IRAN UNIVERSITY OF MEDICAL SCIENCES

A Deep Dive Into The Ocean Of Artificial Intelligence

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Iran University of Medical Sciences

Outline

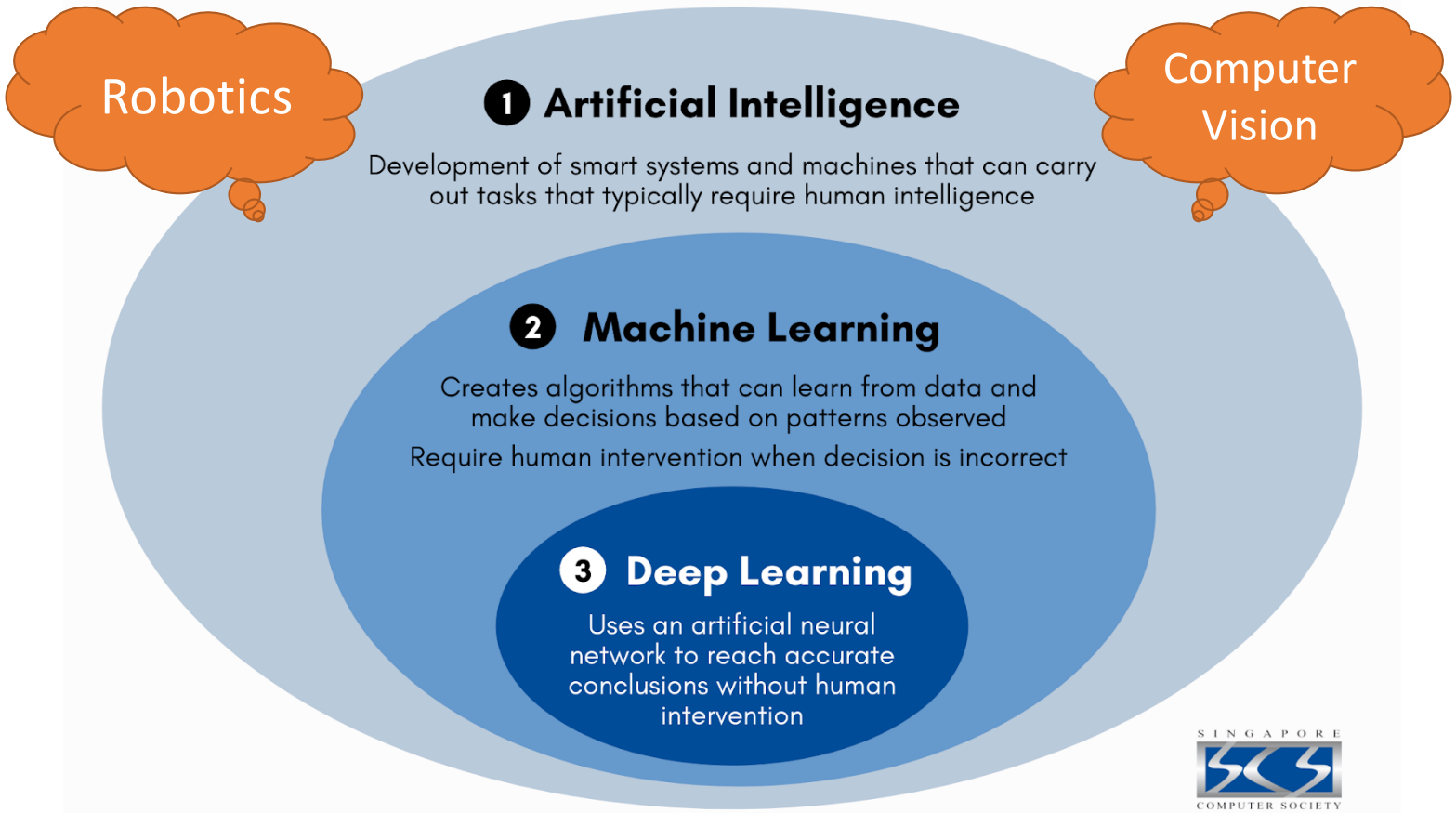
- Definition and Basic Principles of Artificial Intelligence (AI)
- AI in Ophthalmology
- Large Language Models
- Limitations and Challenges
- WHO Guidelines

Artificial Intelligence

- John McCarthy

- “a system which is to evolve intelligence of human order.”

ARTIFICIAL INTELLIGENCE VS MACHINE LEARNING VS DEEP LEARNING



SINGAPORE COMPUTER SOCIETY

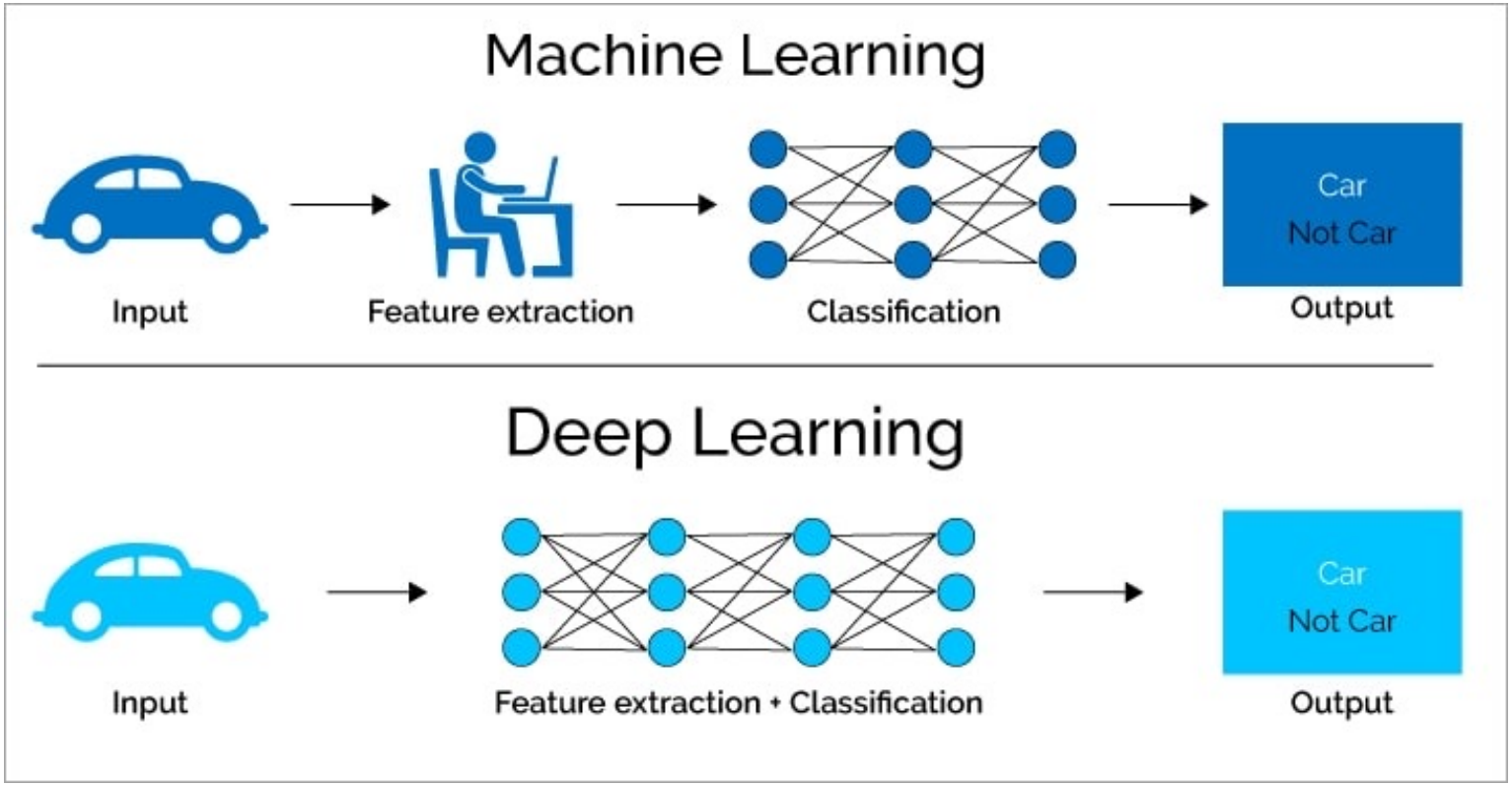
General Principles of AI

Nonlearning versus Learning Systems

- Nonlearning
  - Algorithms react in a predefined way in particular situation

- Learning
  - The algorithms change while processing
  - Neural networks that mimic the human brain
    - Deep learning
  - Alternative architectures

Deep Learning vs. Machine Learning



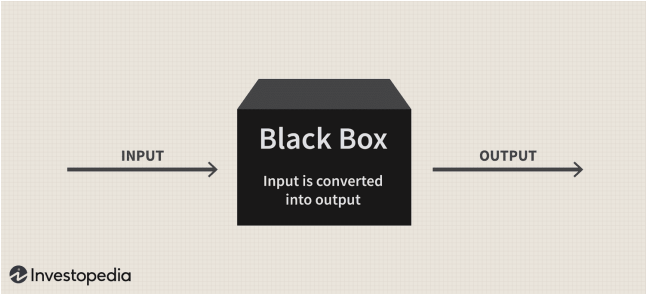
Deep Learning

- Subclass of Machine Learning
  - Using artificial neural networks (ANN)
  - Frank Rosenblatt in 1950s

- ANNs can be composed of many layers
  - The adjective deep
  - First layer: Input
  - Last layer: Output
  - Layers in-between: Hidden layers

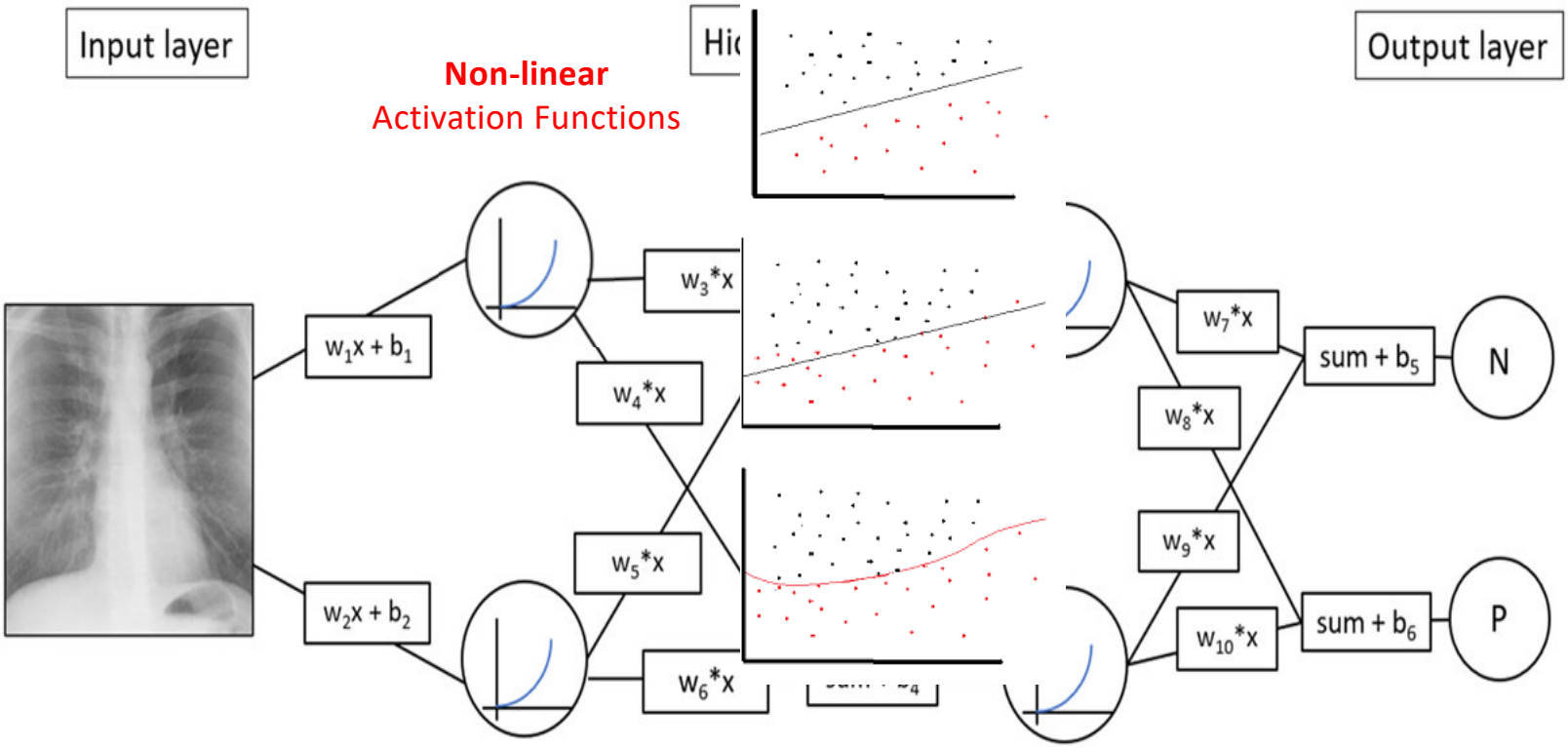
Mystification of Artificial Intelligence

