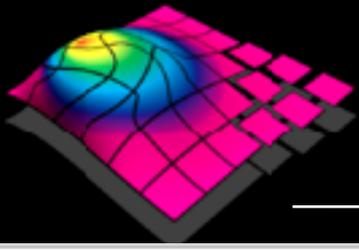
Ambiguous Cases



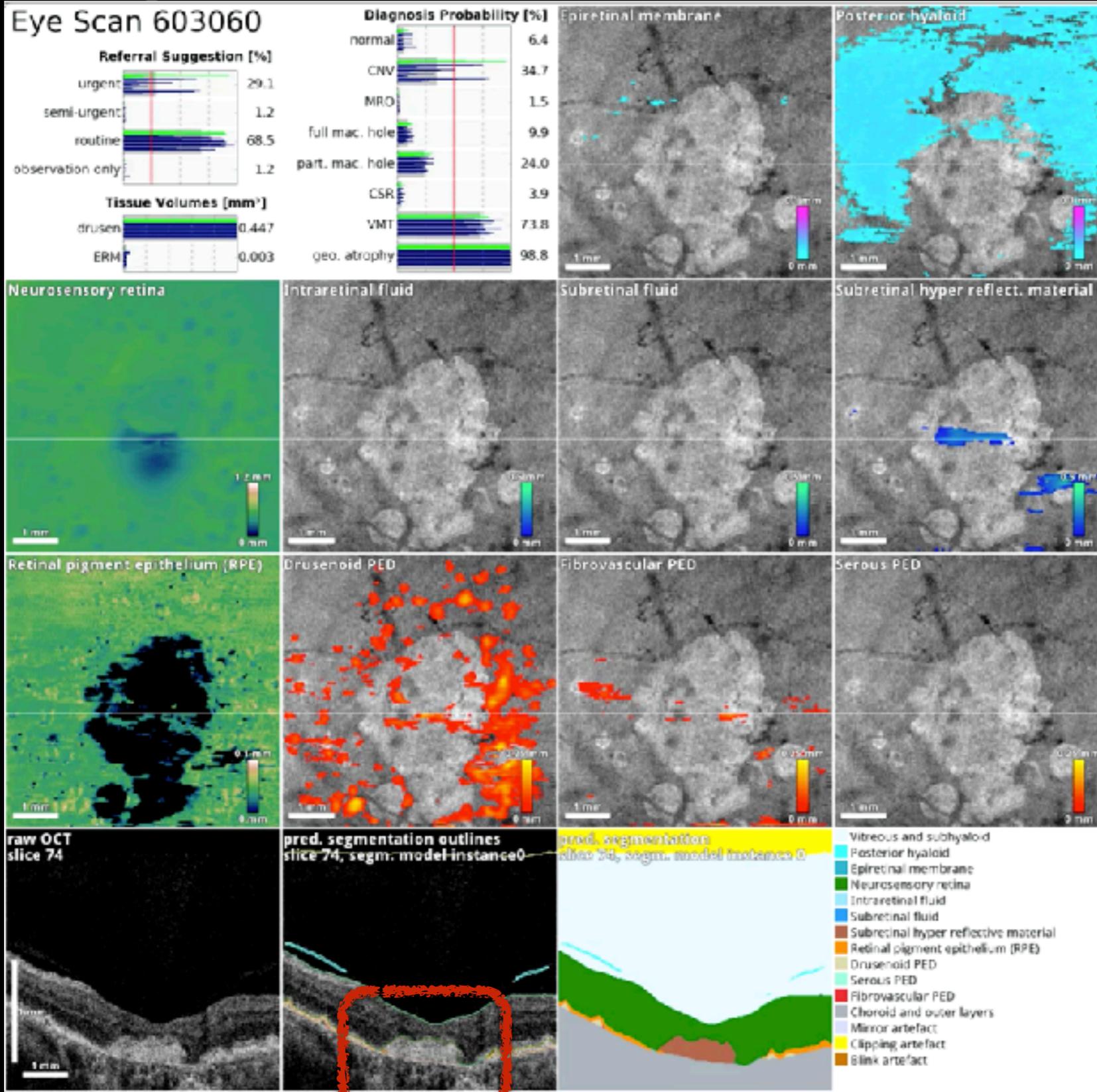
Examples - GA



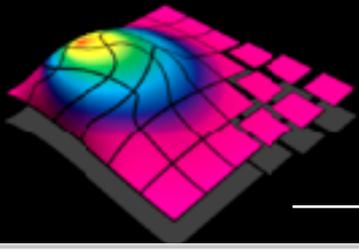
Ambiguous Cases



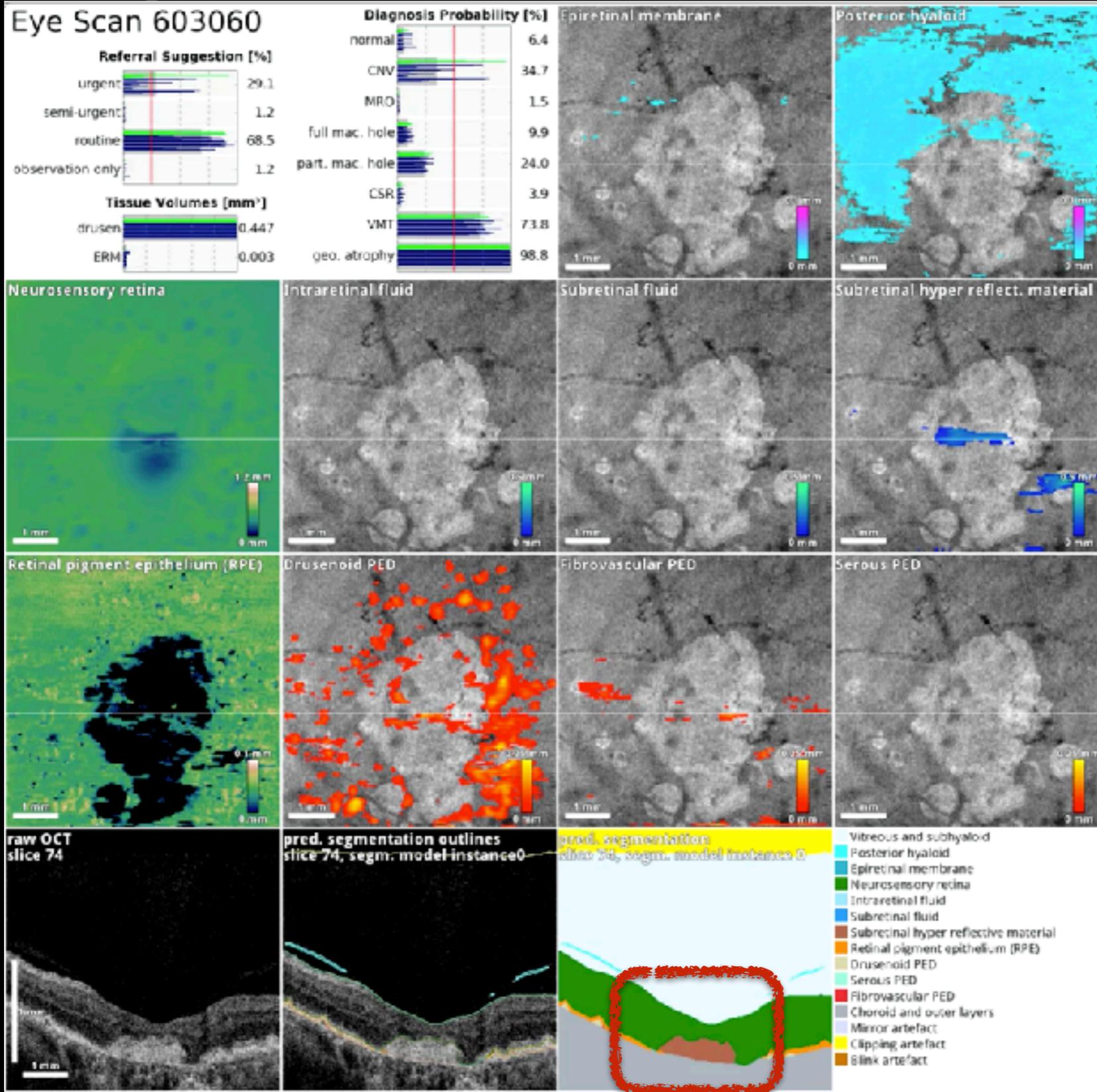
Examples - GA



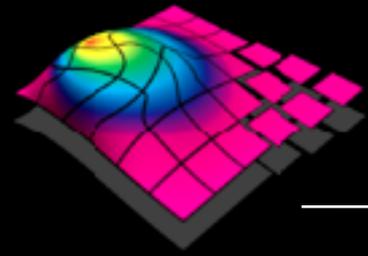
