Medical Applications of Artificial Intelligence: Lessons from Dermatology

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Disclosures

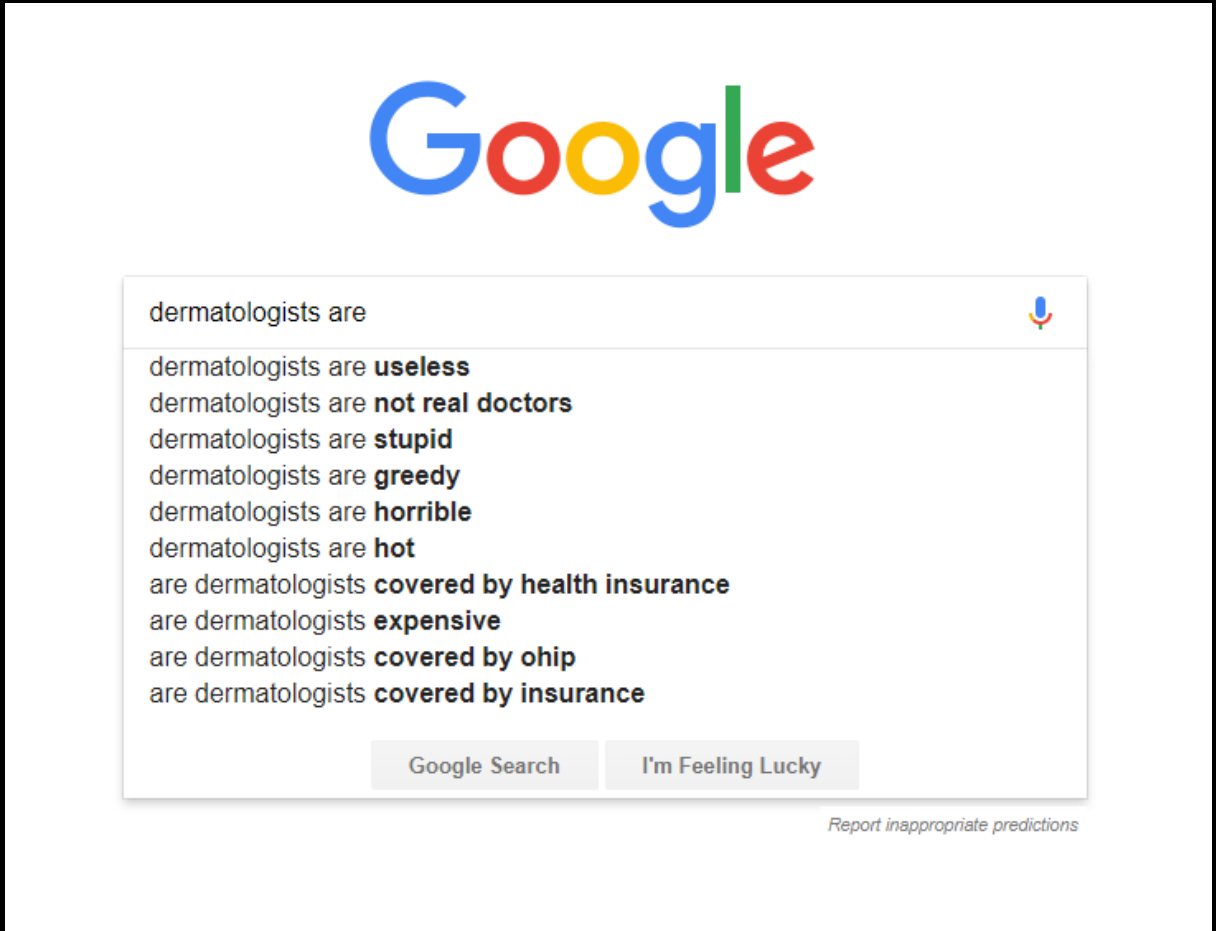
- Enspectra: Consultant
- Grant support: Melanoma Research Alliance, Stanford Predictives and Diagnostics Accelerator
- No relevant disclosures

Melanoma Research Alliance

Objectives

- Discuss applications of artificial intelligence within dermatology
- Highlight challenges and pitfalls to effective and equitable application of AI

