AI AND TELEMEDICINE

GWCO 2022

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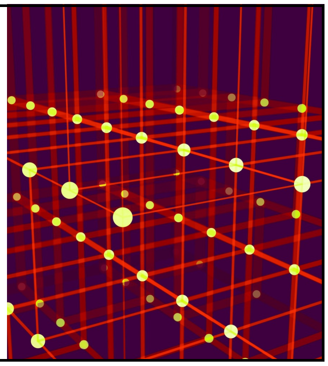

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Leo Semes, OD, FAAO

- Consultant - Apellis
- Speaker Bureau, Consultant - Regeneron, OptoMed
- Scientific Advisory Board (Consultant) - EyePromise
- Stock options - EyePromise (< 0.01% ownership)

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COURSE OBJECTIVES

In this course, the attendee will

- Learn the evolution of artificial intelligence and why that descriptor may be a misnomer
- Appreciate the basis for image analysis by automation
- Appreciate the application of automated image analysis to diabetic retinopathy, age-related macular degeneration and other fundus abnormalities
- Understand the accuracy of automated image analyses

3

What is artificial intelligence?

"If you wish to converse with me, define your terms." -Voltaire

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Artificial Intelligence Defined

The theory and development of computer systems able to perform tasks normally requiring human intelligence, such as visual perception, speech recognition, decision-making, and translation between languages.

https://www.lexico.com/en/definition/artificial_intelligence, Accessed August 8, 2019

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A brief history of AI

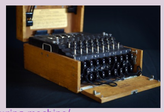
6

TURING <u>MACHINES</u>

Algorithms

“Analytics”

First described by <u>Alan Turing</u> <u>1936–7</u>, are simple abstract computational devices intended to help investigate the extent and limitations of what can be <u>computed</u>.



https://plato.stanford.edu/entries/turing-machine/

https://www.turing.ac.uk/news/enigma-machine-goes-display-alan-turing-institute

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TURING <u>MACHINES</u>

Algorithms

“Analytics”

Turing’s *‘automatic machines’*, as he termed them in 1936, were specifically devised for the computing of real numbers. They were first named ‘Turing machines’ by Alonzo Church (1937). Today, they are considered to be *<u>one of the foundational models of computability and computer science</u>*

https://plato.stanford.edu/entries/turing-machine/

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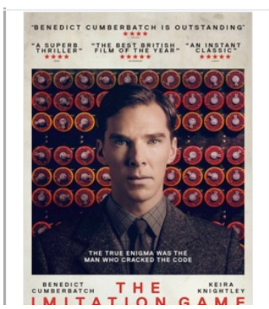

ALGORITHMS

ANALYTICS

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EVOLUTION OF ARTIFICIAL INTELLIGENCE

- 1956 – “Artificial intelligence” coined by John McCarthy on the premise
  - *…that every aspect of learning or any feature of intelligence can be <u>so</u> <u>precisely</u> described that a machine can be made to simulate it.* *[binary decisions, 1 or 0]*

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EVOLUTION OF ARTIFICIAL INTELLIGENCE

1959 – “Machine learning” created by Arthur Samuel

- focuses on the learning feature of intelligence by developing <u>algorithms</u> that extract generalized principles from data.
- ML differs from other automated approaches that required that the *<u>descriptive rules be defined by human experts and implemented by programmers</u>*

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What is an algorithm?

```
  1 1
  4 6 3 7 8
 +2 5 9 2 1
 ----------
  7 2 2 9 9
```

12

Let's do something more complex

4 6 3 7 8 ÷ 2 5 9 2 1 =

13

Let's do something more complex

4 6 3 7 8 ÷ 2 5 9 2 1 = 1.789

Rules for long division . . .

46378 ÷ 25921 =

```
            1.7...
2 5 9 2 1 | 4 6 3 7 8
            2 5 9 2 1
            2 0 4 5 7 0
            1 8 1 4 4 7
              2 3 1 2 3 0
              ...
```

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Racing Daily Form

Regression analysis of "big data" to produce

THE ***Algorithm***

The year was 1973. . .

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CONTEMPORARY EXAMPLES OF AI

Artificial Intelligence
or
Always Intruding?

"inspired by your browsing"

"Based on your zip code"

Google translate

Voice-generated text

Auto-fill text

Sports-related applications ("analytics")

J F G I

"google" as a verb!"

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"Analog" Driving Algorithm

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Automation levels for vehicles

	Level 0	Level 1	Level 2
Concept	No driving automation	Advanced driver-assistance system, assists human with some tasks	Advanced driver-assistance system, full human attention required
Explanation	The human driver does all the driving.	An advanced driver-assistance system (ADAS) on the vehicle can sometimes assist the human driver with either steering or braking/accelerating, but not both simultaneously.	An advanced driver-assistance system (ADAS) on the vehicle can control both steering and braking/accelerating simultaneously under some circumstances. The human driver must continue to pay full attention (monitor the driving environment) at all times and perform the rest of the driving task.

Source: The authors, informed by Automated Vehicles for Safety. U.S. Department of Transportation, National Highway Traffic Safety Administration. Accessed February 7, 2022. https://www.nhtsa.gov/technology-innovation/automated-vehicles-safety.