Ambiguous Cases



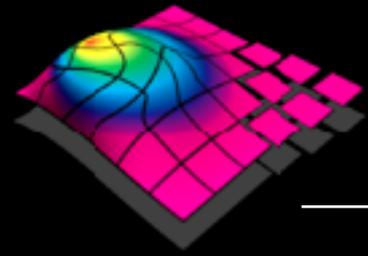
Examples - GA



Ambiguous Cases

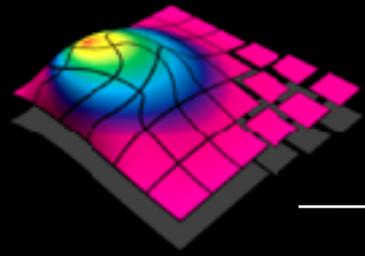


Evaluation of Performance



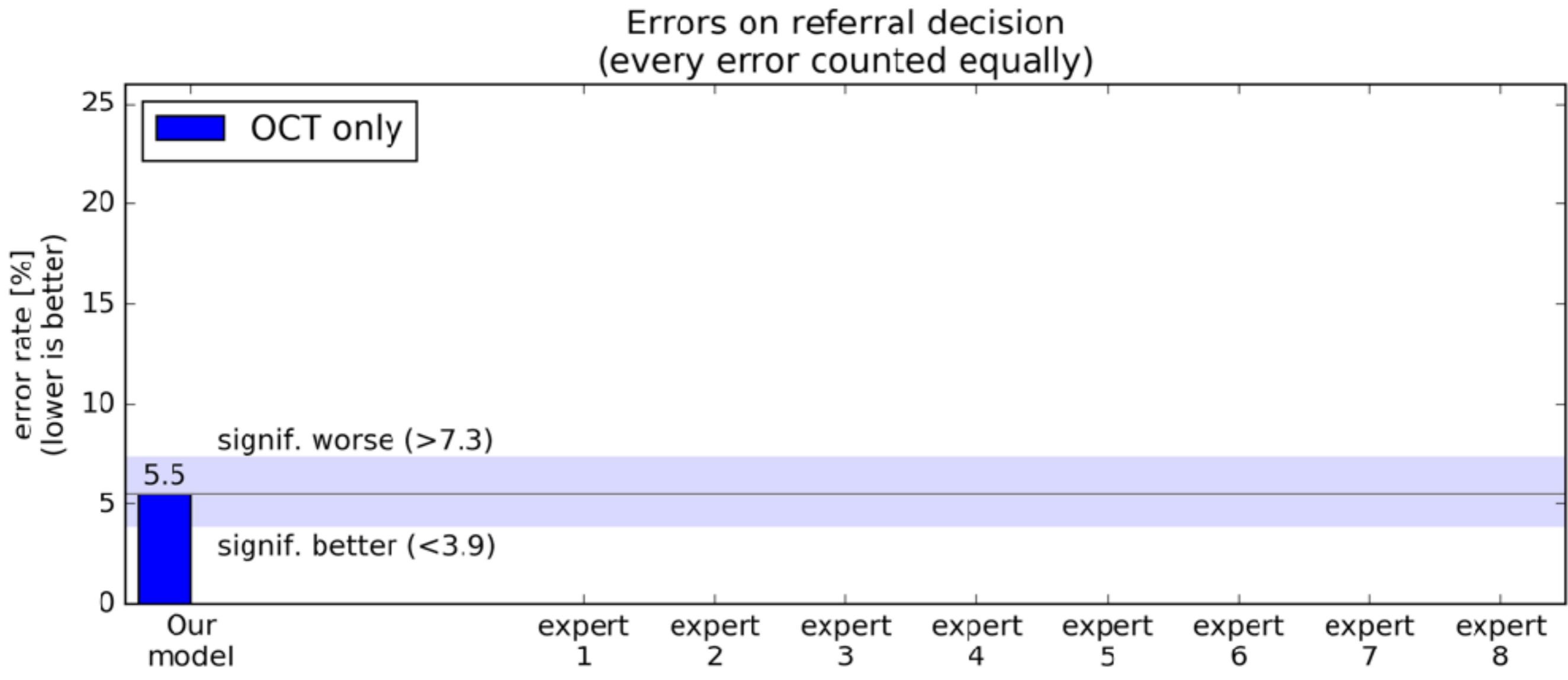
Evaluation of Performance