This is AI


Google
dermatologists are
dermatologists are useless
dermatologists are not real doctors
dermatologists are stupid
dermatologists are greedy
dermatologists are horrible
dermatologists are hot
are dermatologists covered by health insurance
are dermatologists expensive
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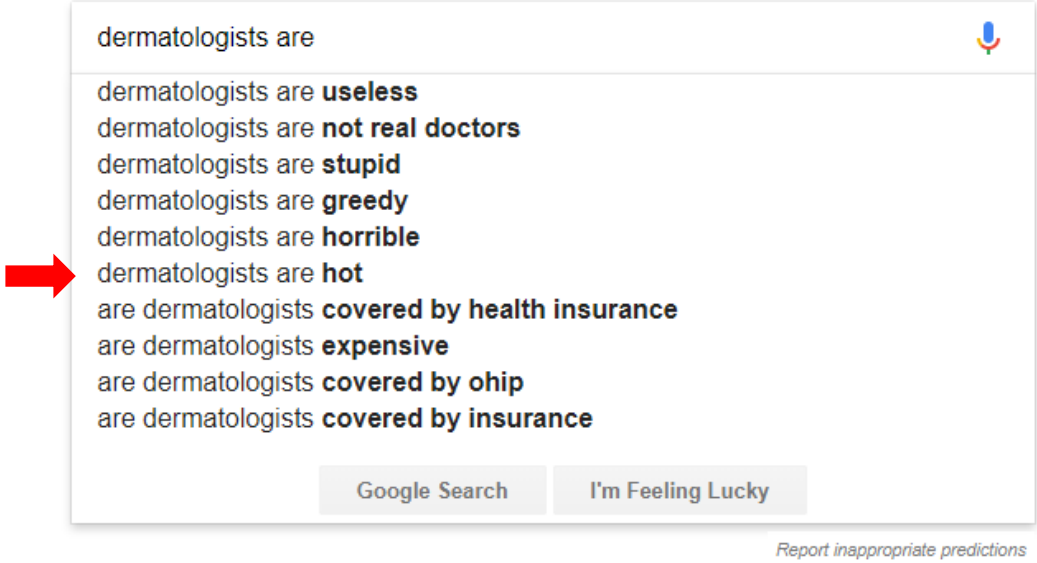
are dermatologists covered by insurance
Google Search
I'm Feeling Lucky
Report inappropriate predictions

This is AI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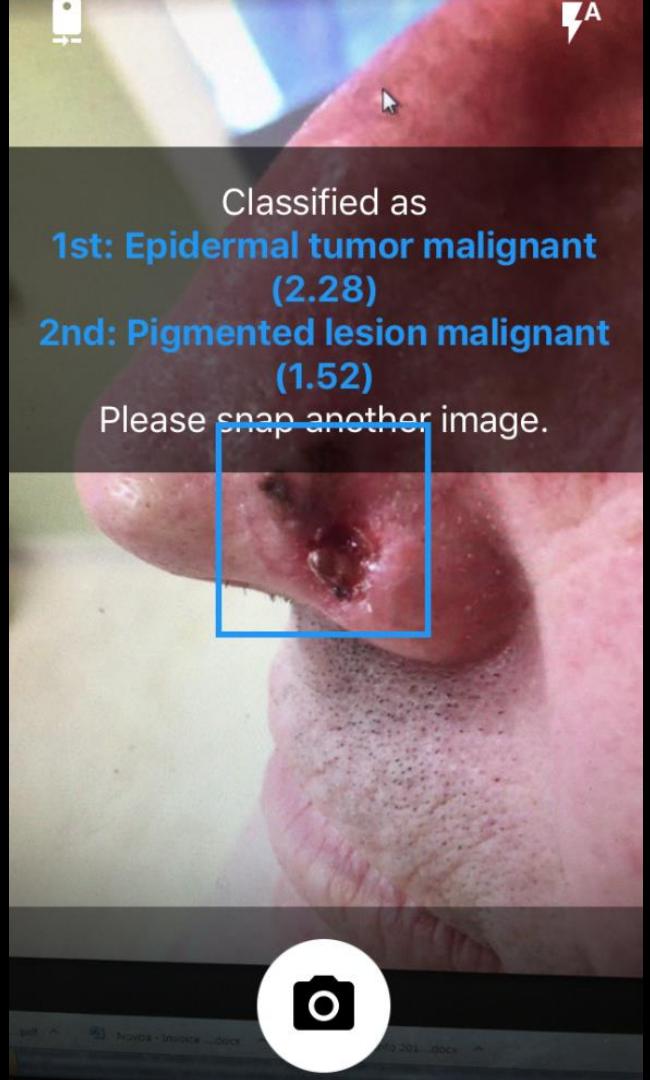
This is AI