- Black box AI

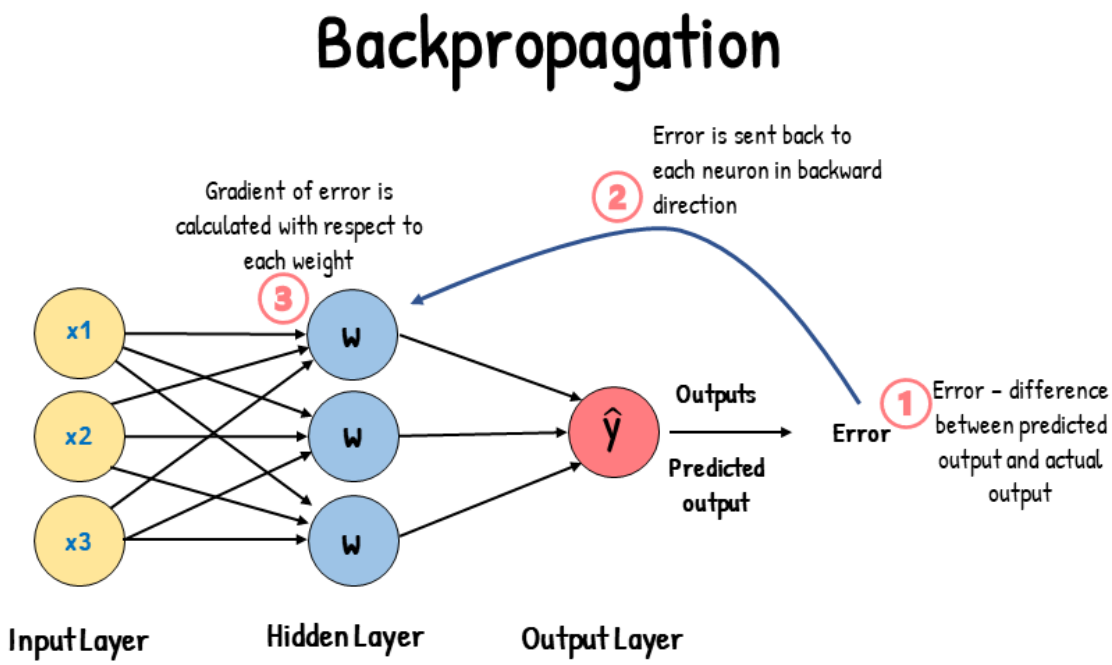


- Many AI models can be traced back to simple mathematical models
  - Large quantity of operations and data
- Large computing capacities, big data, and mathematical algorithms
  - Recognizing patterns in a way that was impossible before

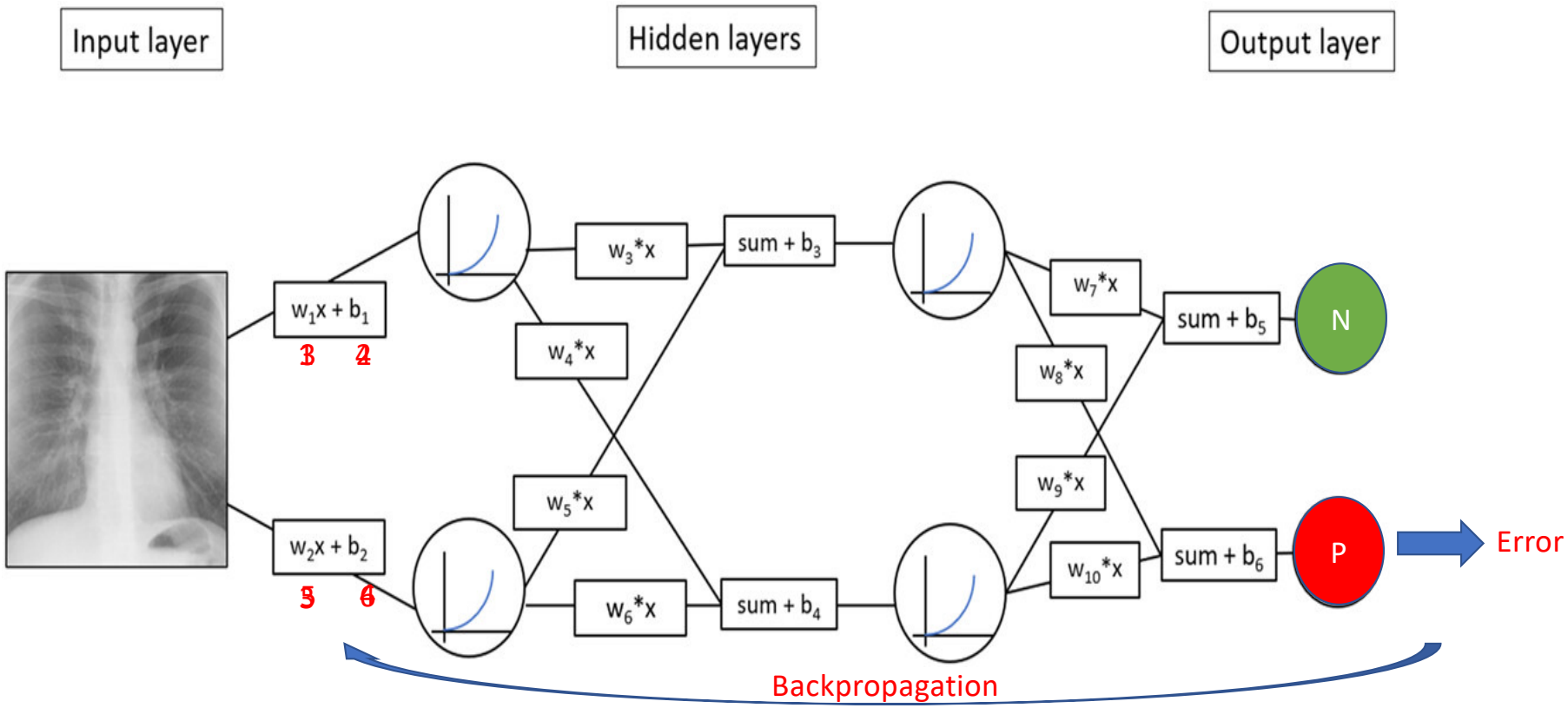
Artificial Neural Networks



Backpropagation in Training Phase

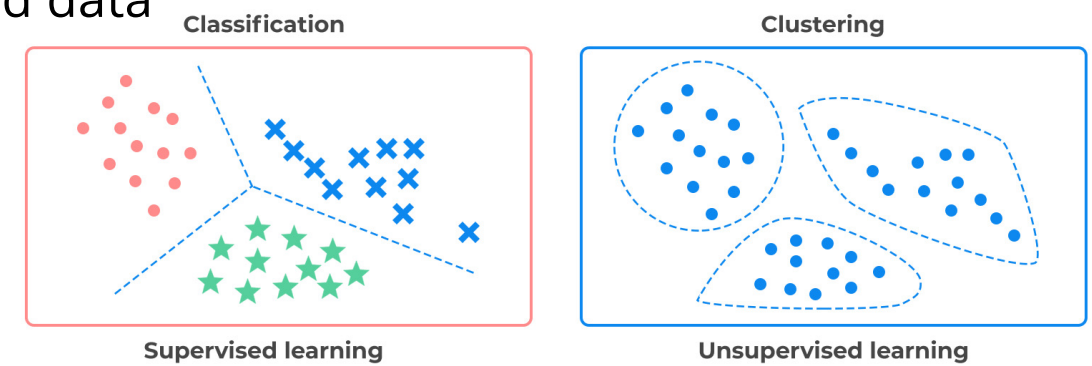


Training

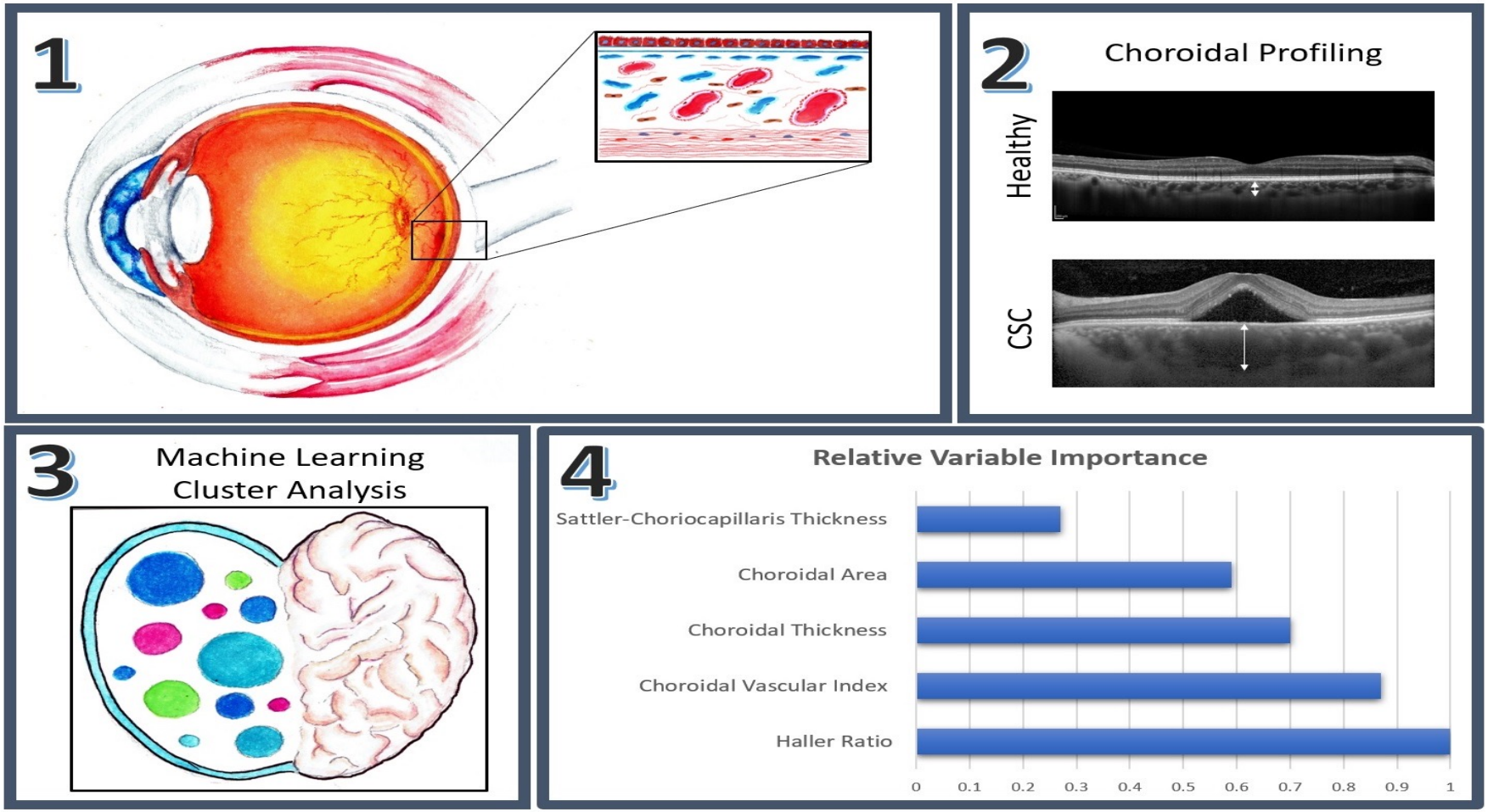

Input layer
Hidden layers
Output layer
$w_1x + b_1$
$w_2x + b_2$
w_3*x
w_4*x
w_5*x
w_6*x
sum + b_3
sum + b_4
w_7*x
w_8*x
w_9*x
$w_{10}*x$
sum + b_5
sum + b_6
N
P
Error
Backpropagation

Supervised vs. Unsupervised Learning

- Supervised learning
  - Training with clearly classified data



- Unsupervised learning
  - Detecting unknown patterns in unlabeled data without human help



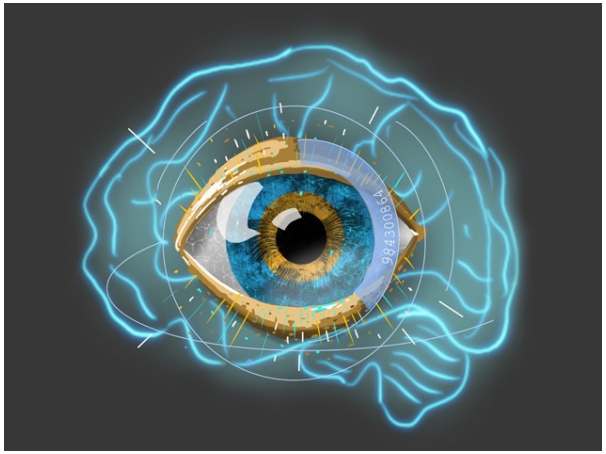
Mirshahi R, Naseripour M, Shojaei A, Heirani M, Alemzadeh SA, Moodi F, Anvari P, Falavarjani KG. Differentiating a pachychoroid and healthy choroid using an unsupervised machine learning approach. Scientific Reports. 2022 Sep 29;12(1):16323.