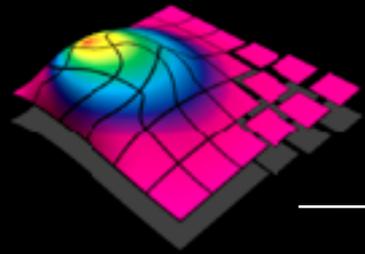
1000 “New” Patients Moorfields



Evaluation of Performance

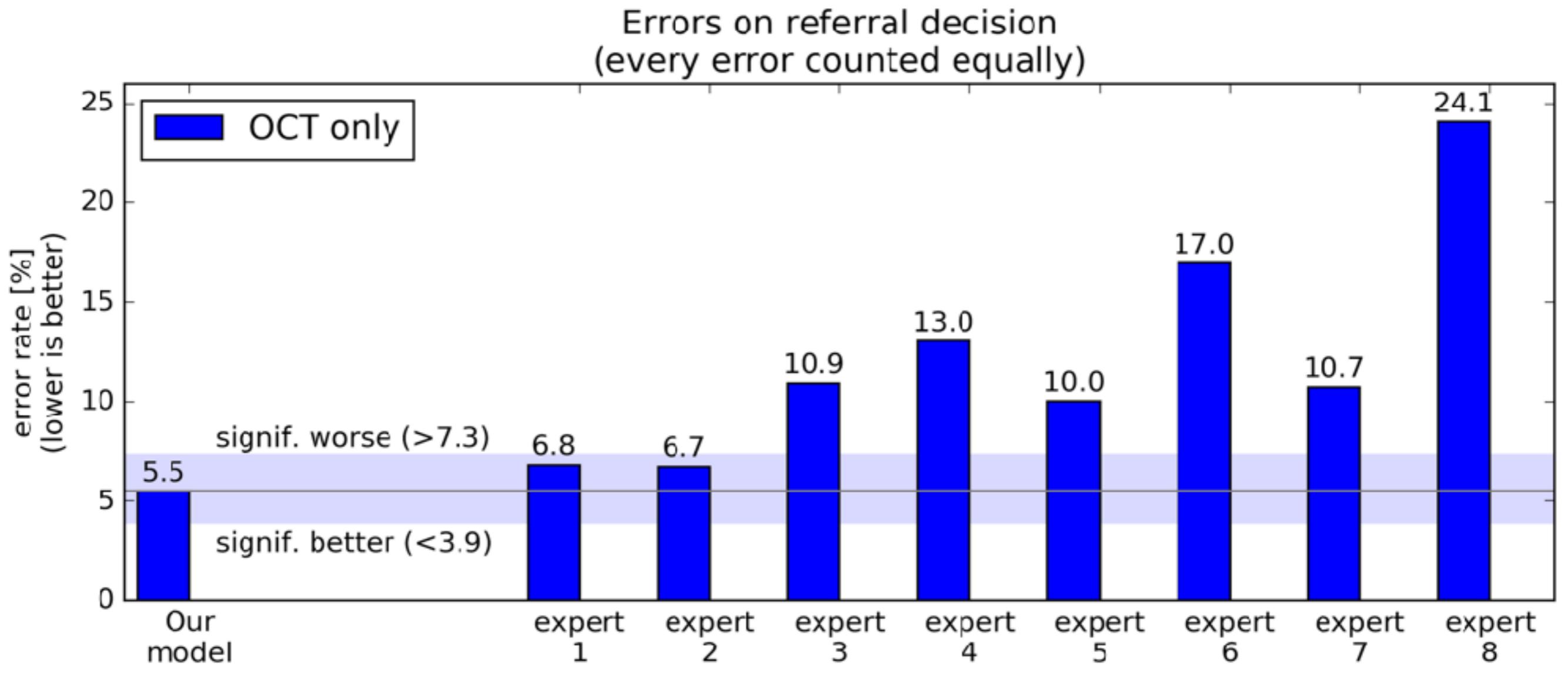
1000 "New" Patients Moorfields

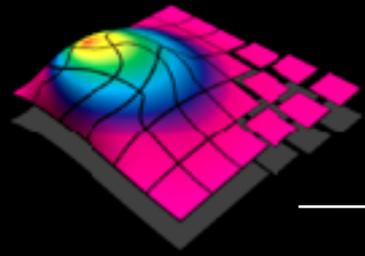




Evaluation of Performance

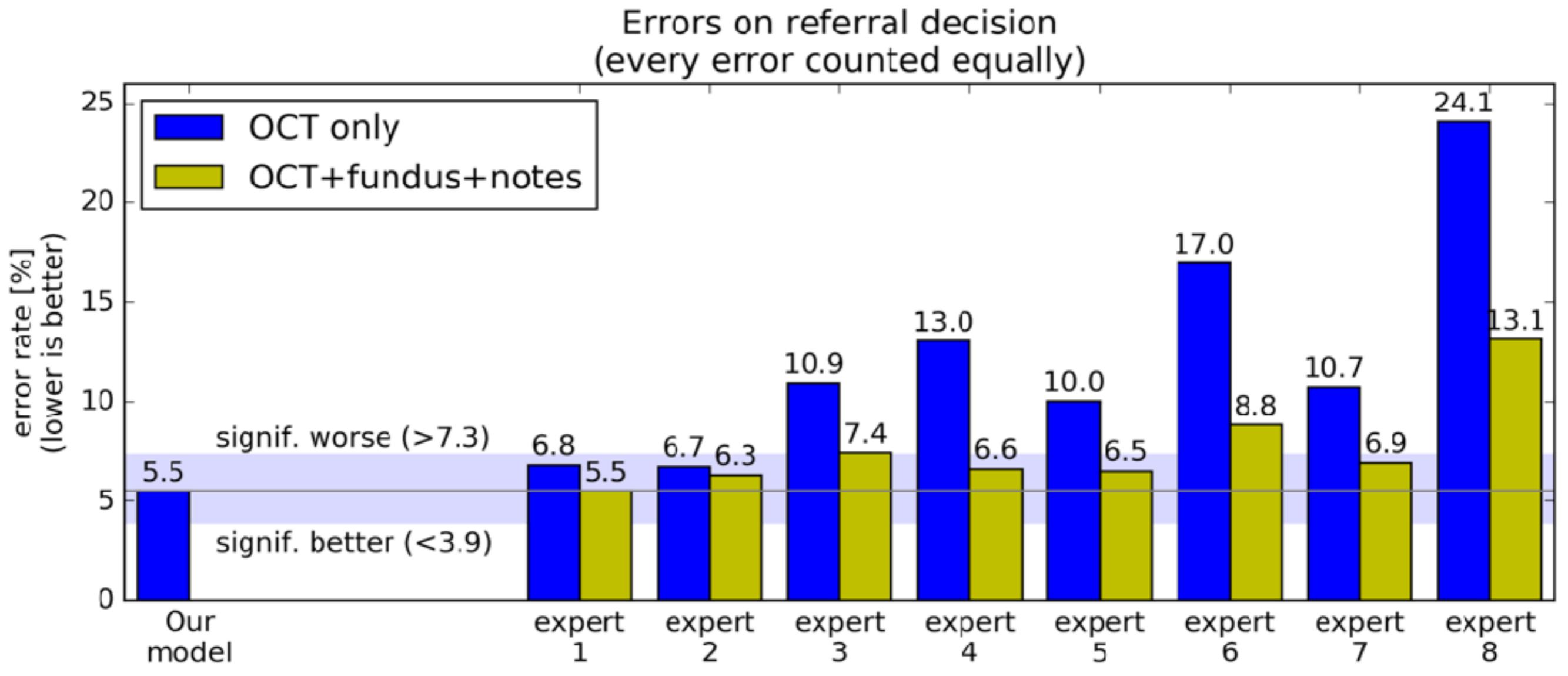
1000 "New" Patients Moorfields

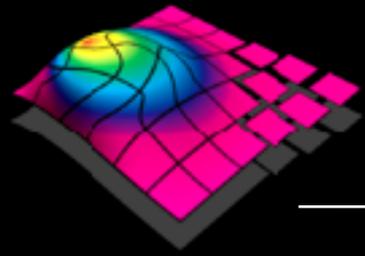




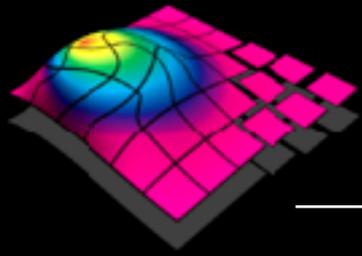
Evaluation of Performance

1000 "New" Patients Moorfields





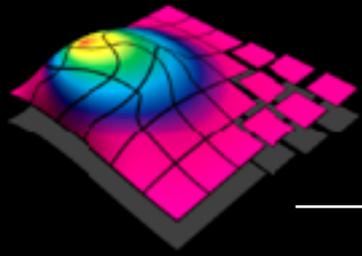
What did it get wrong?