This is AI

https://thispersondoesnotexist.com

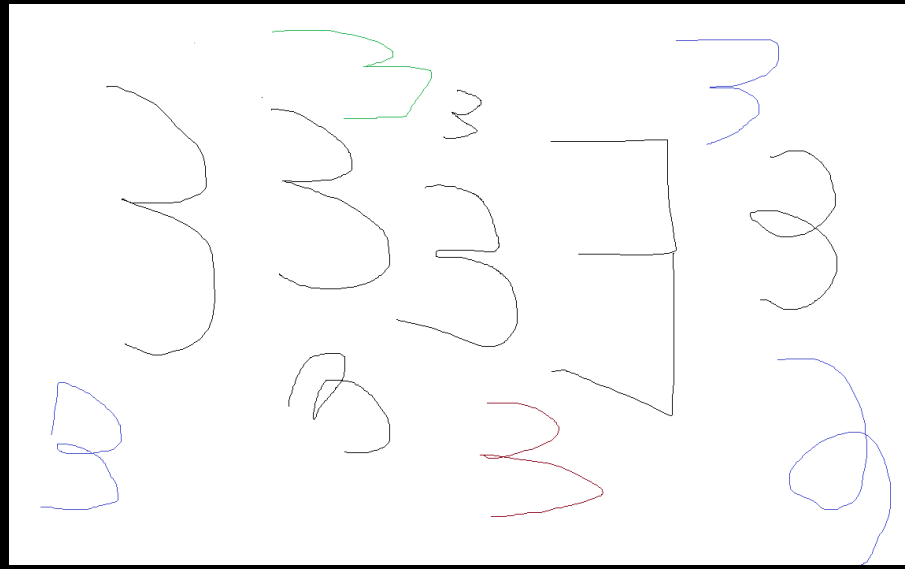

Classified as
1st: Epidermal tumor malignant (2.28)
2nd: Pigmented lesion malignant (1.52)
Please snap another image.

Early artificial intelligence

- Teaching a computer to analyze the world
- Decades old→ 1956
- Top-down

Early artificial intelligence

- Incredibly fragile
- Would not be able to read “3”