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Automation levels for vehicles

	Level 3	Level 4	Level 5
Concept	Automated driving system, for some circumstances	Automated driving system, for certain circumstances	Full driving automation, for all circumstances, humans as passengers
Explanation	An automated driving system (ADS) on the vehicle can perform all aspects of the driving task under some circumstances. In those circumstances, the human driver must be ready to take back control at any time when the ADS requests the human driver to do so. In all other circumstances, the human driver performs the driving task.	An automated driving system (ADS) on the vehicle can perform all driving tasks and monitor the driving environment — essentially, do all the driving — in certain circumstances. The human need not pay attention in those circumstances.	An automated driving system (ADS) on the vehicle can do all the driving in all circumstances. The human occupants are just passengers and need never be involved in driving.

Source: The authors, informed by Automated Vehicles for Safety. U.S. Department of Transportation, National Highway Traffic Safety Administration. Accessed February 7, 2022. https://www.nhtsa.gov/technology-innovation/automated-vehicles-safety.

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Tesla Driving Algorithms

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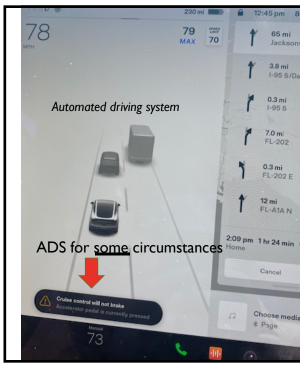

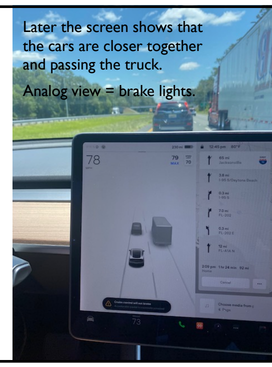

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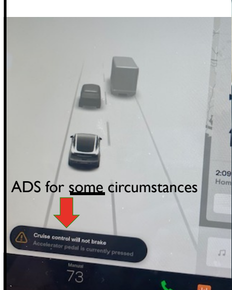

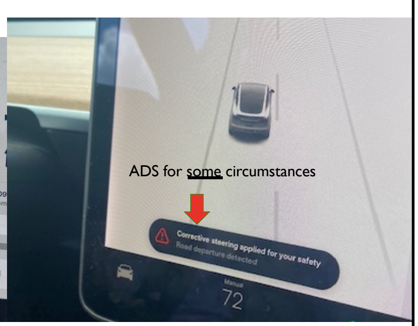

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> *"Getting to 100% automation is the goal for AVs, because the advantages of taking the driver completely out of the equation are clear and compelling. Not so in health care. In fact, quite the contrary, as the doctor-patient relationship is critical to outcomes."*

Autonomous vehicle prototype
Pittsburgh, PA September 2016

Norden JG, Shah NR. What AI in healthcare can learn from the long road to autonomous vehicles. NEJM Catalyst Accessed March 10, 2022.
https://catalyst.nejm.org/doi/pdf/10.1056/CAT.21.0458

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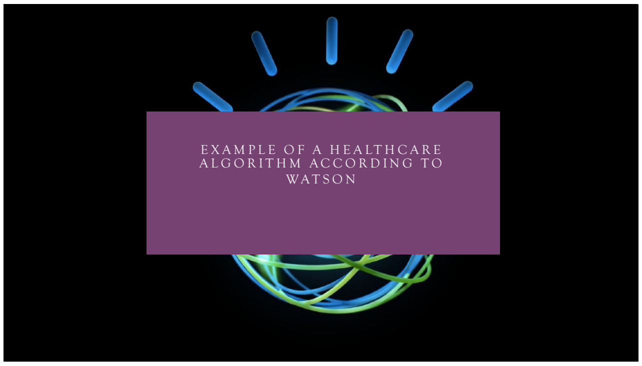

EXAMPLE OF A HEALTHCARE ALGORITHM ACCORDING TO WATSON

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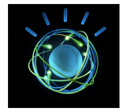

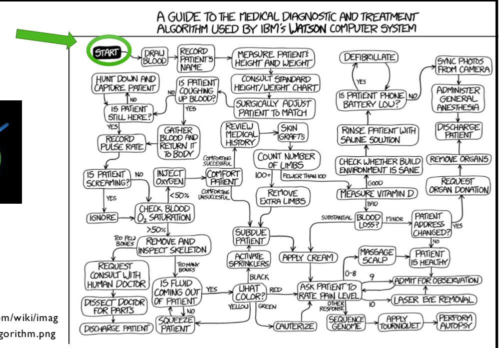

https://www.explainxkcd.com/wiki/images/1/15/watson_medical_algorithm.png

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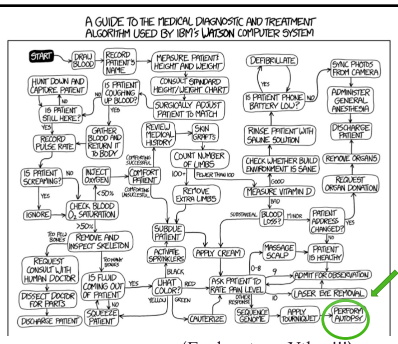
Elementary, my Dear Watson

An *algorithm* for patient care

Templates
Patterns

https://www.explainxkcd.com/wiki/images/1/15/watson_medical_algorithm.png



(End point. Yikes!!!)