What did it get wrong?

b

		Our model (OCT only)			Retina specialist 1 (OCT + fundus + notes)				Retina specialist 2 (OCT + fundus + notes)				
		Predicted referral			Predicted referral				Predicted referral				
		Urgent	Semi-urgent	Routine	Observation	Urgent	Semi-urgent	Routine	Observation	Urgent	Semi-urgent	Routine	Observation
Gold standard referral	Urgent	234	5	13	0	228	4	20	0	231	8	13	0
	Semi-urgent	3	225	2	0	3	223	4	0	1	226	3	0
	Routine	10	2	250	4	2	7	254	3	11	1	250	4
	Observation	1	1	14	233	1	1	10	237	0	2	20	227



What did it get wrong?

b

Gold standard referral	Our model (OCT only)				Retina specialist 1 (OCT + fundus + notes)				Retina specialist 2 (OCT + fundus + notes)			
	Predicted referral			Observation	Predicted referral			Observation	Predicted referral			Observation
	Urgent	Semi-urgent	Routine		Urgent	Semi-urgent	Routine		Urgent	Semi-urgent	Routine	
Urgent	234	5	13	0	228	4	20	0	231	8	13	0
Semi-urgent	3	225	2	0	3	223	4	0	1	226	3	0
Routine	10	2	250	4	2	7	254	3	11	1	250	4
Observation	1	1	14	233	1	1	10	237	0	2	20	227

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Health

Artificial intelligence 'did not miss a single urgent case'

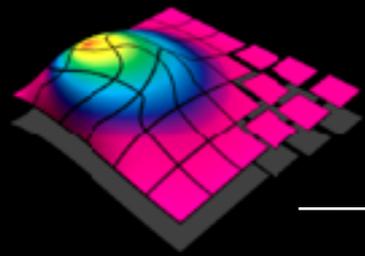
 **Fergus Walsh**
Medical correspondent
@BBCFergusWalsh

13 August 2018

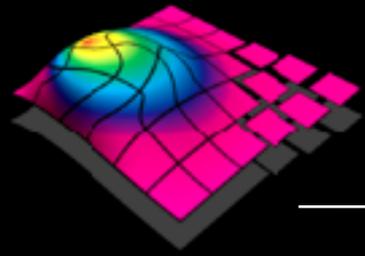
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Elaine Manna had her sight saved at Moorfields Eye hospital in London

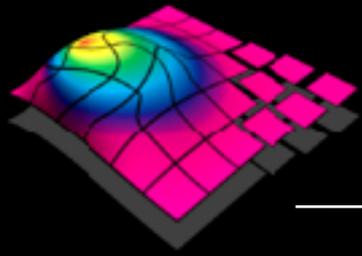


Other OCT Systems?



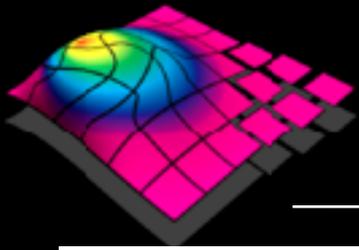
Other OCT Systems?



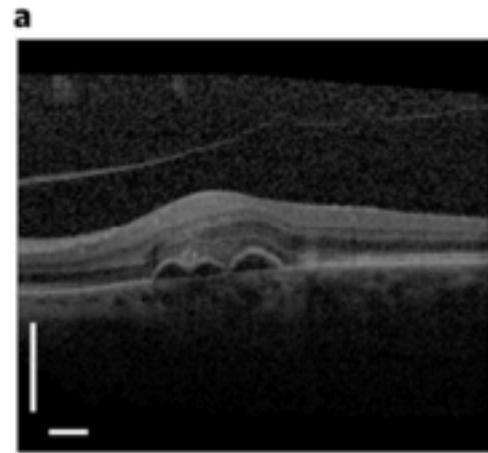


Other OCT Systems?



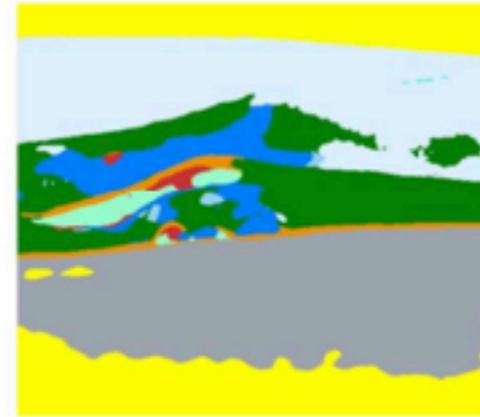


Other OCT Systems?