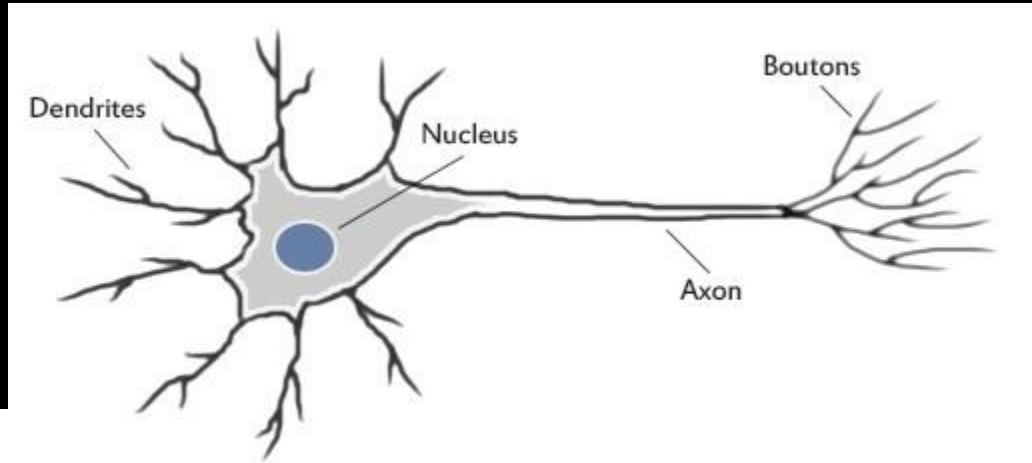


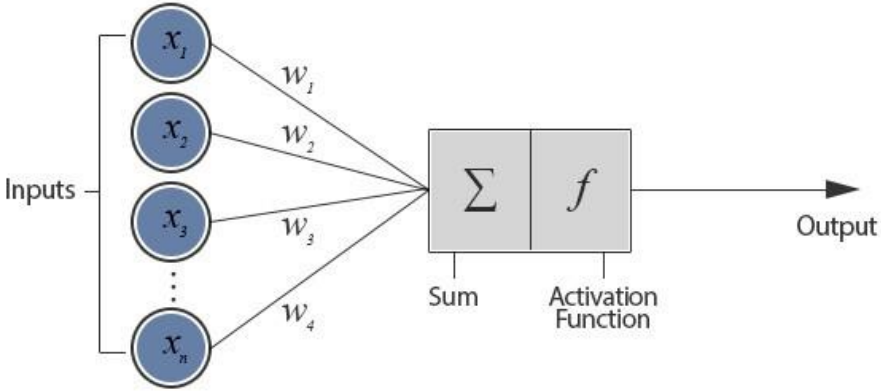
Early artificial intelligence

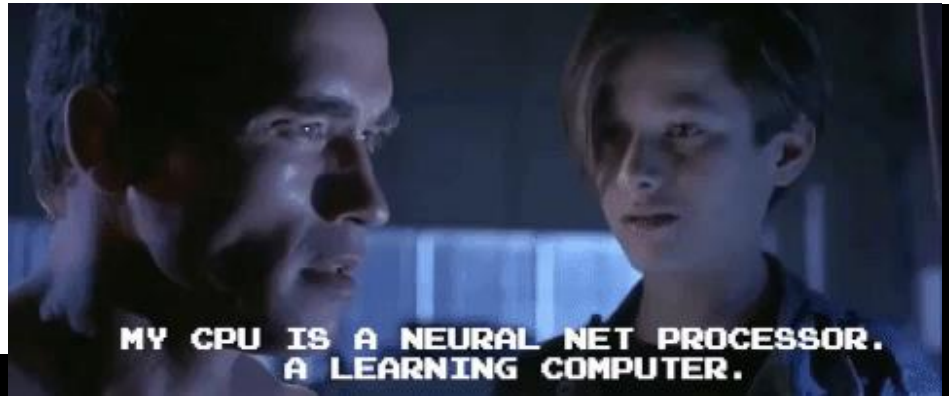
- Bottom-up
  - Observe the world and its rules, learn from there
  - Out of favor for years

1960s: Neural Networks

- Math equations modeled on human neurons
- Inputs
- If > threshold, “fires”



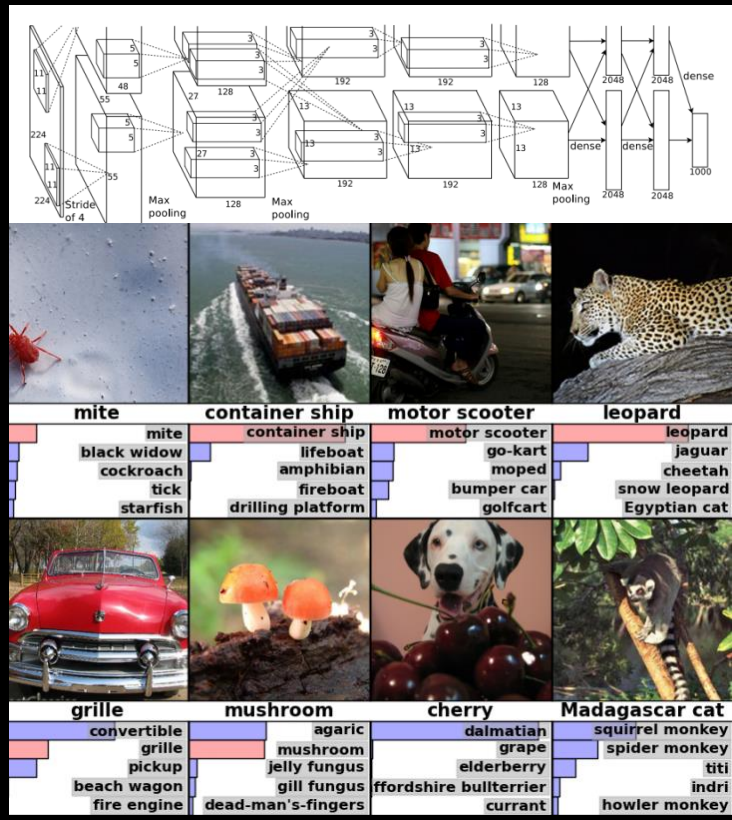




Harsh Pokharna, 2016. Introduction to Neural Networks. Medium.com

Advances in AI

- Breakthroughs in artificial intelligence over past 9 years
- Convolutional neural networks+large databases+processing power= **deep learning**



Krizhevsky, Sutskever, Hinton et al. 2012

AI and Dermatology

- 30+ years
- “Handcrafted features” (ex. ABCDEs)
  - Labor-intensive
  - Fragile

Dermatologica. 1986;173(2):79-84.