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WHAT HEALTHCARE CAN LEARN FROM AUTONOMOUS DRIVING

AI categories and terminology

Evolution of AI Categories		
Term	Explanation	Examples
Rule-based Systems	Translating human knowledge into predetermined actions	Sepsis alerts for flagging an abnormal set of vitals
Supervised Learning	A set of algorithms that builds predictive models from data with known outcomes	A radiologist groups 1,000 chest X-rays into those with lesions and those without, then a supervised learning algorithm is trained on this labeled data to determine a pattern to sort these chest X-rays automatically into these groups
Unsupervised Learning	Sets of algorithms that identify patterns in data without predetermined labels or known outcomes	Using large gene expression data sets, we have discovered 10 breast cancer subtypes that correspond to different patient outcomes and treatment responses
Reinforcement Learning	These are AI algorithms that train toward a certain goal using an iterative approach of trial and error, updating their models dynamically toward the more successful outcomes	Type of AI used to train AlphaGO through iterative self-play, ultimately outperforming the world championship GO player

Norden JG, Shah NR. What AI in healthcare can learn from the long road to autonomous vehicles. NEJM Catalyst
Accessed March 10, 2022.
https://catalyst.nejm.org/doi/pdf/10.1056/CAT.21.0458

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WHAT HEALTHCARE CAN LEARN FROM AUTONOMOUS DRIVING

AI Terminology		
Term	Explanation	Examples
Synthetic Data	This is data created artificially by algorithms that is meant to mimic real-world data	1. People train fall-detection algorithms using artificially generated falls; the synthetic fall data is made by moving stick figure models through human poses that portray how people may fall 2. Use cases today in health care are to create digital twins for control arms in clinical trials instead of recruiting patients who will receive placebo
Computer Vision and Deep Learning	Types of AI techniques that use multilayer artificial neural networks trained off large data sets (deep learning) to find information in images or videos	Hospitals today are using computer-vision algorithms to find strokes in head-computed tomography scans (CTs)
Natural Language Processing (NLP)	These algorithms work to extract or "understand" useful information from human speech or text	Physicians are using NLP tools to transcribe speech to write patient encounter notes

Norden JG, Shah NR. What AI in healthcare can learn from the long road to autonomous vehicles. NEJM Catalyst
Accessed March 10, 2022.
https://catalyst.nejm.org/doi/pdf/10.1056/CAT.21.0458

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How would you, as a clinician, manage this patient?

22 WM

- presents with 2-day history of a unilateral floater
- non-contributory medical, allergy, family histories
- UCVA 20/20

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22 WM

- 2-day history of a unilateral floater
- non-contributory medical, allergy, family histories
- UCVA 20/20
- Initial differentials
  - PVD (not myopic)
  - Post-trauma (denies)
  - Retinal tear
  - Inflammatory etiology
  - Infectious etiology

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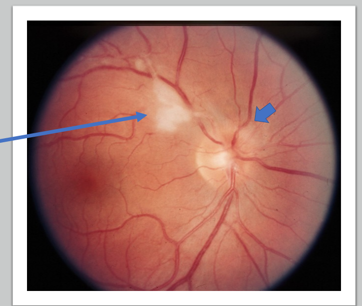
22 WM

- 2-day history of a unilateral floater
- non-contributory medical, allergy, family histories
- UCVA 20/20

Clinical observations:
Granuloma
\+ indistinct disc margin =
Neuroretinitis!

(Clinician's machine-learning conclusion)



Etiology? Kitten as vector for *B. Henselae* infection

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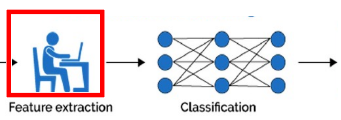
Requires human intervention

- Further history
- Fundus photo features
- Order additional testing?



Schmidt-Erfurth U, Sadeghipour A, Gerendas BS, Waldstein SM, Bogunović H. Artificial intelligence in retina. Prog Retin Eye Res. 2018 Nov;67:1-29.

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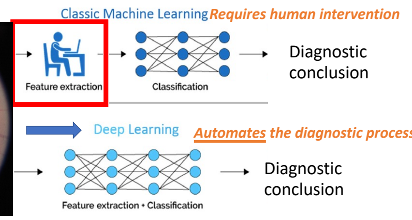
Machine learning *aids* in diagnosis
Deep learning can *make* the diagnosis



Schmidt-Erfurth U, Sadeghipour A, Gerendas BS, Waldstein SM, Bogunović H. Artificial intelligence in retina. Prog Retin Eye Res. 2018 Nov;67:1-29.

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What if erroneous information is generated?

(False positives/negatives)

Apple watch -
Did you fall?

I was shaking the sunscreen to the end of the tube.

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Additional terminology

Machine Learning (ML)

Deep Neural Networks (DNN) / Deep Learning

Convolutional Neural Networks (CNN)

Redundancies!

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What is the difference between classic machine learning and deep learning?