Discriminative vs. Generative AI

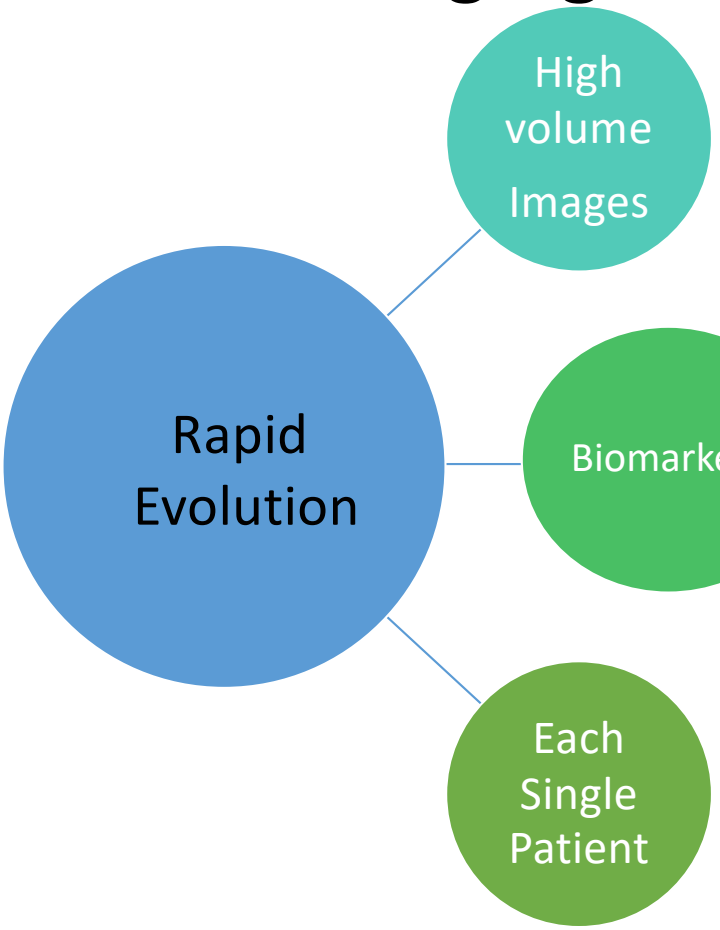
- Discriminative algorithms
  - Divide a data set into groups that share common properties
    - Normal x-ray vs. Malignancy

- Generative algorithms
  - Generate new and original content like pictures and text
    - ChatGPT
    - Data augmentation

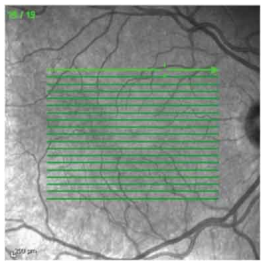
Artificial Intelligence and Ophthalmology



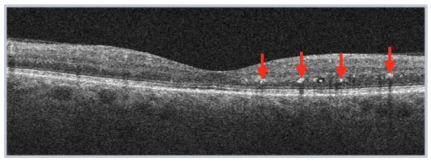
Ophthalmic Imaging Imaging



- 250-512 bscans/OCT

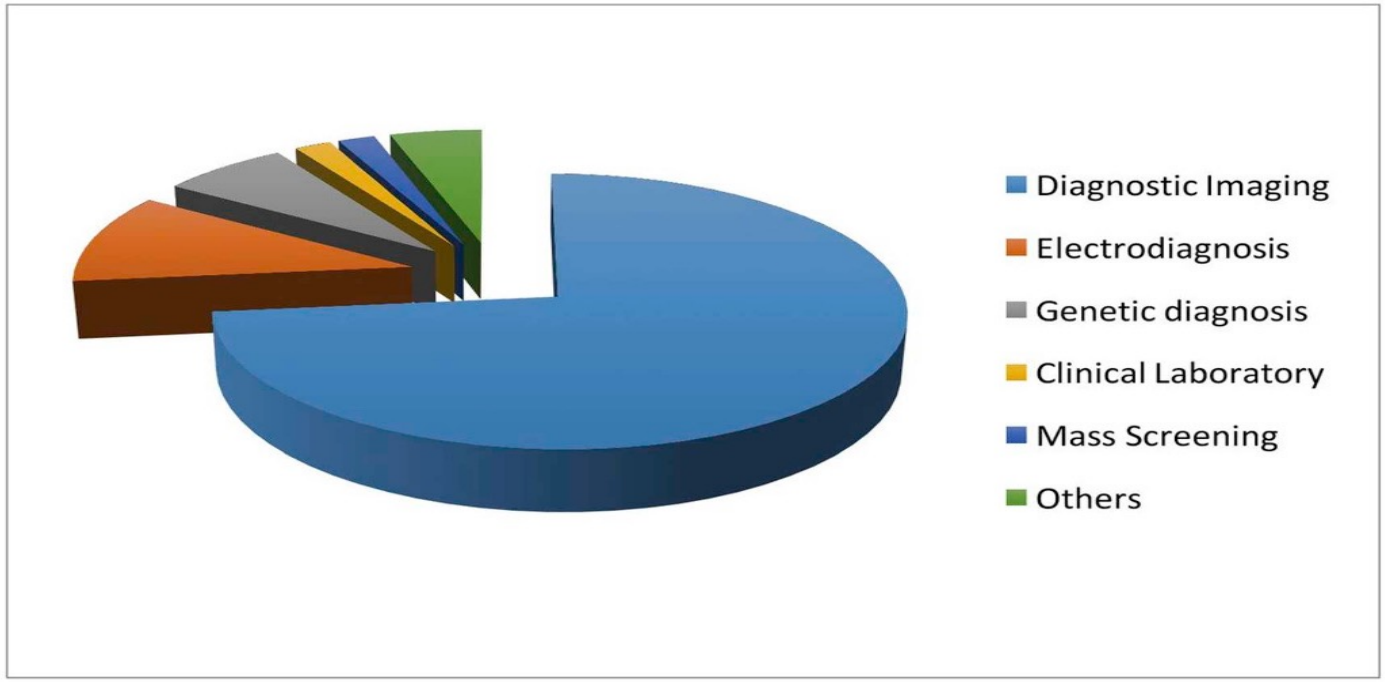


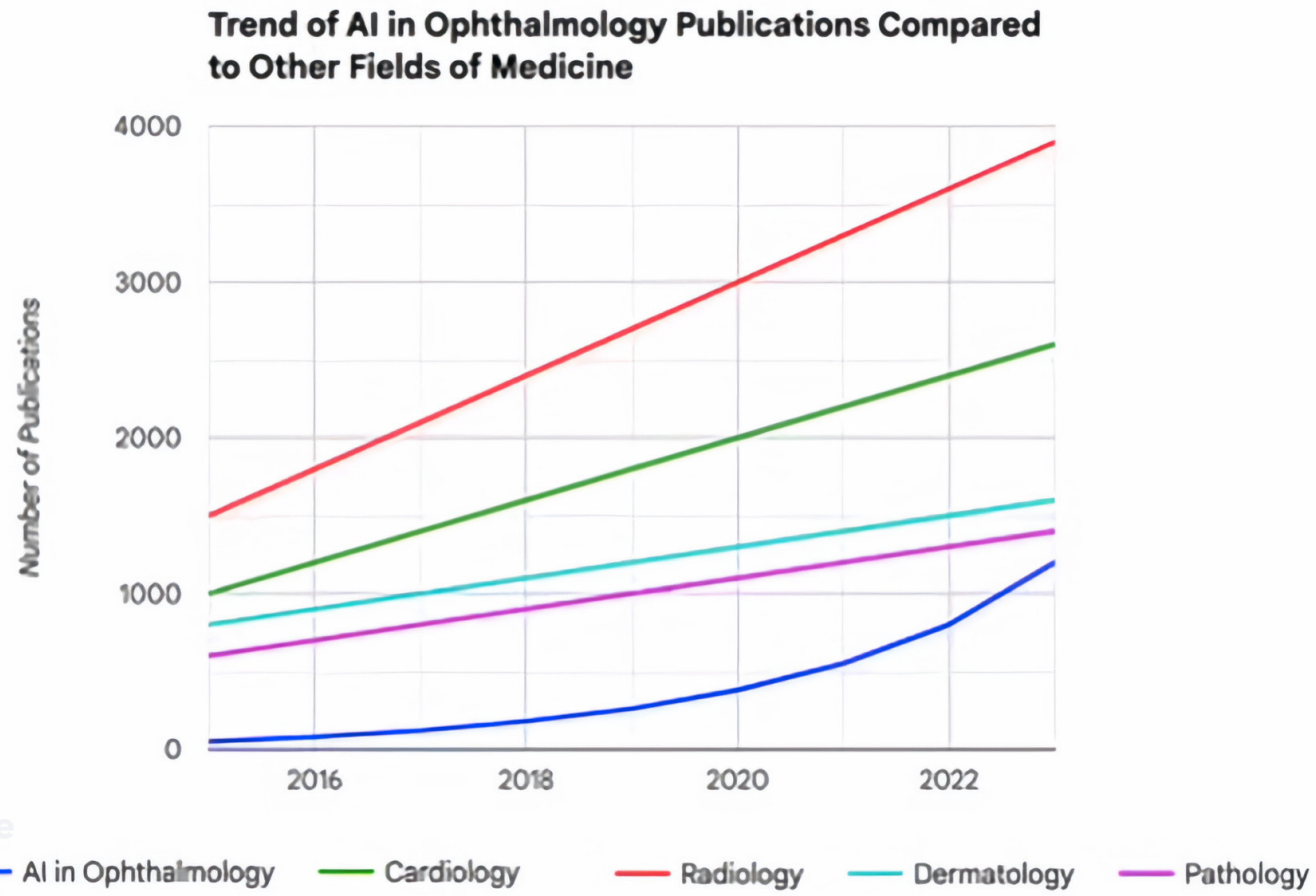
- High amount of Subclinical features



- “Big Data”

Artificial intelligence (AI) in Medicine





Courtesy of Ellias Khalilpour

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1. **Artificial intelligence for ocular oncology**
Neslihan Dilruba Koseoglu, Zélia Maria Corrêa, T.Y. Alvin Liu
Curr Opin Ophthalmol. 2023 Sep; 34(5): 437–440. Published online 2023 Jun 19.
doi: 10.1097/ICU.0000000000000982
PMCID: PMC10399931
Article PubReader PDF–174K Cite

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1. Prognostic Biomarkers in **Uveal Melanoma**: The Status Quo, Recent Advances and Future Directions
   Nuno Jorge Lamas, Arnaud Martel, Sacha Nahon-Estève, Samantha Goffinet, Adam Macocco, Corine Bertolotto, Sandra Lassalle, Paul Hofman
   Cancers (Basel) 2022 Jan; 14(1): 96. Published online 2021 Dec 25. doi: 10.3390/cancers14010096
   PMCID: PMC8749988
   Article PubReader PDF–3.9M Cite