Expert systems in dermatology: the computer potential. The example of facial tumour diagnosis.

Finlay AY, Hammond P.

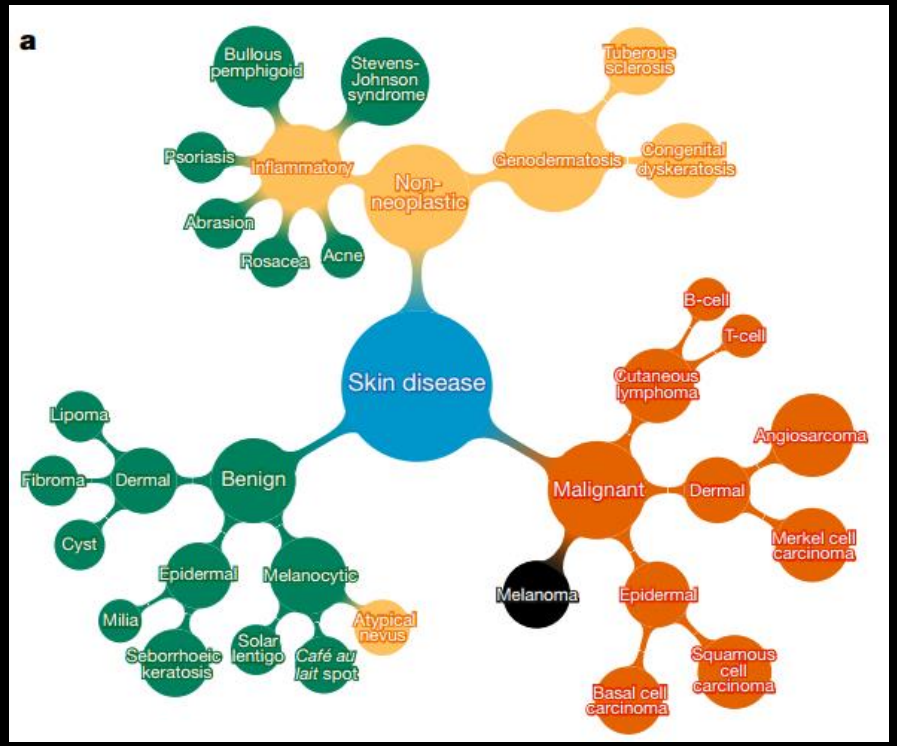
Abstract

The expert system approach to computer diagnosis uses a non-algorithmic method to represent and manipulate an expert's knowledge and reasoning. This information, which may be provided by a dermatologist, is represented by rules in a logic-based computer language in order to provide interactive and explanatory features. The major advantages of using expert system techniques for computer-aided diagnosis in dermatology are that knowledge is made explicit, the heuristic nature of an expert's knowledge can be more easily captured and the more easily readable programs make modification easier. In the example described, the differential diagnosis of nine facial skin tumours was considered. The program, using the language 'micro-PROLOG' in an expert system shell 'APES', consists of 'rules' and 'facts' which define a relationship between patient and symptom, symptom and disease or disease and therapy. The 'strength' of each relationship is defined and 'key symptoms' identified. The system finally offers a diagnosis, an estimate of certainty and simple management advice.

PMID: 3539654

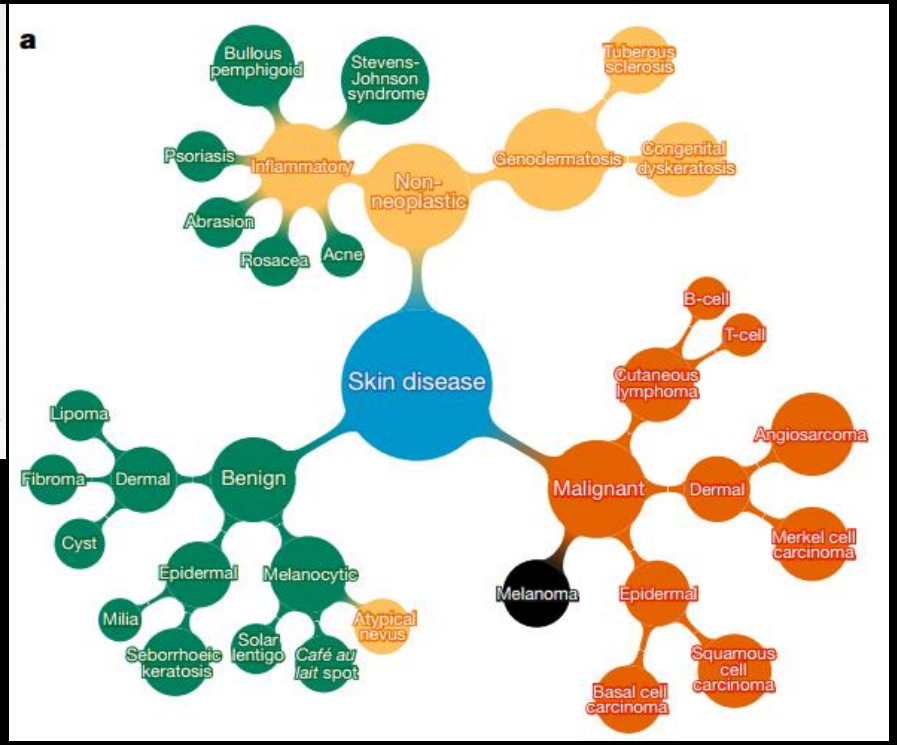
Esteva et al (2017) methods:

- 129,000+ image dataset
  - Internet+Stanford images
  - Variety of labels
- Biopsy-proven databases
- Visual taxonomy



Methods

https://www.melissacarmon.com/artist-blog/in-search-of-the-lost-cyan-manganese-blue

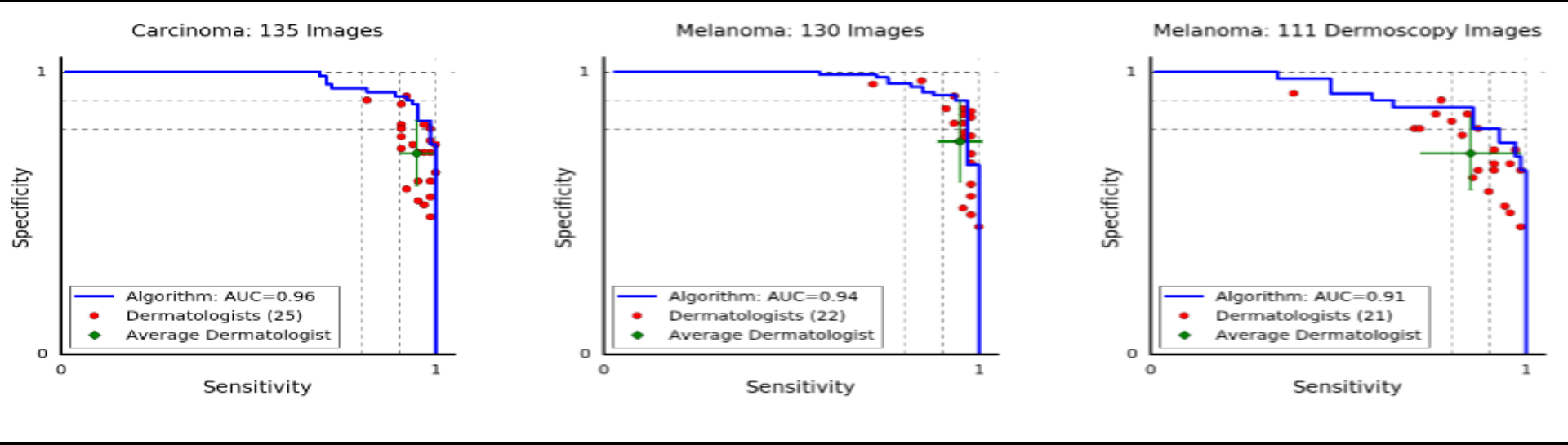


https://www.melissacarmon.com/artist-blog/in-search-of-the-lost-cyan-manganese-blue