Classic machine learning
- Learning to play checkers
- Learning to win at checkers

Deep learning
- Learning to play chess, then
- Learning to beat a grand-master at chess

Can you see the danger here?

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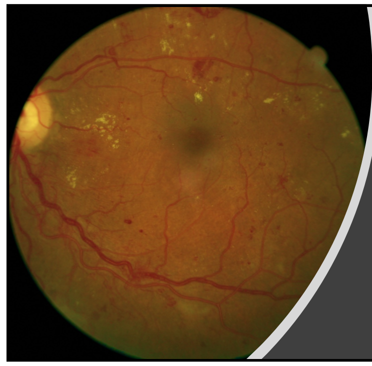

Diabetic retinopathy -

The "poster child" for the application of AI?

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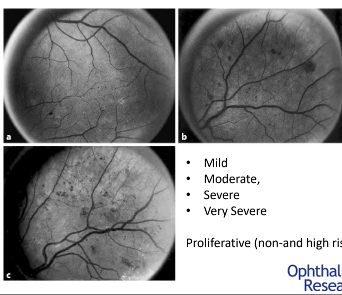
KARGER

Solomon SD, Goldberg MF ETDRS Grading of Diabetic Retinopathy: Still the Gold Standard? Ophthalmic Res. 2019 Aug 27:1-6.

Standard photographs 1, 2A

2B



- Mild
- Moderate,
- Severe
- Very Severe

Proliferative (non-and high risk)

© 2019 S. Karger AG, Basel

Ophthalmic Research

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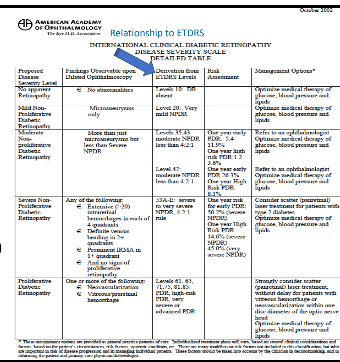
Another algorithm for diabetic retinopathy staging

The diabetic retinopathy disease severity scale DRSS

(note detailed *descriptions and levels*)



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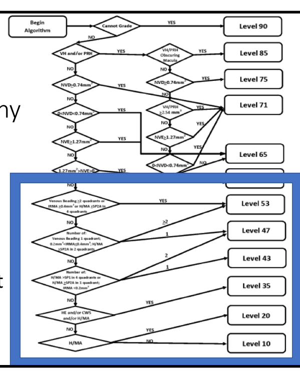
Automated algorithm for diabetic retinopathy

Trains machines in image reading

Focus on this segment



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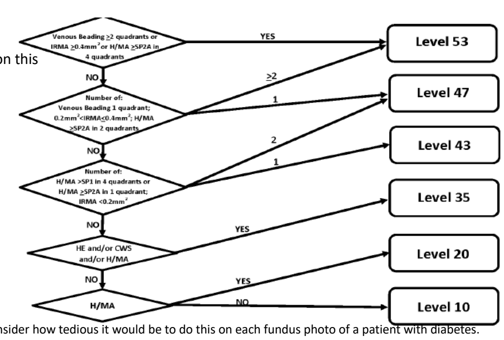
Focus on this



Consider how tedious it would be to do this on each fundus photo of a patient with diabetes. It's easier to have a machine decide on the 1's and 0's

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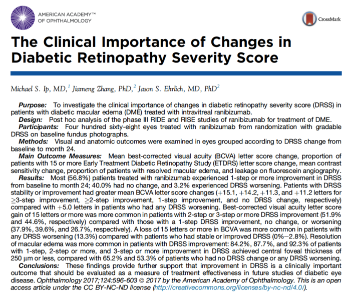
Why would such an exacting staging system have any significance?



AMERICAN ACADEMY™ OF OPHTHALMOLOGY

The Clinical Importance of Changes in Diabetic Retinopathy Severity Score

Michael S. Ip, MD,[1] Jiameng Zhang, PhD,[2] Jason S. Ehrlich, MD, PhD[2]

Purpose: To investigate the clinical importance of changes in diabetic retinopathy severity score (DRSS) in patients with diabetic macular edema (DME) treated with intravitreal ranibizumab.
Design: Post hoc analysis of the phase III RIDE and RISE studies of ranibizumab for treatment of DME.
Participants: Four hundred sixty-eight eyes treated with ranibizumab from randomization with gradable DRSS on baseline fundus photographs.
Methods: Visual and anatomic outcomes were examined in eyes grouped according to DRSS change from baseline to month 24.
Main Outcome Measures: Mean best-corrected visual acuity (BCVA) letter score change, proportion of patients with 15 or more Early Treatment Diabetic Retinopathy Study (ETDRS) letter score change, mean contrast sensitivity change, proportion of patients with resolved macular edema, and leakage on fluorescein angiography.
Results: Most (56.8%) patients treated with ranibizumab experienced 1-step or more improvement in DRSS from baseline to month 24; 40.0% had no change, and 3.2% experienced DRSS worsening. Patients with DRSS stability or improvement had greater mean BCVA letter score changes (+15.1, +14.2, +11.3, and +11.2 letters for ≥3-step improvement, ≥2-step improvement, 1-step improvement, and no DRSS change, respectively) compared with +5.0 letters in patients who had any DRSS worsening. Best-corrected visual acuity letter score gain of 15 letters or more was more common in patients with 2-step or 3-step or more DRSS improvement (51.9% and 44.6%, respectively) compared with those with a 1-step DRSS improvement, no change, or worsening (37.9%, 39.6%, and 26.7%, respectively). A loss of 15 letters or more in BCVA was more common in patients with any DRSS worsening (13.3%) compared with patients who had stable or improved DRSS (0%–2.8%). Resolution of macular edema was more common in patients with DRSS improvement: 84.2%, 87.7%, and 92.3% of patients with 1-step, 2-step or more, and 3-step or more improvement in DRSS achieved central foveal thickness of 250 µm or less, compared with 65.2% and 53.3% of patients who had no DRSS change or any DRSS worsening.
Conclusions: These findings provide further support that improvement in DRSS is a clinically important outcome that should be evaluated as a measure of treatment effectiveness in future studies of diabetic eye disease. *Ophthalmology 2017;124:596-603 © 2017 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