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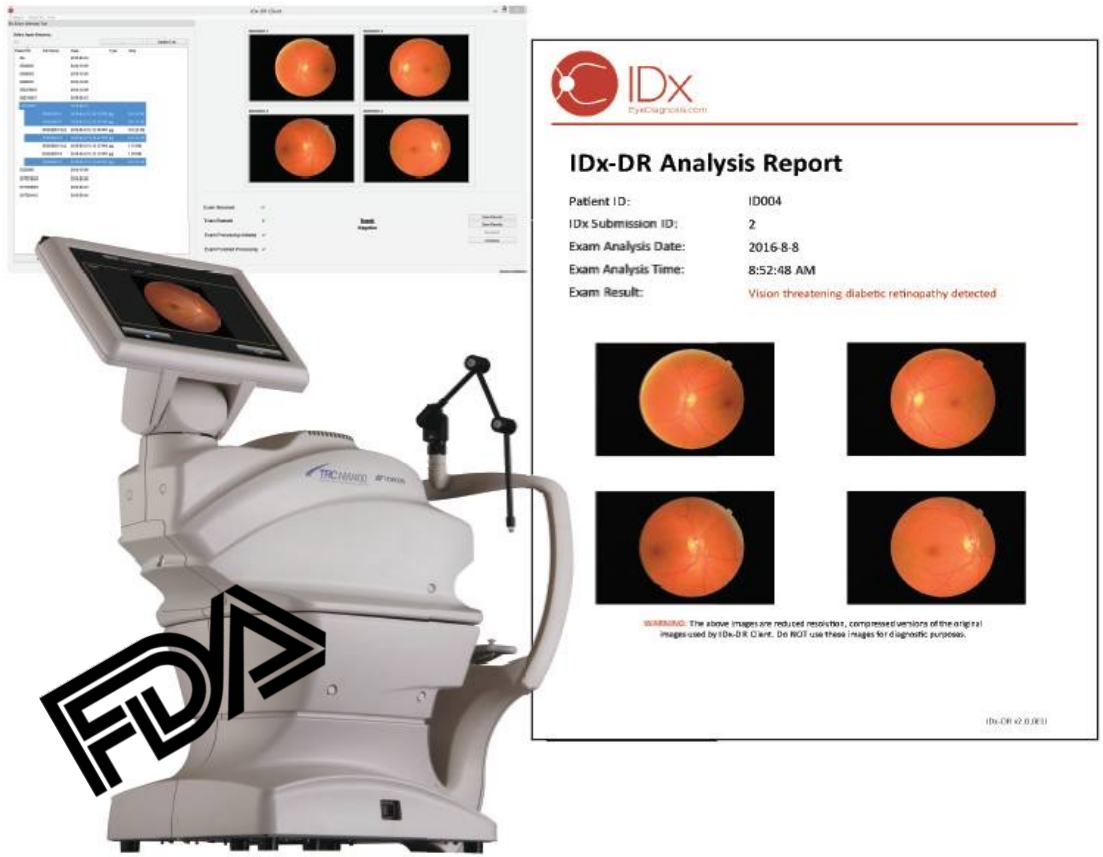
```
"artificial intelligence"[All Fields] AND ("Ocular oncology"[All Fields] OR "retinoblastoma"[All Fields] OR "Uveal Melanoma"[All Fields])
```

AI roles in Ophthalmology

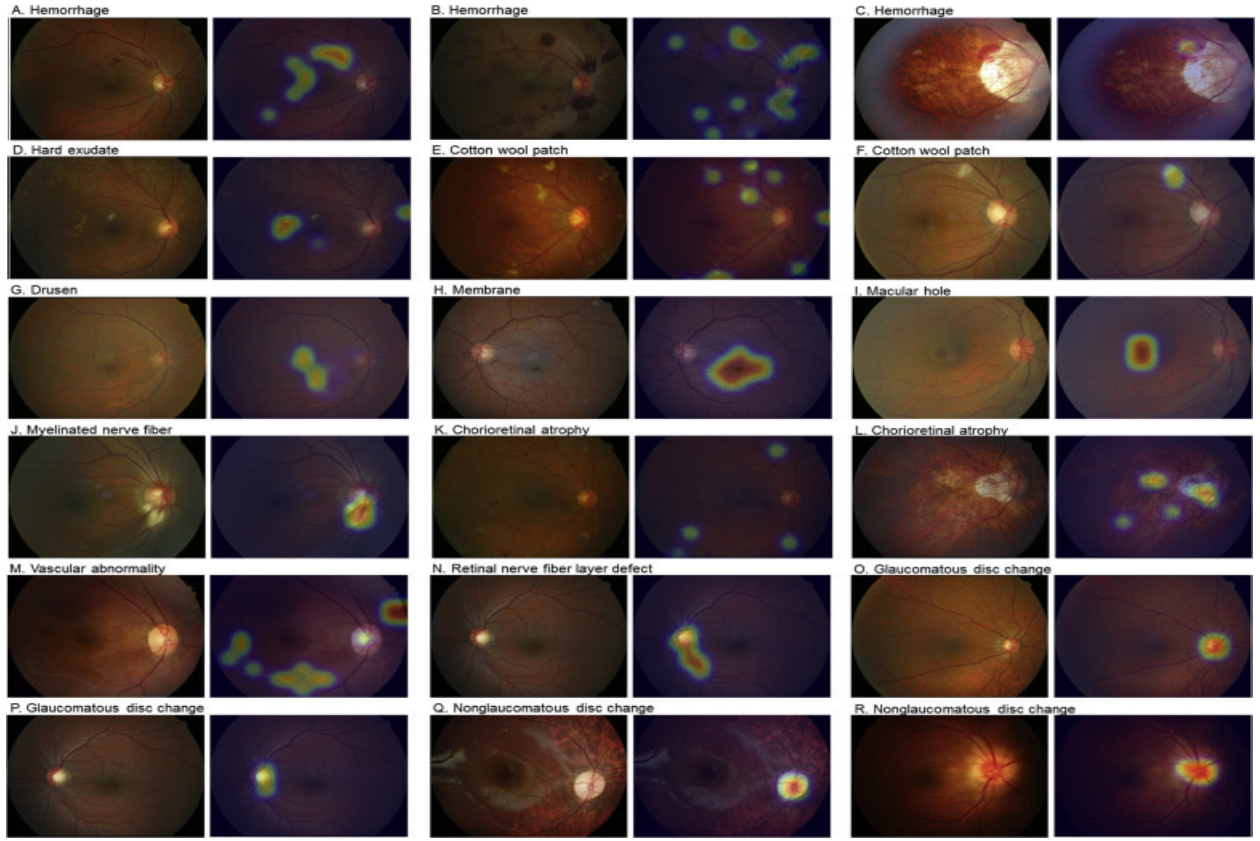
- To detect and “learn” features
- To reduce diagnostic and therapeutic errors
- Foster personalized medicine
- To reduce healthcare costs
- Disease-specific patterns
  - To gain innovative scientific insights

Disease Classification and Screening

Diabetic Retinopathy



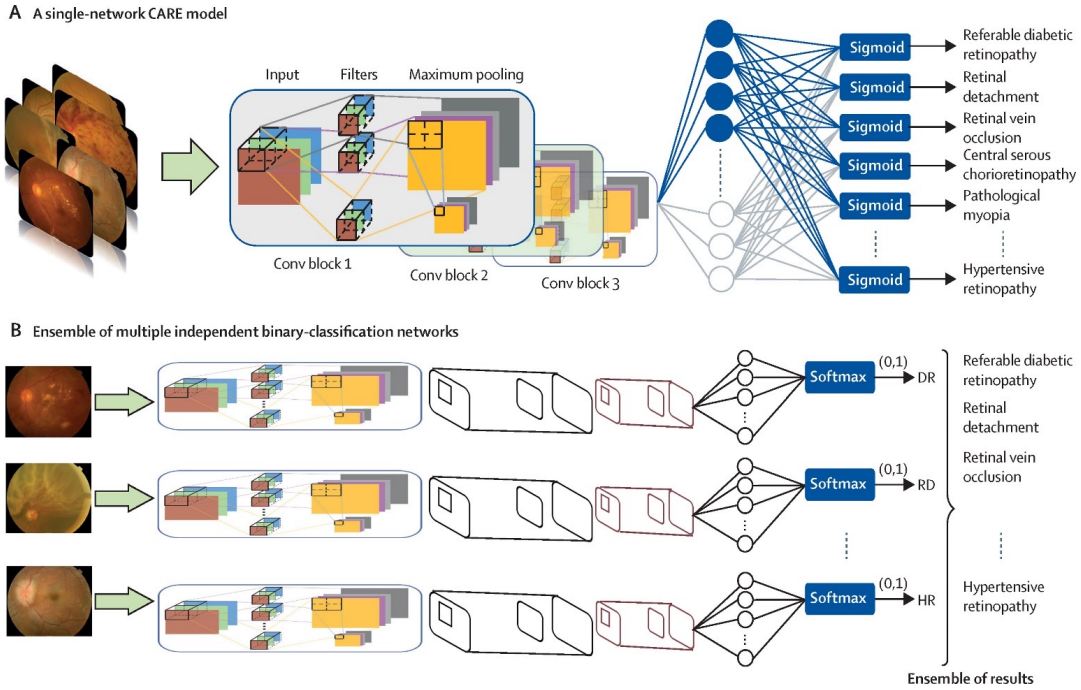
Simultaneous Screening



Son, Jaemin, et al. "Development and validation of deep learning models for screening multiple abnormal findings in retinal fundus images." Ophthalmology 127.1 (2020): 85-94.

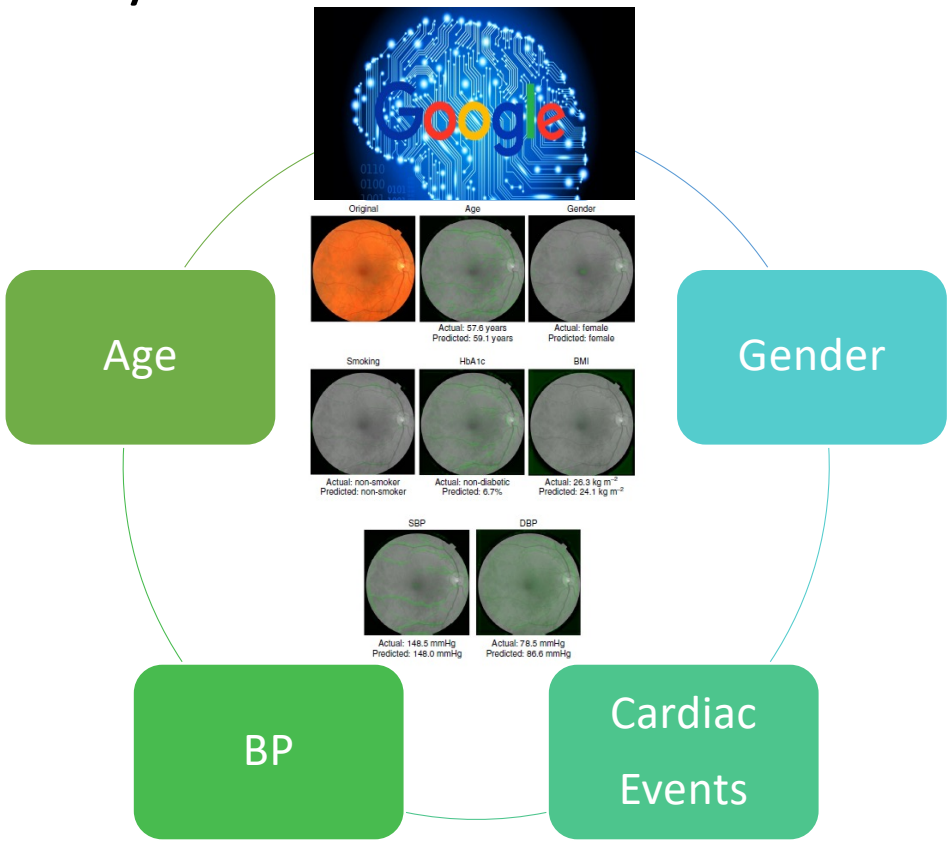
Simultaneous Screening

- Comprehensive Artificial intelligence Retinal Expert (CARE)



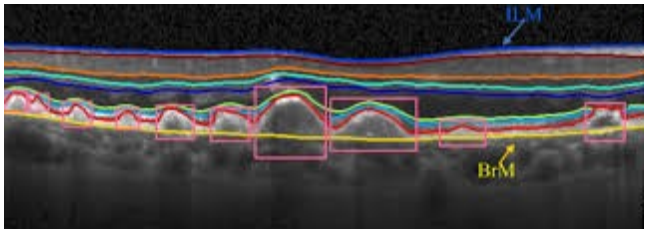
Lin, Duoru, et al. "Application of Comprehensive Artificial intelligence Retinal Expert (CARE) system: a national real-world evidence study." The Lancet Digital Health 3.8 (2021): e486-e495.