Esteva et al, 2017

Increasing the dataset

Results: Biopsy vs Reassure

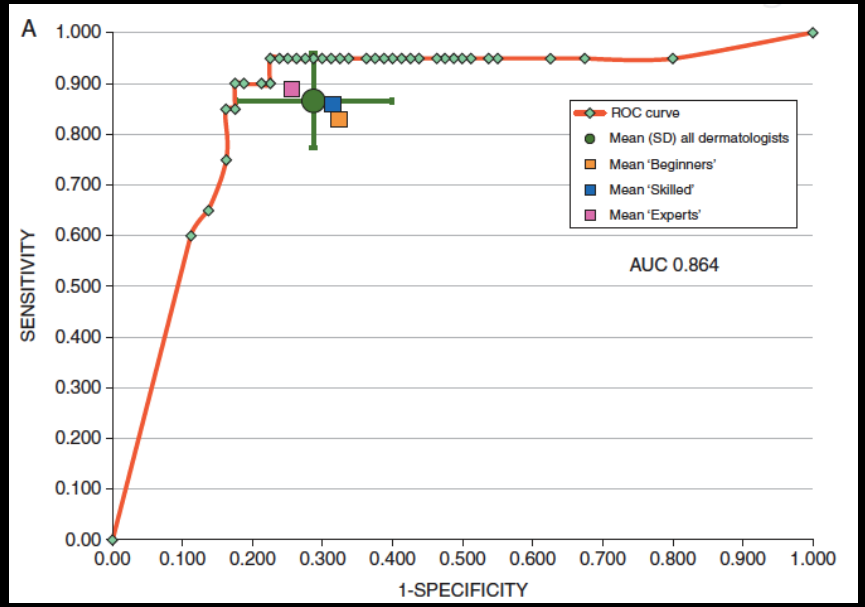


Esteva et al, 2017

Advances in Derm AI

Man against machine: diagnostic performance of a deep learning convolutional neural network for dermoscopic melanoma recognition in comparison to 58 dermatologists

- Demonstrated excellent performance by CNNs
- Compared different levels of expertise
- Provided clinical information



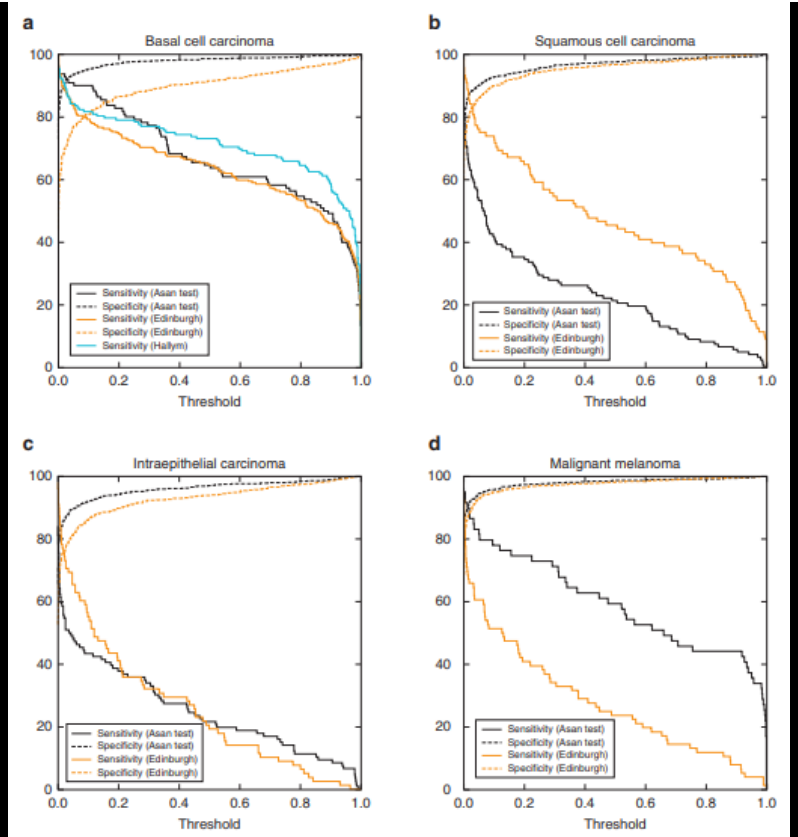
Haenssle HA et al, 2018

Advances in Derm AI

- Released dataset
- Differential performance based on dataset/ skin type
- https://modelderm.com

Classification of the Clinical Images for Benign and Malignant Cutaneous Tumors Using a Deep Learning Algorithm

Seung Seog Han[1,7], Myoung Shin Kim[2,7], Woohyung Lim[3], Gyeong Hun Park[4], Ilwoo Park[5] and Sung Eun Chang[6]