OCT scan from new device

Original
segmentation
network

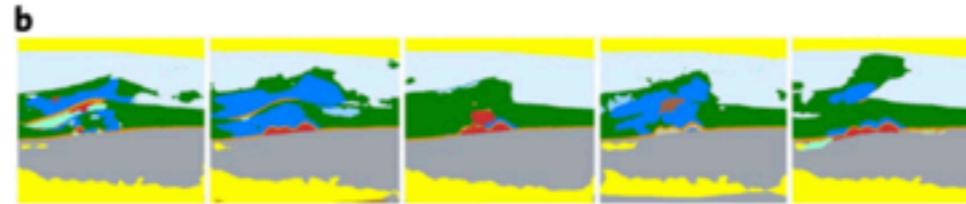


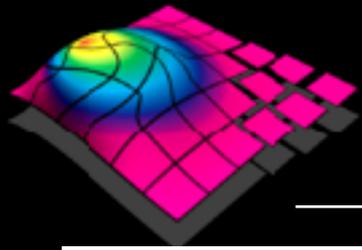
Original
classification
network

Gold standard referral

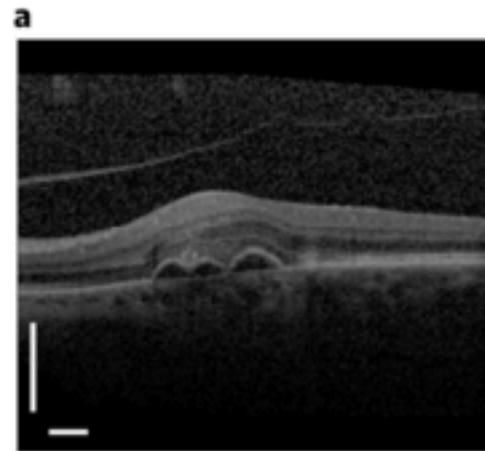
	Predicted referral			Observation
	Urgent	Semi-urgent	Routine	
Urgent	10	3	21	0
Semi-urgent	1	19	8	0
Routine	0	2	33	0
Observation	0	0	19	0

Total error rate: 46.6%



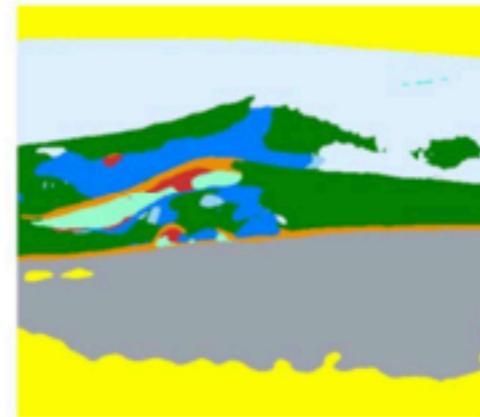


Other OCT Systems?



OCT scan from new device

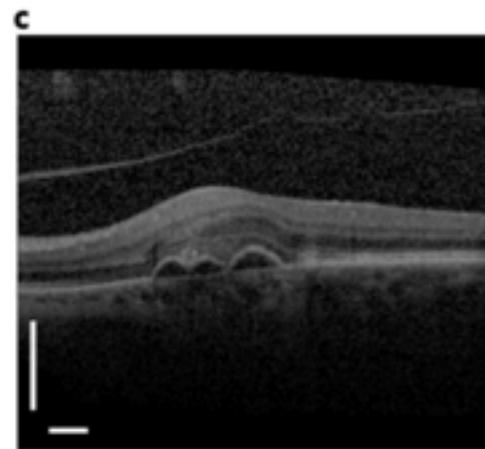
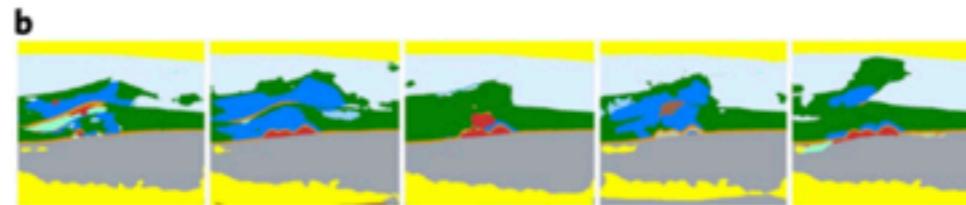
Original
segmentation
network



Original
classification
network

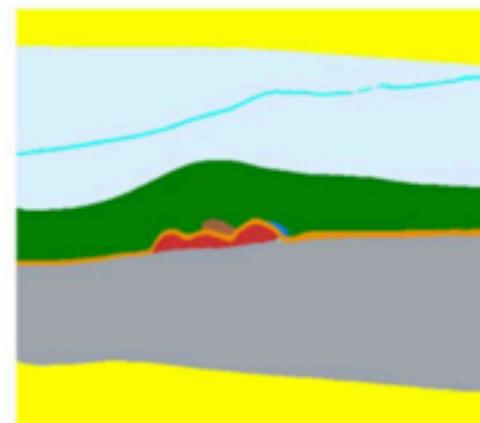
	Predicted referral			Observation
	Urgent	Semi-urgent	Routine	
Urgent	10	3	21	0
Semi-urgent	1	19	8	0
Routine	0	2	33	0
Observation	0	0	19	0

Total error rate: 46.6%



OCT scan from new device

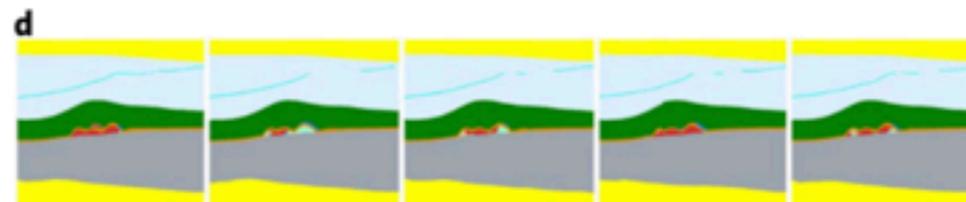
Retrained
segmentation
network

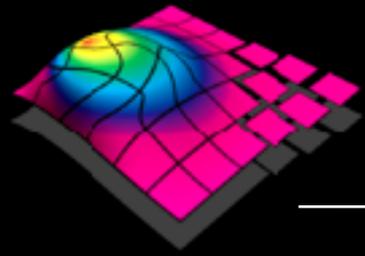


Original
classification
network

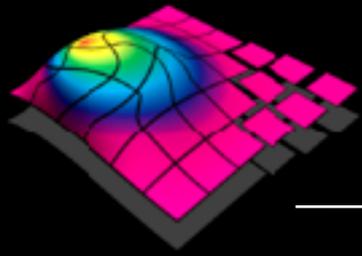
	Predicted referral			Observation
	Urgent	Semi-urgent	Routine	
Urgent	33	0	1	0
Semi-urgent	1	27	0	0
Routine	0	0	35	0
Observation	0	0	2	17