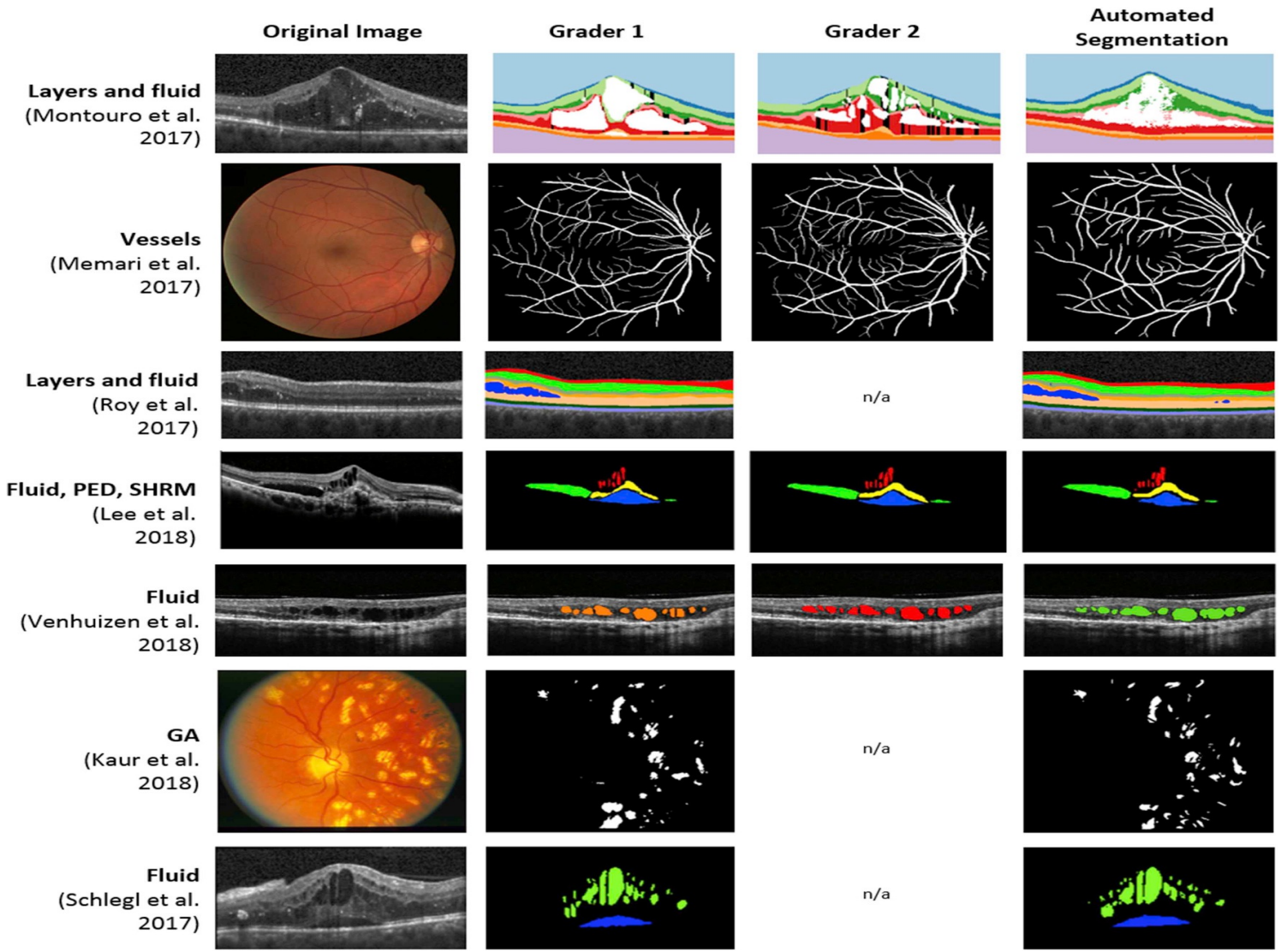
It's All in the Eyes



Poplin, Ryan, et al. "Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning." Nature Biomedical Engineering 2.3 (2018): 158.

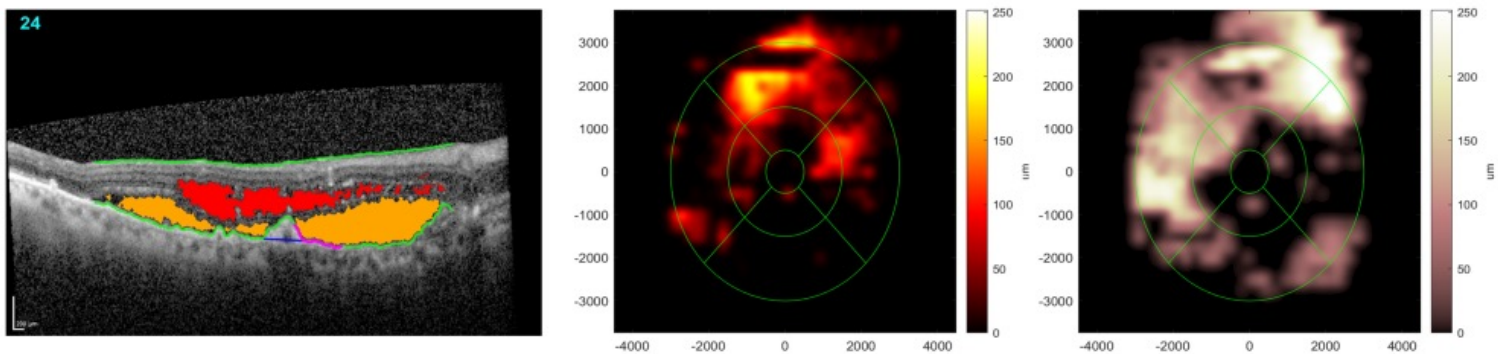
Image Segmentation




Original Image
Grader 1
Grader 2
Automated Segmentation
Layers and fluid (Montouro et al. 2017)
Vessels (Memari et al. 2017)
Layers and fluid (Roy et al. 2017)
n/a
Fluid, PED, SHRM (Lee et al. 2018)
Fluid (Venhuizen et al. 2018)
GA (Kaur et al. 2018)
n/a
Fluid (Schlegl et al. 2017)
n/a

Retinal Specialist vs. AI

- Detection of fluid in OCT
- AI outperformed the specialist!



Keenan, Tiarnan DL, et al. "Retinal specialist versus artificial intelligence detection of retinal fluid from OCT: age-related eye disease study 2: 10-year follow-on study." Ophthalmology 128.1 (2021): 100-109.

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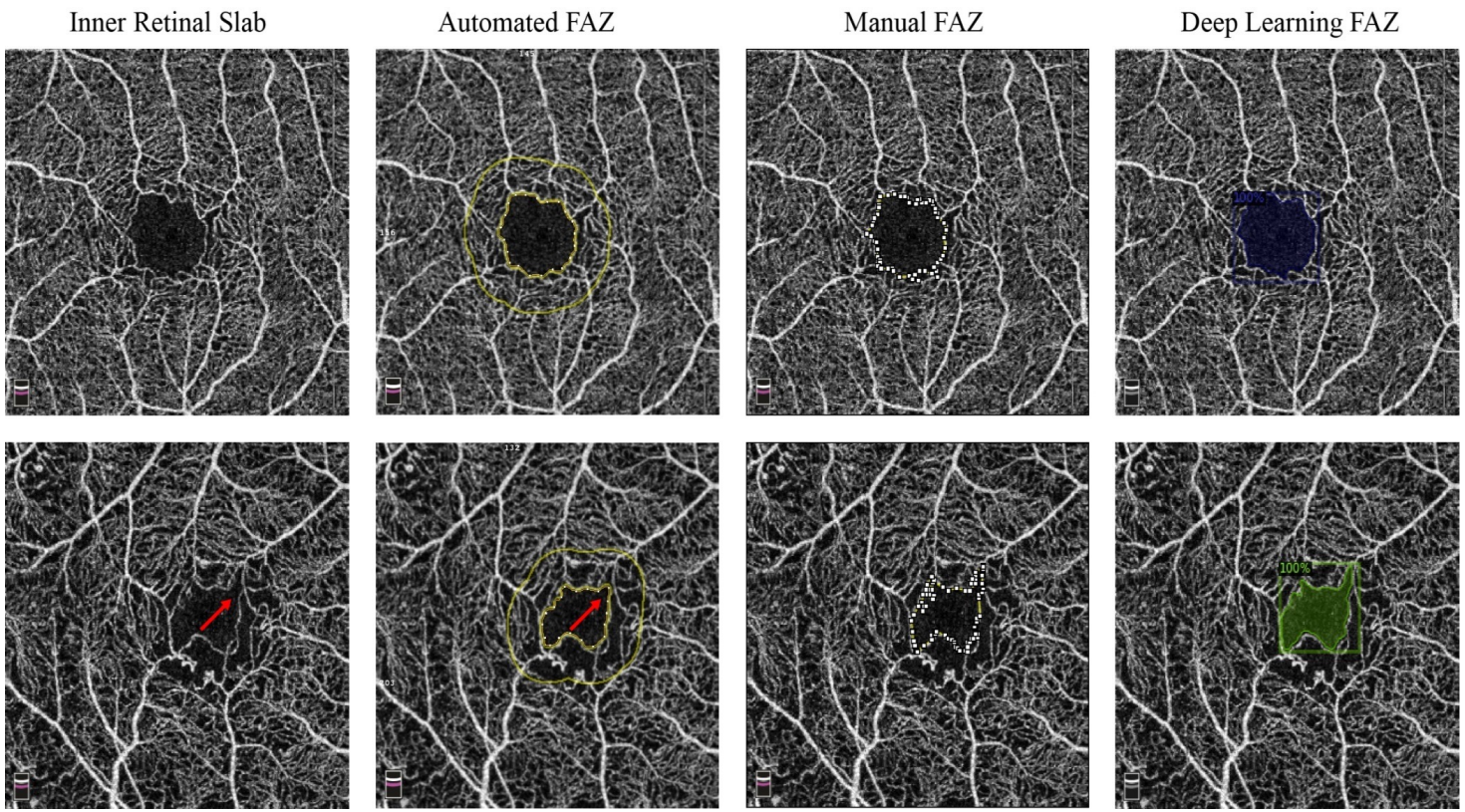
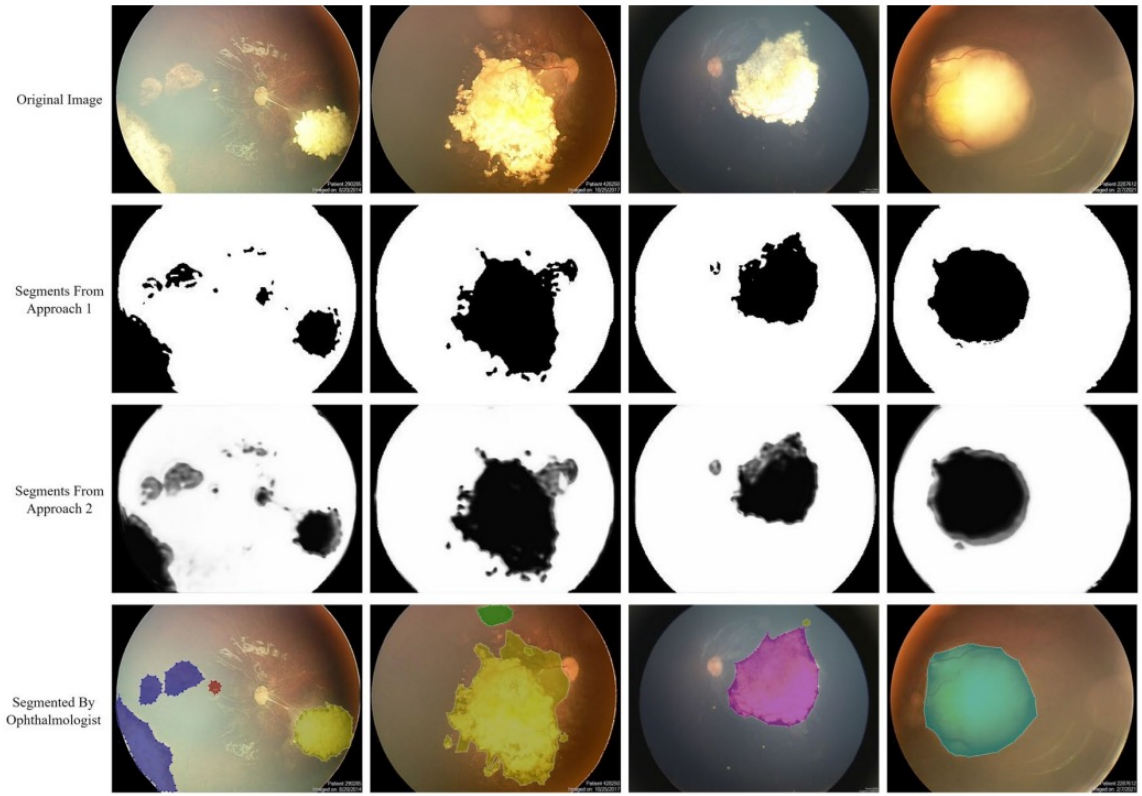
Our Experience



Mirshahi, Reza, et al. "Foveal avascular zone segmentation in optical coherence tomography angiography images using a deep learning approach." Scientific reports 11.1 (2021): 1-8.