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Conclusions
(post-hoc analysis of RIDE and RISE data)

- 58.6% of patients treated for DME with ranibizumab showed at least a one-step (*not level*) improvement @ 24 months.
- 40% had no improvement and 3.2% had regression.
- Patients with stability or improvement (98.6%) had BSCVA *gains* of 15.1, 14.2, 11.3 and 11.2 ETDRS letters for 3-, 2-, 1- and No-step (*not level*) improvement.

Clinically significant improvement in staging and performance!

Ip MS, Zhang J, Ehrlich JS. The Clinical Importance of Changes in Diabetic Retinopathy Severity Score. Ophthalmology. 2017 May;124(5):596-603.

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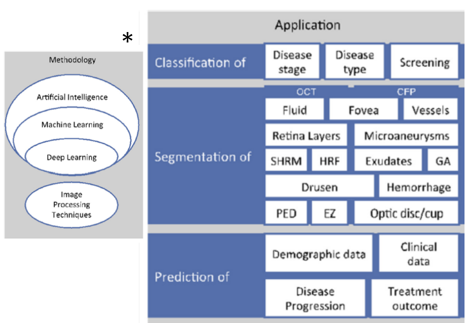

- Classification
- Segmentation
- Prediction

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Evolution of automated analysis for diabetic retinopathy

Autonomous artificial intelligence in a setting of *non-contact patient care*

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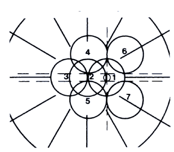
Remote screening for NPDR

- Joslin Vision Network™ (JVN) [1,2] 2001-2003
  - Compared seven standard field 35-mm stereoscopic color fundus photographs (ETDRS) using nonmydriatic digital-video color retinal images *with favorable results.* [3]



1. Bursell SE, Cavallerano JD, Cavallerano AA, Clermont AC, Birkmire-Peters D, Aiello LP, Aiello LM. Stereo non- mydriatic digital-video color retinal imaging compared with Early Treatment Diabetic Retinopathy Study seven standard field 35-mm stereo color photos for determining level of diabetic retinopathy. Ophthalmology. 2001;108(3): 572–85.

2. Cavallerano AA, Cavallerano JD, Katalinic P, Tolson AM, Aiello LP, Aiello LM, Joslin Vision Network Clinical Team. Use of Joslin Vision Network digital-video nonmy- driatic retinal imaging to assess diabetic retinopathy in a clinical program. Retina. 2003;23(2):215–23.

3. 3. Bursell SE, Cavallerano JD, Cavallerano AA, Clermont AC, Birkmire-Peters D, Aiello LP, Aiello LM; Joslin Vision Network Research Team. Stereo nonmydriatic digital-video color retinal imaging compared with Early Treatment Diabetic Retinopathy Study seven standard field 35-mm stereo color photos for determining level of diabetic retinopathy. Ophthalmology. 2001 Mar;108(3):572-85.

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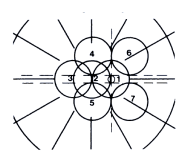

Remote screening for NPDR

Key conclusions:

- Image evaluation by trained readers comparable to standard (7-field) dilated images
- NPDR level assessed accurately
- The protocol identified those requiring management of significant vision-threatening conditions
- It is an appropriate tool for enhancing access to recommended eye examinations
- It is ***NOT*** a replacement for comprehensive eye evaluations

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Every silver lining has a cloud . . .

Advantages

- Greater adherence to follow-up ophthalmic (dilated fundus examination) and endocrinologic care.
- Improved characterization of early fundus changes*

Potential barriers

- Obtaining optimal gradable images (media opacities, small pupil,
- Presence of co-morbidities (e.g., AMD, glaucoma)

**Ophthalmoscopy fails to detect about half of microaneurysms confirmed by trained readers. [Recall OHTS]*

Conlin PR, Fisch BM, Cavallerano AA, Cavallerano JD, Bursell SE, Aiello LM. Nonmydriatic teleretinal imaging improves adherence to annual eye examinations in patients with diabetes. J Rehabil Res Dev. 2006 Sep-Oct;43(6):733-40.