Total error rate: 3.4%

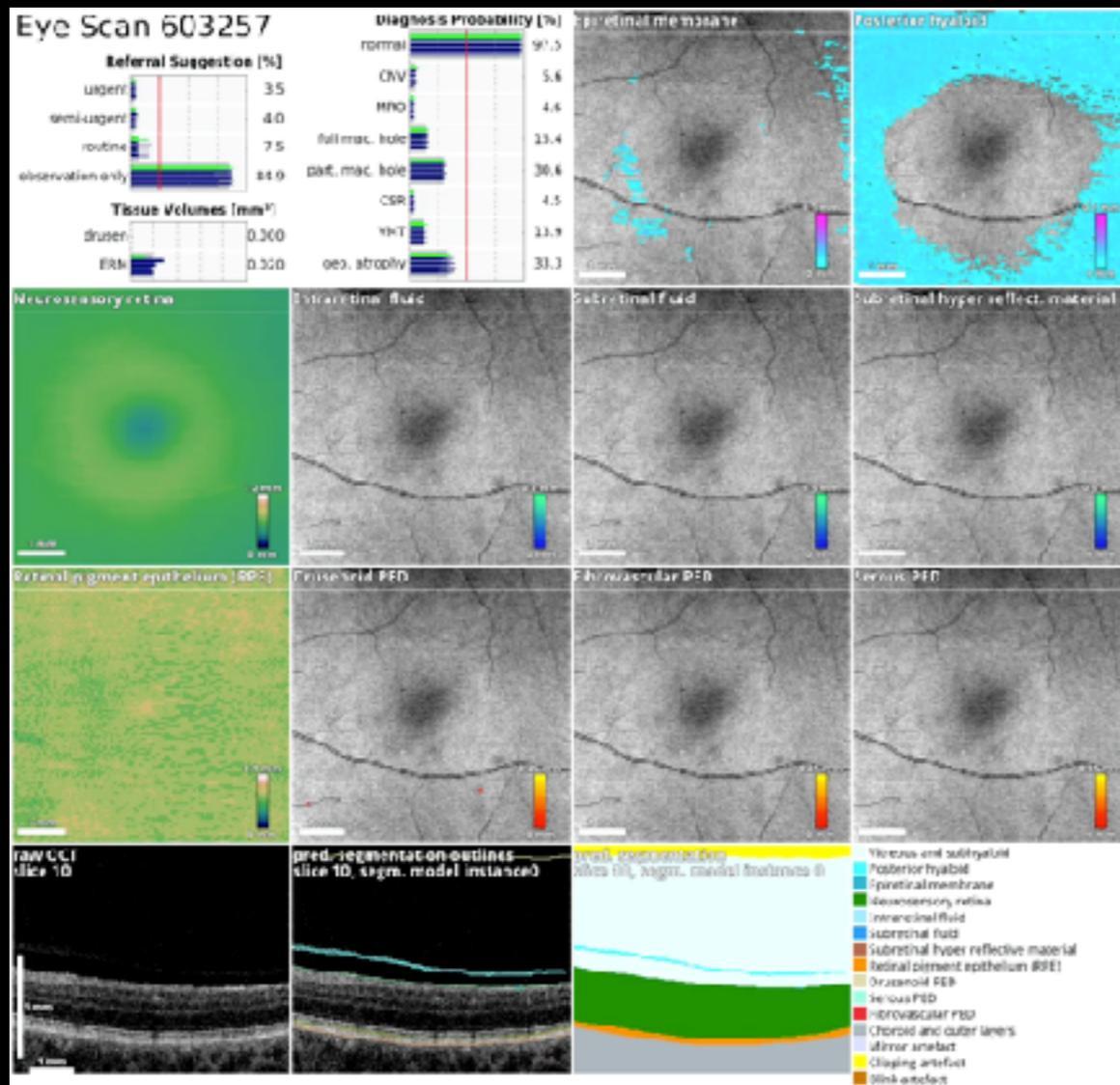


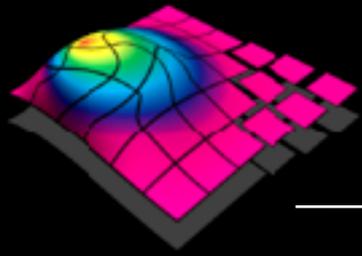


Medical Education?