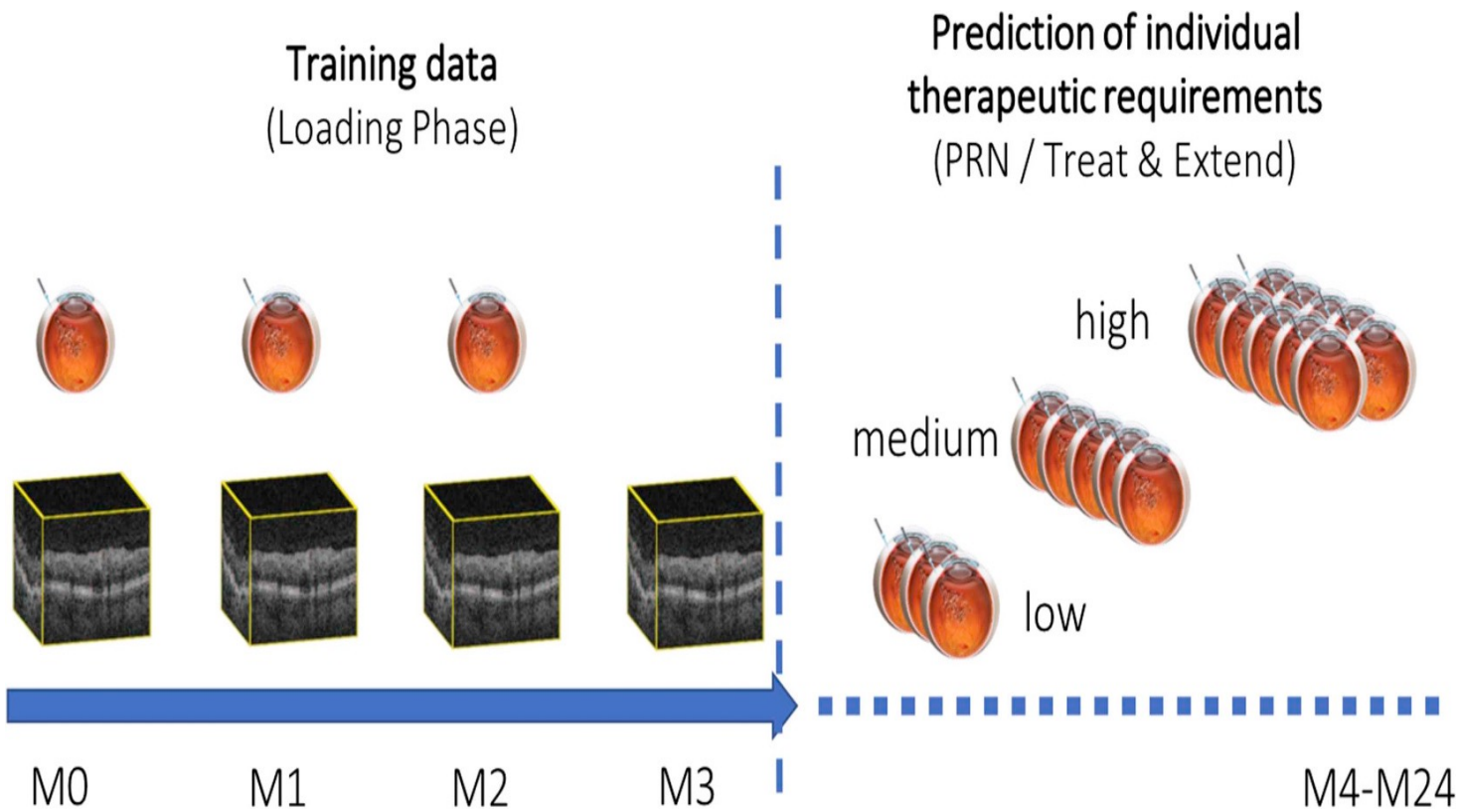
AI and Ocular Oncology: Iran



Rahdar, A., Ahmadi, M. J., Naseripour, M., Akhtari, A., Sedaghat, A., Hosseinabadi, V. Z., ... & Mirshahi, R.. Semi-supervised segmentation of retinoblastoma tumors in fundus images. Sci Rep 13, 13010 (2023). https://doi.org/10.1038/s41598-023-39909-6

Guidance of Therapy

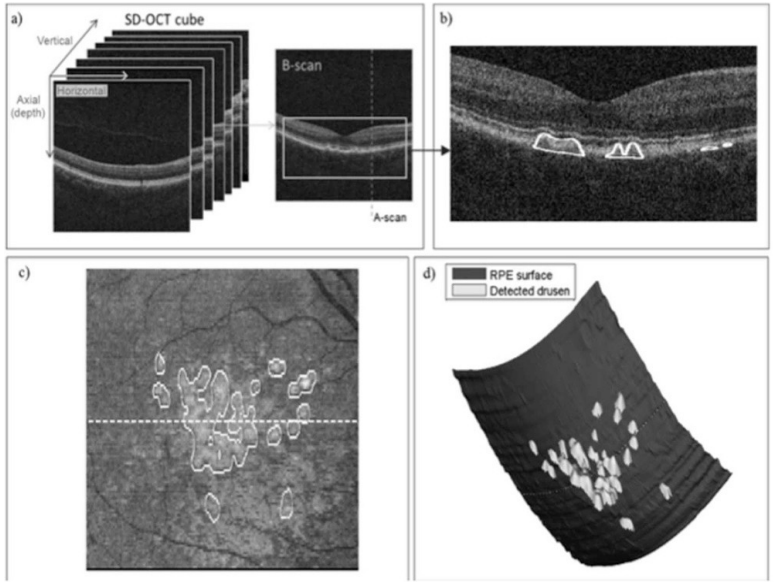
Need For ReTx

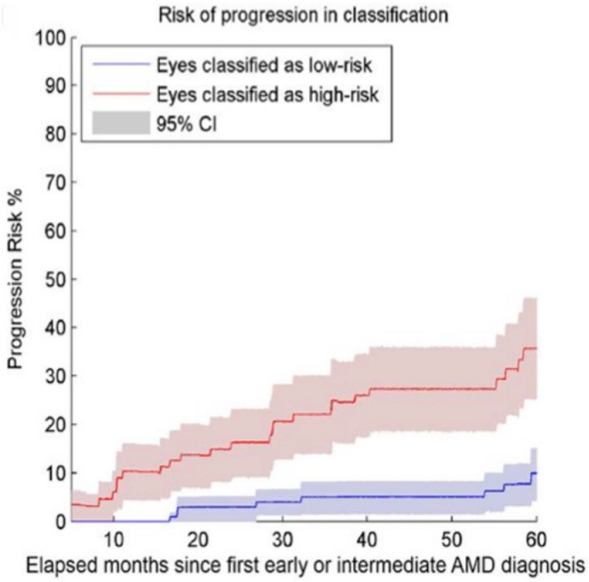


Schmidt-Erfurth, Ursula, et al. "Machine learning to analyze the prognostic value of current imaging biomarkers in neovascular age-related macular degeneration." Ophthalmology Retina 2.1 (2018): 24-30.

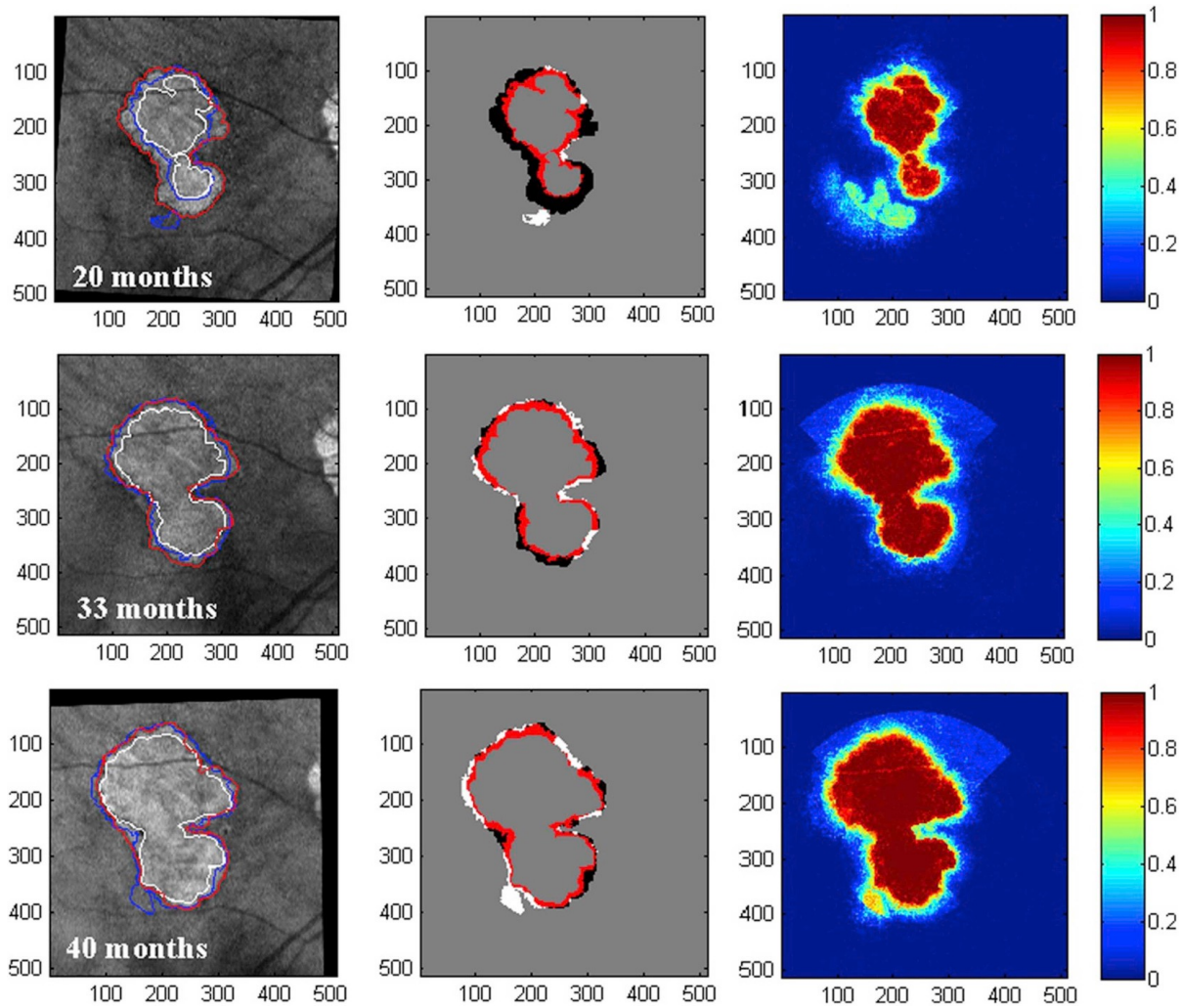
Predictions and Prognosis

Risk Stratification





Schmidt-Erfurth, U., Waldstein, S.M., Klimscha, S., Sadeghipour, A., Hu, X., Gerendas, B.S., Osborne, A., Bogunovic, H., 2018b. Prediction of individual disease conversion in early AMD using artificial intelligence. Invest. Ophthalmol. Vis. Sci. 59, 3199–3208.

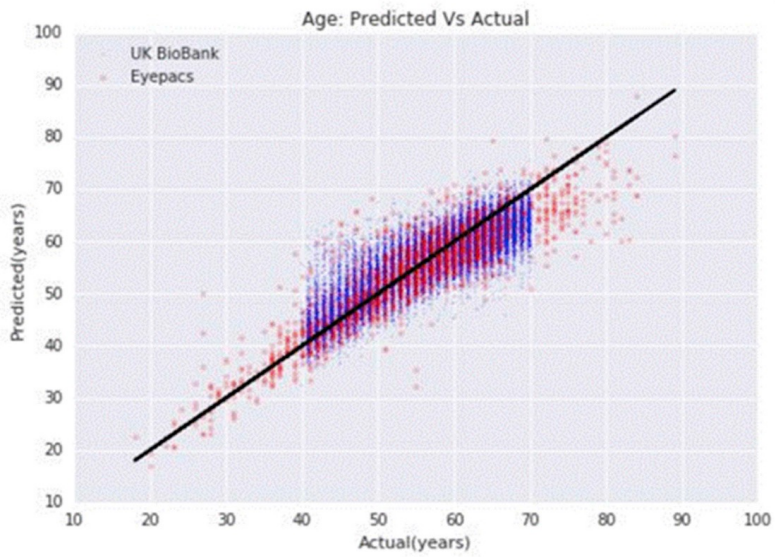


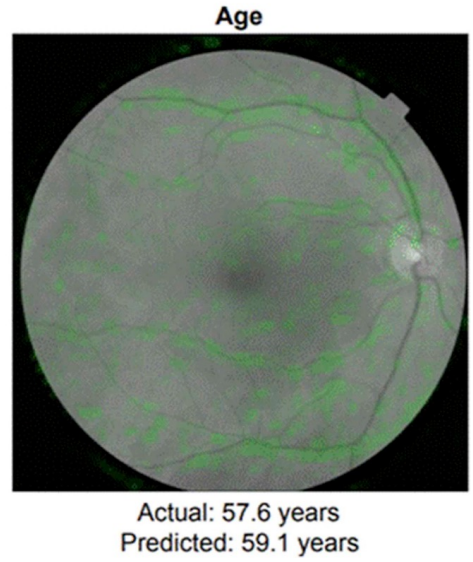
Bogunović, Hrvoje, et al. "Machine learning of the progression of intermediate age-related macular degeneration based on OCT imaging." Investigative ophthalmology & visual science 58.6 (2017): BIO141-BIO150.