Kinyoun JL, Martin DC, Fujimoto WY, Leonetti DL. Ophthalmoscopy versus fundus photographs for detecting and grading diabetic retinopathy. Invest Ophthalmol Vis Sci. 1992 May;33(6):1888-93.

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Some Recent Advances in Assessing NPDR

- 7-field fundus photography (Gold Standard - posterior pole)
- Ultrawide fundus photography (for Predominantly Peripheral Diabetic Retinopathy PPDR) 2015-2016

Silva PS, Horton MB, Clary D, et al.. Identification of Diabetic Retinopathy and Ungradable Image Rate with Ultrawide Field Imaging in a National Teleophthalmology Program. Ophthalmology. 2016 Jun;123(6):1360-7. doi: 10.1016/j.ophtha.2016.01.043. Epub 2016 Mar 2.

Silva PS, Dela Cruz AJ, Ledesma MG, et al. Diabetic Retinopathy Severity and Peripheral Lesions Are Associated with Nonperfusion on Ultrawide Field Angiography. Ophthalmology. 2015 Dec;122(12):2465-72. doi: 10.1016/j.ophtha.2015.07.034. Epub 2015 Sep 6.

Silva PS, Cavallerano JD, Haddad NM, et al. Peripheral Lesions Identified on Ultrawide Field Imaging Predict Increased Risk of Diabetic Retinopathy Progression over 4 Years. Ophthalmology. 2015 May;122(5):949-56. doi: 10.1016/j.ophtha.2015.01.008. Epub 2015 Feb 19

- And most recently . . . *Automated* assessment of diabetic retinopathy.

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Into the periphery - revealing an unmet need

- Recognition of the relative inaccessibility but significance of predominantly peripheral diabetic retinopathy (PPDR) lead to further refinements in diagnostic imaging.
  - 80% coverage,
  - PPLs as sentinels for progression of NPDR,
  - substantially increased image readability,
  - visualization of significantly more retinal abnormalities,
  - more accurate characterization and quantitation of total retinal nonperfusion

Which can lead to *improved outcomes* for managing NPDR in general and diabetic macular edema (DME) in particular.

Ashraf M, Shokrollahi S, Salongcay RP, Aiello LP, Silva PS. Diabetic retinopathy and ultrawide field imaging. Semin Ophthalmol. 2020 Jan 2;35(1):56-65.

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Contemporary Remote Triage Strategies

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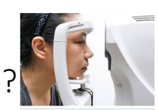
Medscape October 19, 20?

"The Future of Teleretinal Imaging for Diabetic Retinopathy *Screening*"



Take Note

Telemedicine has proven value as a screening tool in the detection of diabetic retinopathy (DR).

Certain obstacles need to be overcome before telemedicine DR screening programs can be implemented in the US on a wide basis.

These hurdles involve patient standardization of imaging methods, DR grading, and other telemedicine processes; reimbursement policies; and establishment of an infrastructure to manage those patients identified with DR in a time-sensitive manner.

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Medscape October 19, *2016*

"The Future of Teleretinal Imaging for Diabetic Retinopathy *Screening*"

Hurdles to navigate

- Patient acceptance
- Standardization of imaging and grading protocols
- Reimbursement policies
- Establishment of time-efficient infrastructure

Ogunyemi O, George S, Patty L, Teklehaimanot S, Baker R. Teleretinal screening for diabetic retinopathy in six Los Angeles urban safety-net clinics: final study results. AMIA Annu Symp Proc. 2013 Nov 16;2013:1082-8.

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I Dx-DR is FDA cleared

FDA grants breakthrough device designation to artificial intelligence diagnostic system

February 5, 2018

The FDA is expediting the review of an artificial intelligence-based diagnostic system for the autonomous detection of diabetic retinopathy, according to a press release from IDx.

The company filed a de novo submission, and the FDA granted the system breakthrough device designation, allowing it to receive expedited review, the release said.

"The FDA's designation of IDx-DR as a breakthrough device confirms what we have believed for a long time," **Michael Abramoff, MD, PhD,** the company's founder and president, said in the release. "The health care system desperately needs a more efficient and cost-effective way to detect diabetic retinopathy. Too many patients go blind needlessly because they aren't diagnosed in time."

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Breaking News!

Medscape

AI Screening for Diabetic Retinopathy Moves to Retail Clinics

Roxanne Nelson, RN, BSN

November 26, 2019

However, an ophthalmologist won't make the diagnosis at the clinic; instead, it will be made by an artificial intelligence (AI) system called IDx-DR. Testing will be offered through CarePortMD, the first retail health clinic to adopt this type of AI diagnostic technology, and offered at clinics inside Albertsons grocery stores. The second largest grocery chain in the United States, Albertsons added five CarePortMD clinics to stores in Delaware and Pennsylvania this year

2019

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Foundation for FDA clearance

Retina

Improved Automated Detection of Diabetic Retinopathy on a Publicly Available Dataset Through Integration of Deep Learning

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Citation: Abràmoff MD, Lou Y, Erginay A, et al. Improved automated detection of diabetic retinopathy on a publicly available dataset through integration of deep learning. *Invest Ophthalmol Vis Sci.* 2016;57:5200–5206. DOI:10.1167/iovs.16-19964

PURPOSE. To compare performance of a deep-learning enhanced algorithm for automated detection of diabetic retinopathy (DR), to the previously published performance of that algorithm, the Iowa Detection Program (IDP)–without deep learning components–on the same publicly available set of fundus images and previously reported consensus reference standard set, by three US Board certified retinal specialists.