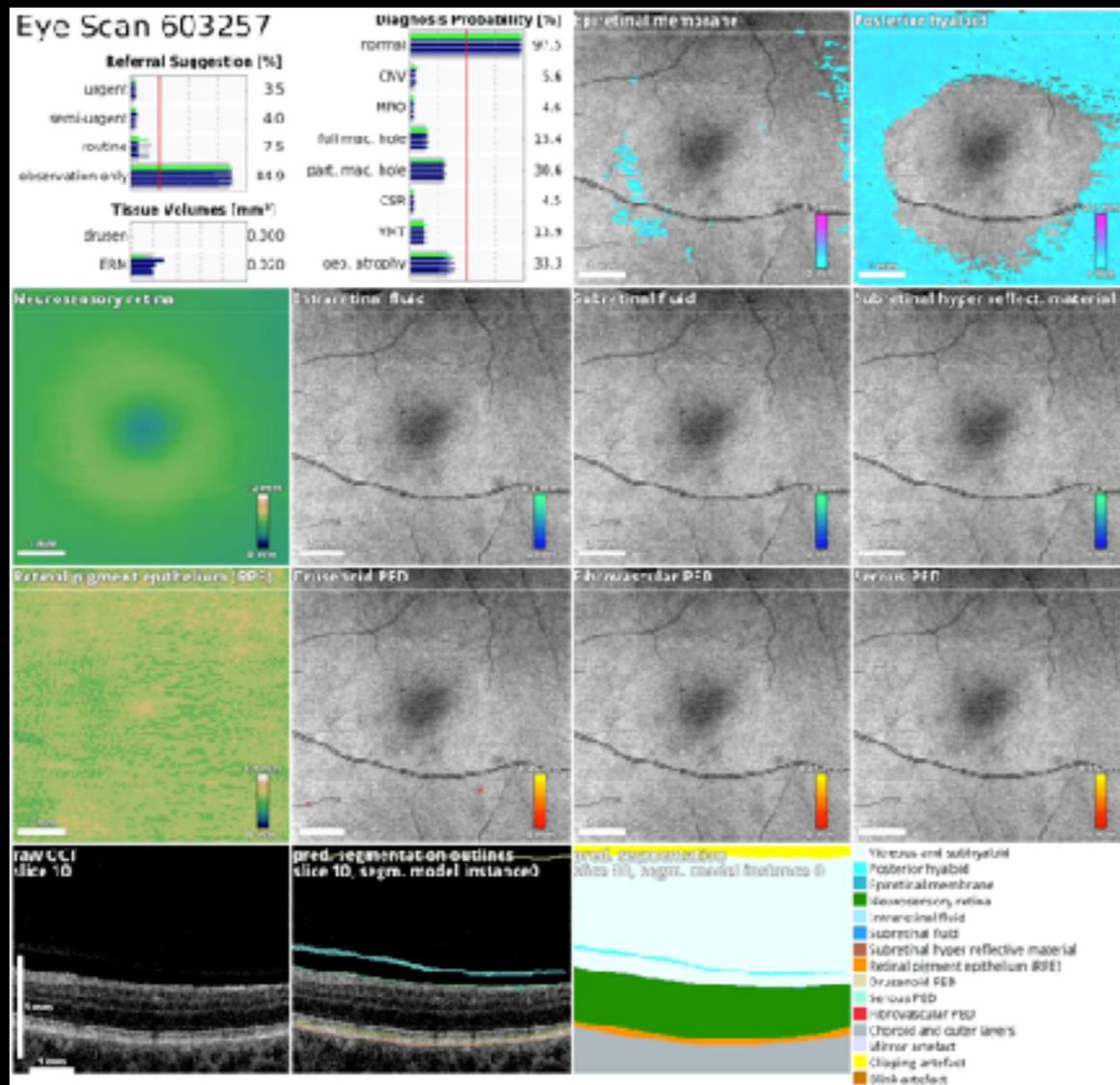


Medical Education?





Medical Education?



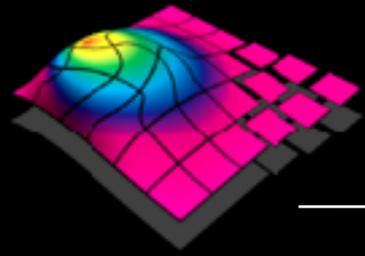
DEEP THINKING

Where Artificial Intelligence Ends... ...And Human Creativity Begins

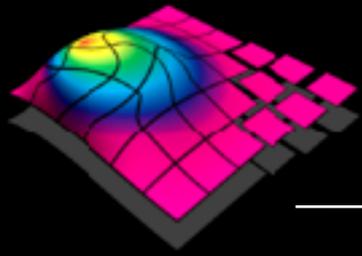
GARRY KASPAROV

'An absorbing page-turning thriller... not just a tale of human vs. machine, this is also a story about one man vs. The Man'

Observer

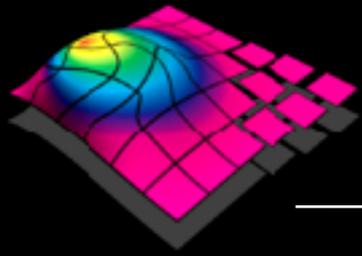


Next Steps?



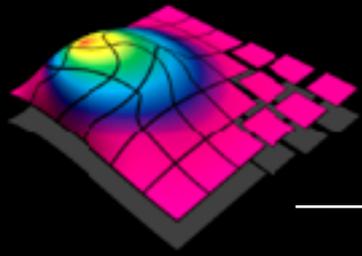
Next Steps?

1. Prospective clinical trials



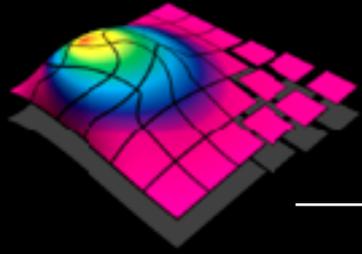
Next Steps?

- 1. Prospective clinical trials**
- 2. AI-assisted Science**



Next Steps?

- 1. Prospective clinical trials**
- 2. AI-assisted Science**
- 3. Reinventing the Eye Exam!**



Next Steps?

1. Prospective clinical trials
2. AI-assisted Science
3. Reinventing the Eye Exam!

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