Novel Insights

Google Brain

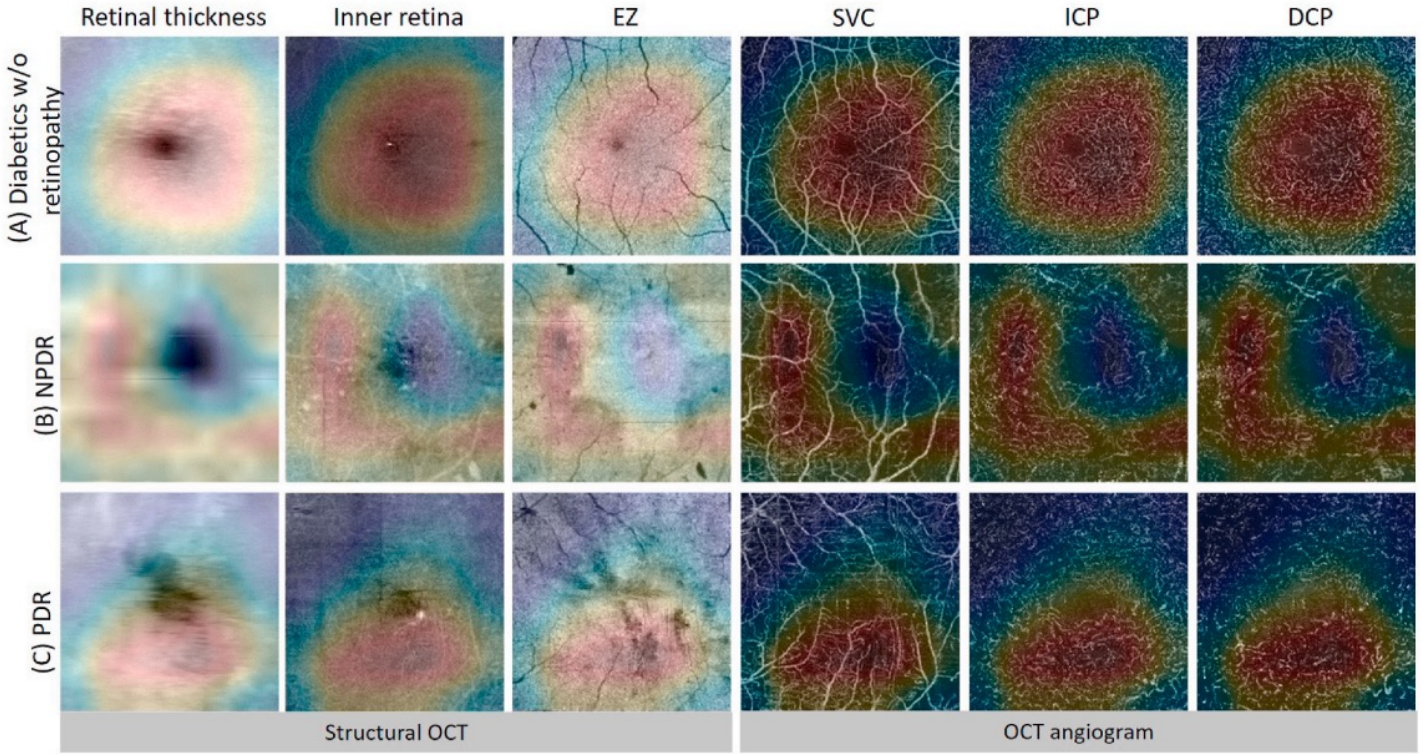
- How to predict AGE!!??





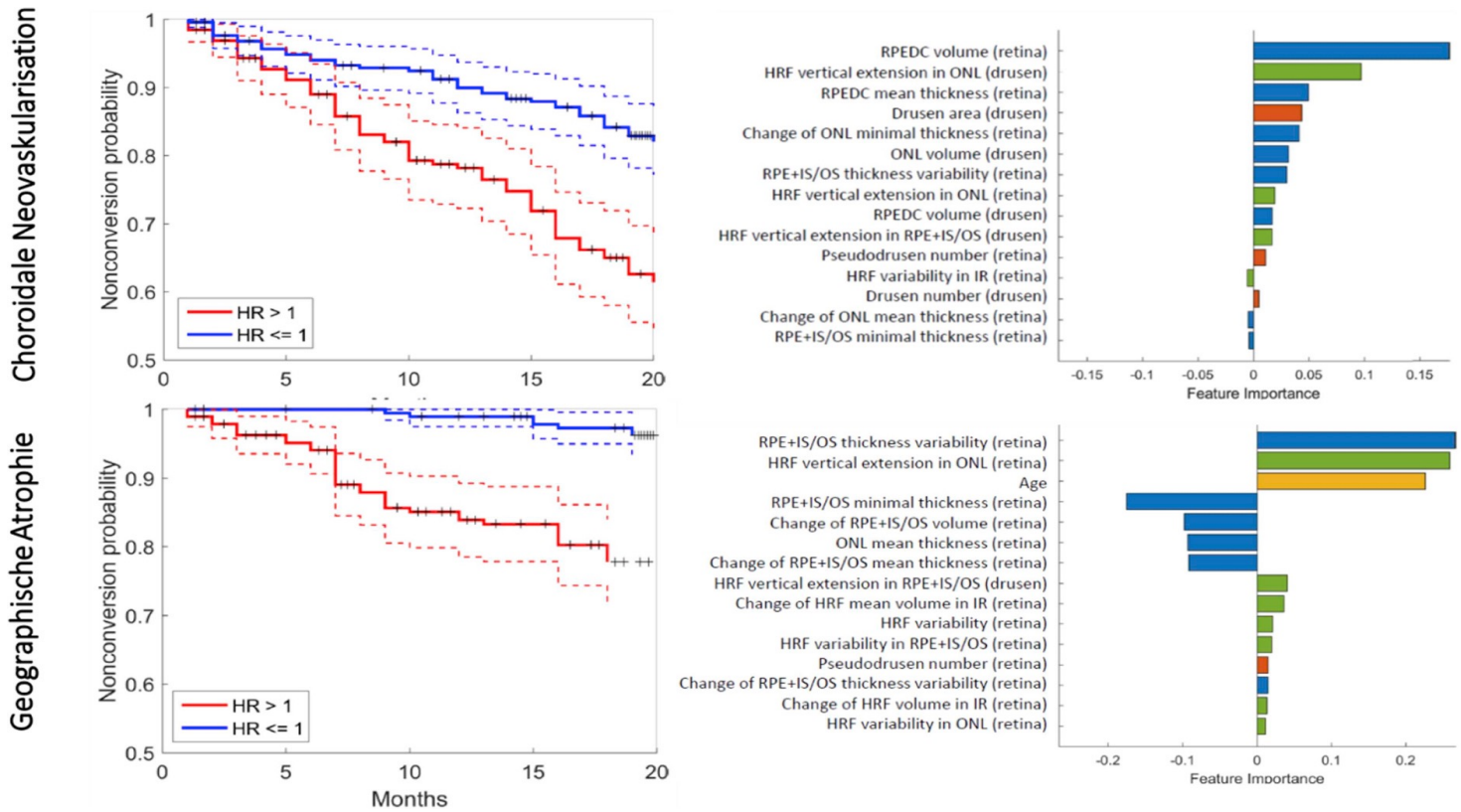
Poplin, Ryan, et al. "Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning." Nature Biomedical Engineering 2.3 (2018): 158.

Heatmaps
Class Activation Maps



Hormel, Tristan T., et al. "Artificial intelligence in OCT angiography." Progress in Retinal and Eye Research (2021): 100965.

Novel Insights in Age-Related Macular Degeneration



Schmidt-Erfurth, Ursula, et al. "Prediction of individual disease conversion in early AMD using artificial intelligence." Investigative ophthalmology & visual science 59.8 (2018): 3199-3208.

AI and Personalized Medicine

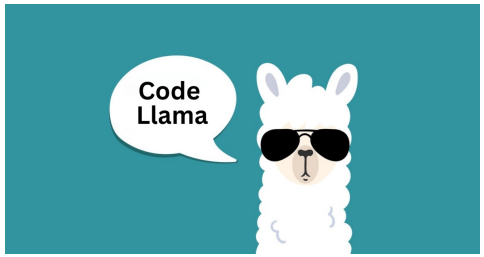
- Individualized treatment selection

- In servicing electronic medical records
  - Speech recognition and image analysis
  - More time for human-to-patient interactions

- Patient-accessible automated scanners
  - AI enabled

Large Language Models (LLM)

- “Advanced artificial intelligence (AI) systems designed to understand and generate human-like text. They are trained on vast amounts of text data and use deep learning techniques to learn the intricacies of language, enabling them to perform tasks like text generation, translation, summarization, and more.”
- GPT (Generative Pre-trained Transformer) series by OpenAI,
- PaLM 2 by Google
- LLaMA by Meta
- Bing AI by Microsoft

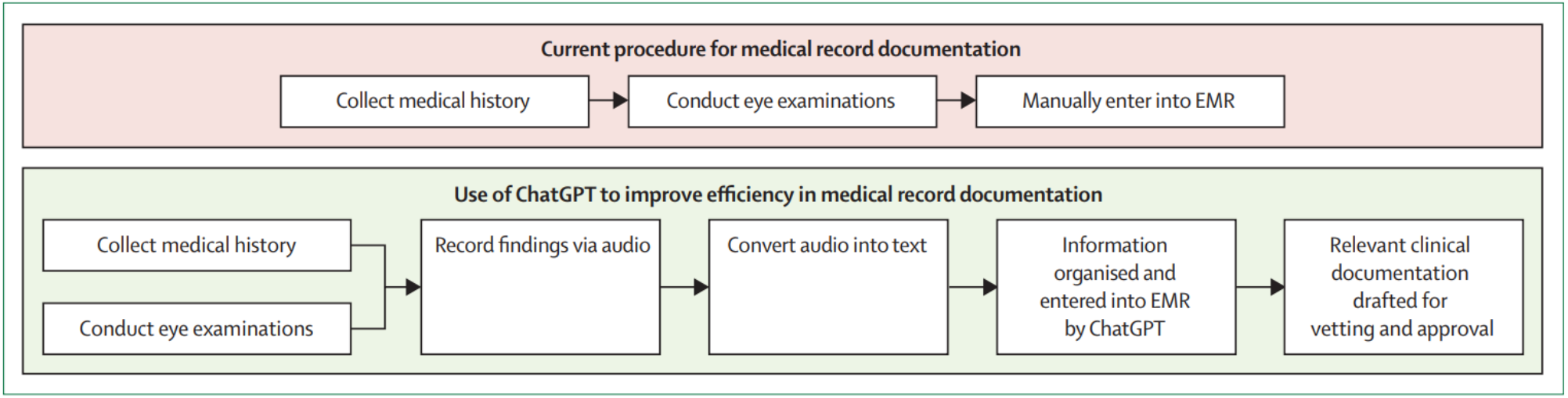


GPT - 4

LLMS in Assisting Clinicians

- Doubling time for medical knowledge: 73 days.
  - Rapidly review, distill, and summarize scientific papers, trials, guidelines
- Compiling and cross-referencing digitized patient health records
  - Family history, past medical history, imaging, histopathology, and other data modalities
  - E.g. Highlight a patient's need to undergo BAP1 germline mutation testing
- Research and Education Tasks

Enhance Efficiency in Medical Record Documentation



LLMS in Enhancing Patient Care

- Personalized responses in plain language
  - Diagnosis, treatments, side effects, prognosis etc.
- Improve patient satisfaction, adherence, and outcomes
  - Patient’s emotional state, preferences, and needs
- 24/7 Responding
  - Answer postoperative related questions and concerns