METHODS. We used the previously reported consensus reference standard of referable DR (rDR), defined as International Clinical Classification of Diabetic Retinopathy moderate, severe nonproliferative (NPDR), proliferative DR, and/or macular edema (ME). Neither Messidor-2 images, nor the three retinal specialists setting the Messidor-2 reference standard were used for training IDx-DR version X2.1. Sensitivity, specificity, negative predictive value, area under the curve (AUC), and their confidence intervals (CIs) were calculated.

RESULTS. Sensitivity was 96.8% (95% CI: 93.3%–98.8%), specificity was 87.0% (95% CI: 84.2%–89.4%), with 6/874 false negatives, resulting in a negative predictive value of 99.0% (95% CI: 97.8%–99.6%). No cases of severe NPDR, PDR, or ME were missed. The AUC was 0.980 (95% CI: 0.968–0.992). Sensitivity was not statistically different from published IDP sensitivity, which had a CI of 94.4% to 99.3%, but specificity was significantly better than the published IDP specificity CI of 55.7% to 63.0%.

CONCLUSIONS. A deep-learning enhanced algorithm for the automated detection of DR, achieves significantly better performance than a previously reported, otherwise essentially identical, algorithm that does not employ deep learning. Deep learning enhanced algorithms have the potential to improve the efficiency of DR screening, and thereby to prevent visual loss and blindness from this devastating disease.

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The algorithm – 3 categories of disease

Used a training base of 10,000 – 1.25M images and convolutional neural networks (CNN)

Using the previously reported ICDR and ME gradings, four levels of disease for each subject (per DRSS):

- DR – ICDR level 0 (no DR) or 1 (mild DR), and no ME
- Referable DR (rDR) – ICDR level 2 (moderate nonproliferative DR), 3 (severe nonproliferative DR), 4 (proliferative DR), or ME

Abramoff MD, et al. Improved Automated Detection of Diabetic Retinopathy on a Publicly Available Dataset Through Integration of Deep Learning. Invest Ophthalmol Vis Sci. 2016;57:5200–5206.

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The algorithm – 3 categories of disease

Used a training base of 10,000 – 1.25M images and convolutional neural networks (CNN)

Using the previously reported ICDR and ME gradings, four levels of disease for each subject (per DRSS):

- Vision threatening DR (vtDR) – ICDR level 3 (severe nonproliferative DR), 4 (proliferative DR), or ME. A new disease category for this study, to evaluate the performance on this category of disease.
- Macular edema, the adjudicated reference standard for the presence of ME. A new, separate category for this study, all subjects with ME appear in both vtDR and rDR.

Abramoff MD, et al. Improved Automated Detection of Diabetic Retinopathy on a Publicly Available Dataset Through Integration of Deep Learning. Invest Ophthalmol Vis Sci. 2016;57:5200–5206.

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Tabular results,

for any statisticians in the audience

TABLE. IDx-DR X2.1 Sensitivity, Specificity, Negative and Positive Predictive Value, and AUC and Corresponding 95% CIs for rDR Output to Detect rDR, ME, and vtDR, and vtDR Output to Detect vtDR

IDx Output For	Disease Level	Sensitivity (95% CI)	Specificity (95% CI)	Negative Predictive Value (95% CI)	Positive Predictive Value (95% CI)	AUC (95% CI)
rDR	rDR	96.8% (93.3%-98.8%)	87.0% (84.2%-89.4%)	99.0% (97.8%-99.6%)	67.4% (61.5%-72.9%)	0.980 (0.968, 0.992)
rDR	vtDR	100% (96.1%-100%)	N.A.	N.A.	N.A.	N.A.
rDR	ME	100% (95.6%-100%)	N.A.	N.A.	N.A.	N.A.
vtDR	vtDR	100.0% (96.1%-100.0%)	90.8% (88.5%-92.7%)	100.0% (99.5%-100.0%)	56.4% (48.4%-64.1%)	0.989 (0.984, 0.994)

N.A., not calculated.

What does AUC mean?

("…if it's not >90% nobody will read it.")

Abramoff MD, et al. Improved Automated Detection of Diabetic Retinopathy on a Publicly Available Dataset Through Integration of Deep Learning. Invest Ophthalmol Vis Sci. 2016;57:5200–5206. DOI:10.1167/iovs.16-19964

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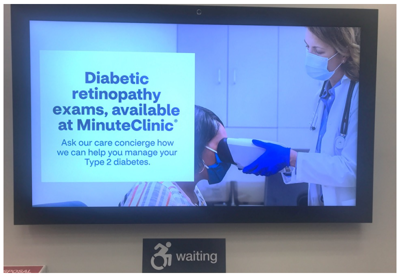
Fast forward . . .2022

At my local CVS



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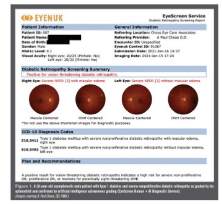
From Optometry Times

Embrace, don't fear, AI in diabetic retinopathy

May 11, 2021
A. Paul Chous, MA, OD, FAAO
Optometry Times Journal, May digital edition 2021, Volume 13, Issue 5



Challenges exist in diagnosing and grading diabetic retinopathy (DR). Multiple analyses show that many patients with diabetes are not receiving dilated eye examinations at recommended intervals, with

A. PAUL CHOUS, MA, OD, FAAO, has a practice emphasizing diabetes eye care and education in Tacoma, Washington.

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Where do we go from here?