Workflow: Ophthalmology Facilities

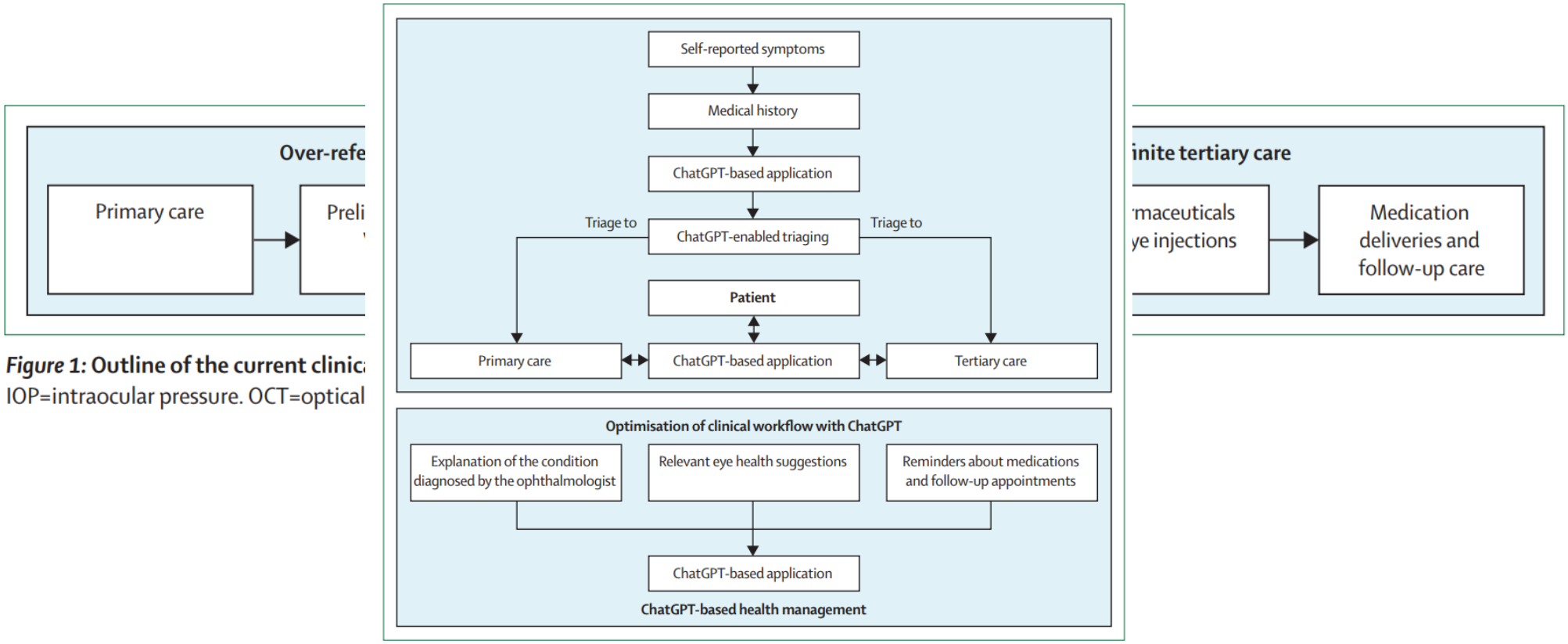


Figure 1: **Outline of the current clinic**
IOP=intraocular pressure. OCT=optical

Betzler, Bjorn Kaijun, et al. "Large language models and their impact in ophthalmology." The Lancet Digital Health 5.12 (2023): e917-e924.

Table. Ophthalmologist Evaluation of Chatbot-Generated and Human-Written Responses

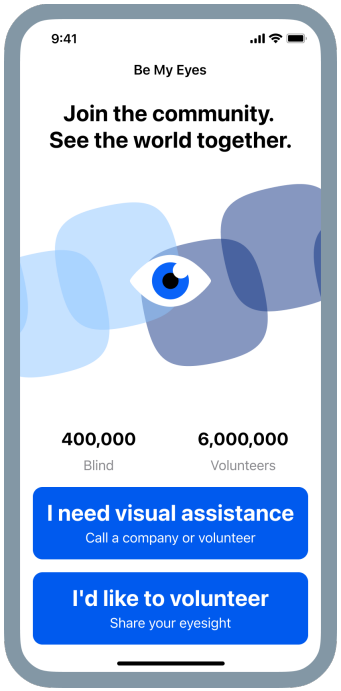
Question	No. (%)		*P* value[a]
	Chatbot	Human	
Was the answer written by a human ophthalmologist or AI?			
Definitely written by a human	93 (11.6)	56 (7.0)	<.001
Probably written by a human	75 (9.4)	227 (28.4)	
Probably written by AI	341 (42.6)	197 (24.6)	
Definitely written by AI	291 (36.4)	320 (40.0)	
Any incorrect or inappropriate material in the answer?			
No	619 (77.4)	603 (75.4)	.58
Yes, little clinical significance	144 (18.0)	153 (19.1)	
Yes, great clinical significance	37 (4.6)	44 (5.5)	
What is the likelihood of possible harm?			
Harm unlikely	692 (86.5)	672 (84.0)	.35
Potentially harmful	101 (12.6)	121 (15.1)	
Definitely harmful	7 (0.9)	7 (0.9)	
What is the extent of possible harm?			
No harm	655 (81.9)	653 (81.6)	.84
Mild or moderate harm	118 (14.8)	116 (14.5)	
Vision-threatening injury or severe harm	23 (2.9)	27 (3.4)	
How does the answer relate to the consensus in the medical community?			
No consensus in the medical community	526 (65.8)	505 (63.1)	.35
Aligned with consensus	221 (27.6)	229 (28.6)	
Opposed to consensus	49 (6.1)	62 (7.8)	

Bernstein, Isaac A., et al. "Comparison of ophthalmologist and large language model chatbot responses to online patient eye care questions." JAMA Network Open 6.8 (2023): e2330320-e2330320.

LLMS in Aiding The Visually Impaired

- Visual input capability
  - Describe objects and scenes in rich detail

- Discerning individual needs and preferences



LLMS for The Policymakers

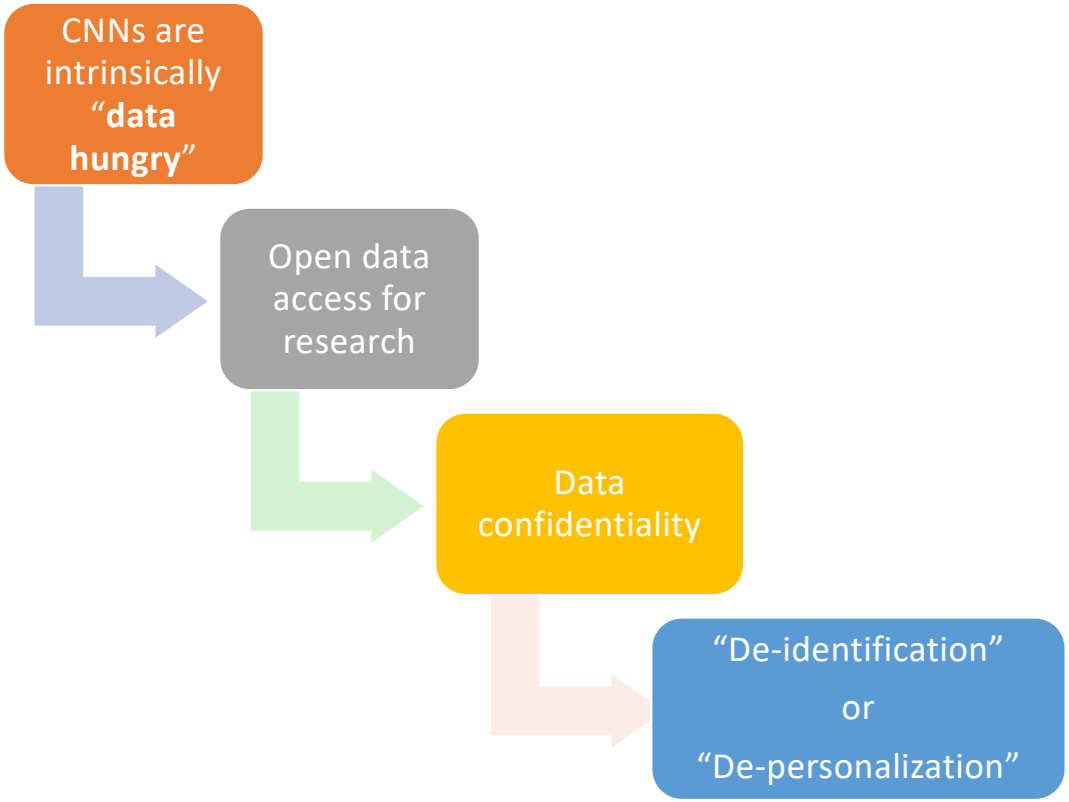
- AI-assisted writing, evidence synthesis, and administrative work

- Drafting, writing, refining, and proofreading
  - Guidelines, regulations, and other document

Tan, Ting Fang, et al. "Generative Artificial Intelligence Through ChatGPT and Other Large Language Models in Ophthalmology: Clinical Applications and Challenges." Ophthalmology Science 3.4 (2023): 100394.

Limitations of AI

Limitations and Challenges



Limitations and Challenges

- Data bias and algorithmic fairness
  - Quality of the data
  - Discrimination of vulnerable groups

- Security risks
  - Adversarial attacks are malicious inputs to ML algorithm
  - Misclassificatios

- Impact on clinical outcome
  - Randomized clinical trial (RCT)

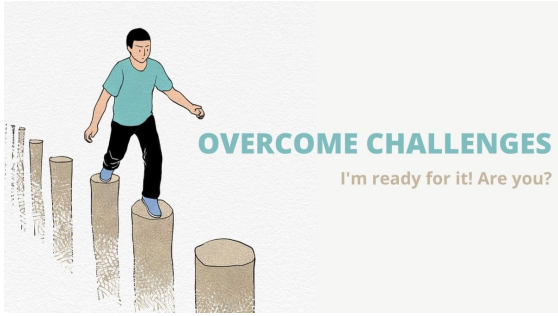
Limitations and Challenges

- Cybersecurity and data privacy
  - Solution: blockchain technology??
    - Cryptographic algorithms and intrinsic transparency of blockchain
- Regulations
  - Health Insurance Portability and Accountability Act in the USA
  - The General Data Protection Regulation in the EU
- False responses by LLMs
  - AI hallucinations
  - Wrong answer to a wrong question instead of probing
  - Out of date knowledge of offline chatbots

Yaghy, Antonio, et al. "Large Language Models in Ophthalmology: Potential and Pitfalls." Seminars in Ophthalmology. Taylor & Francis, 2024.

Limitations and Challenges

- Not incorporating the latest research findings or clinical guideline
- Not cater to all languages
  - Specialized medical vocabulary
- Lack of the clinicians' hard-won acumen and experience
- True Empathy?
- Ethical and legal considerations
  - Misinformation, medical deepfakes
  - Promising avenues for democratizing knowledge and empowering patients



Yaghy, Antonio, et al. "Large Language Models in Ophthalmology: Potential and Pitfalls." Seminars in Ophthalmology. Taylor & Francis, 2024.

Limitations and Challenges

Scenario	AI recommendation	AI accuracy	Physician action	Patient outcome	Legal outcome (probable)
1	Standard of care	Correct	Follows	Good	No injury and no liability
2			Rejects	Bad	Injury and liability
3		Incorrect (standard of care is incorrect)	Follows	Bad	Injury but no liability
4			Rejects	Good	No injury and no liability
5	Nonstandard care	Correct (standard of care is incorrect)	Follows	Good	No injury and no liability
6			Rejects	Bad	*Injury but no liability*
7		Incorrect	Follows	Bad	*Injury and liability*
8			Rejects	Good	No injury and no liability

Price, W. Nicholson, Sara Gerke, and I. Glenn Cohen. "Potential liability for physicians using artificial intelligence." Jama 322.18 (2019): 1765-1766.

WHO Guiding Principles for AI in Healthcare

1. **Protecting human autonomy**
   - Humans should remain in control of health-care systems
   - Privacy and confidentiality

2. **Promoting human well-being and safety and the public interest**
   - Regulatory requirements for safety, accuracy and efficacy of AI

3. **Ensuring transparency, explainability and intelligibility**
   - Sufficient information be published or documented

WHO Guiding Principles for AI in Healthcare

4. **Fostering responsibility and accountability**
   - effective mechanisms should be available for questioning and for redress

5. **Ensuring inclusiveness and equity**
   - The widest possible equitable use and access

6. **Promoting AI that is responsive and sustainable**
   - Continuously and transparently assess AI applications
   - Environmental consequences and increase energy efficiency
   - Potential job losses

Thank you!!!