"The era of subclinical diagnosis has begun and a novel approach to interpretation is required."
Schmidt-Erfurth U, Sadeghipour A, Gerendas BS, Waldstein SM, Bogunović H. Artificial intelligence in retina. Prog Retin Eye Res. 2018 Nov;67:1-29.

- If we are to retain control over our future, we will have to learn to harness output from intelligent algorithms and apply AI in a constructive manner (Safe, Efficacious and Equitable, SEE).
- Will home-based monitoring and imaging platforms equipped with AI be the next big step in retina?

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Durability & Longevity

With Cautions…(Peterson , ED. Machine Learning, Predictive Analytics, and Clinical Practice: Can the Past Inform the Present? 2019 JAMA) Published Online: November 22, 2019. doi:10.1001/jama.2019.17831

- The widespread availability of EHR data and the latest ML analytic techniques offer unique opportunities for achieving better health outcomes.
- Combined, data and ML will likely facilitate the development of numerous *predictive* analytic tools in medicine.
- However, before such advances can transform how clinical decisions are made, the challenges of effective application will need to be overcome.

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Demands of AI for healthcare

- Decrease costs without increasing burden on providers (like EHRs ?).
- Improve quality without imparting bias or violating privacy.

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Accurate outcomes, etc

"Regulatory and professional bodies should ensure the advanced algorithms meet accepted standards of clinical benefit, just as they do for clinical therapeutics and predictive biomarkers"

e.g., Does the algorithm apply equally to all clinical settings?

Parikh RB, Obermeyer Z, Navathe AS. Regulation of predictive analytics in medicine. Science 2019;363(6429):810-2.

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SEE paradigm - *S*afe, *E*fficacious and *E*thical

Channa R, Wolf R, Abramoff MD. Autonomous Artificial Intelligence in Diabetic Retinopathy: From Algorithm to Clinical Application. J Diabetes Sci Technol. 2021 May;15(3):695-698. doi: 10.1177/1932296820909900. Epub 2020 Mar 4. PMID: 32126819; PMCID: PMC8120059.

CopyDownload .nbibFormat: AMA APA MLA NLM

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S E E (+) truthful claims, privacy and security [1,2]

- ***S*afety** - *"First, do no harm."* -Hippocrates
  - Employs the *Sensitivity* metric (how many with the disease are correctly identified)
    - Early computer-assisted mammograms were less accurate for malignancy detection than non-computer-assisted. Fenton JJ, Taplin SH, Carney PA, et al. Influence of computer-aided detection on performance of screening mammography. N Engl J Med. 2007;356(14):1399-1409.
    - *AI will not replace the clinical examination but will be complementary to the clinician*

1. Channa R, Wolf R, Abramoff MD. Autonomous Artificial Intelligence in Diabetic Retinopathy: From Algorithm to Clinical Application. J Diabetes Sci Technol. 2021 May;15(3):695-698.
2. Augmented Intelligence in health care. AMA Foundational Policy Annual 2018.

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S E E (+) truthful claims, privacy and security [1,2]

- ***E*fficacy**
  - Uses the *Specificity* metric (how many normal are correctly identified)

1. Channa R, Wolf R, Abramoff MD. Autonomous Artificial Intelligence in Diabetic Retinopathy: From Algorithm to Clinical Application. J Diabetes Sci Technol. 2021 May;15(3):695-698.
2. Augmented Intelligence in health care. AMA Foundational Policy Annual 2018.

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S E E (+) truthful claims, privacy and security [1,2]

- ***E*quitable**
  - Is the algorithm applicable to all using the "diagnosability" and "bias" metrics.
    - *Valid* vs. uninterpretable result
    - Stratification of sensitivity and specificity by race, ethnicity and age to identify differences that lead to *bias* in generalizing results.

1. Channa R, Wolf R, Abramoff MD. Autonomous Artificial Intelligence in Diabetic Retinopathy: From Algorithm to Clinical Application. J Diabetes Sci Technol. 2021 May;15(3):695-698.
2. Augmented Intelligence in health care. AMA Foundational Policy Annual 2018.

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WE HAVE ENTERED THE ERA OF "NO-TOUCH" PATIENT EXAMINATION

and it has been accelerated by the pandemic

The Mayo Clinic Jacksonville set a strategic benchmark of 30% of *eligible* visits being online by 2030.

↓

At the beginning of 2022, 60% of eligible visits were being conducted online!

Klaas J.Wierenga, M.D. Personal communication March 8, 2022

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Artificial Intelligence

- is transforming medicine
- is making inroads in the ophthalmic space
- will allow telemetric data analysis
- is here to stay in our daily lives and practices
- *will be as transformative for optometry as the last few decades of scope-of-practice expansion*

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