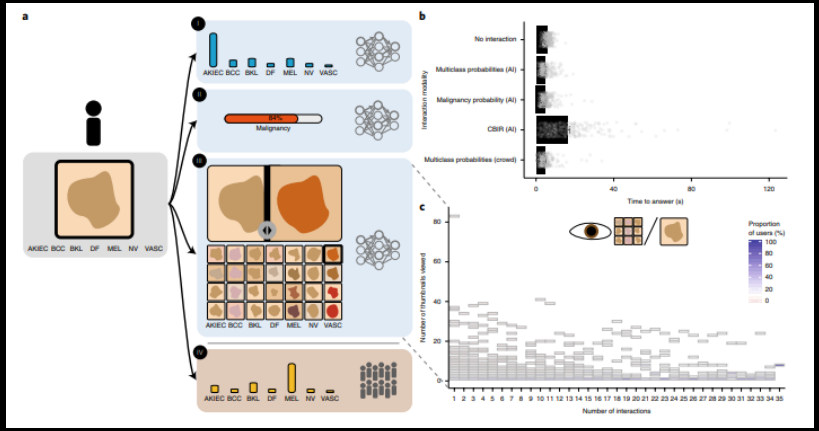
Human+AI: 2020

- Online *in-silico* evaluation of lesions
- More improvement for novices
- Performed best w showing classes and probabilities
- Confidence and experts
- Faulty AI misled all participants

nature medicine
LETTERS
https://doi.org/10.1038/s41591-020-0942-0
Check for updates

Human–computer collaboration for skin cancer recognition

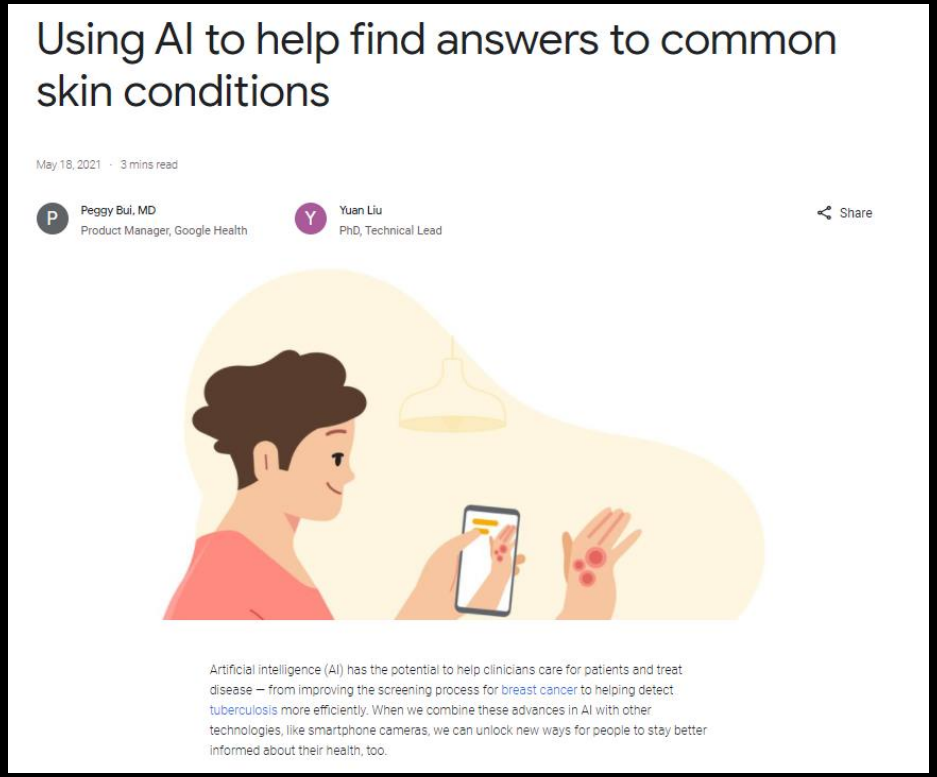
Philipp Tschandl[1,17], Christoph Rinner[2,17], Zoe Apalla[3], Giuseppe Argenziano[4], Noel Codella[5], Allan Halpern[6], Monika Janda[7], Aimilios Lallas[3], Caterina Longo[8,9], Josep Malvehy[10,11], John Paoli[12,13], Susana Puig[10,11], Cliff Rosendahl[14], H. Peter Soyer[15], Iris Zalaudek[16] and Harald Kittler[1]



NATURE MEDICINE | VOL 26 | AUGUST 2020 | 1229–1234 | www.nature.com/naturemedicine

Advances in Derm AI: 2021

- Google released **public** facing app for skin conditions
- Significant challenges
  - Representation?
  - Positive predictive value?



Using AI to help find answers to common skin conditions

May 18, 2021 · 3 mins read

Peggy Bui, MD
Product Manager, Google Health

Yuan Liu
PhD, Technical Lead

Share

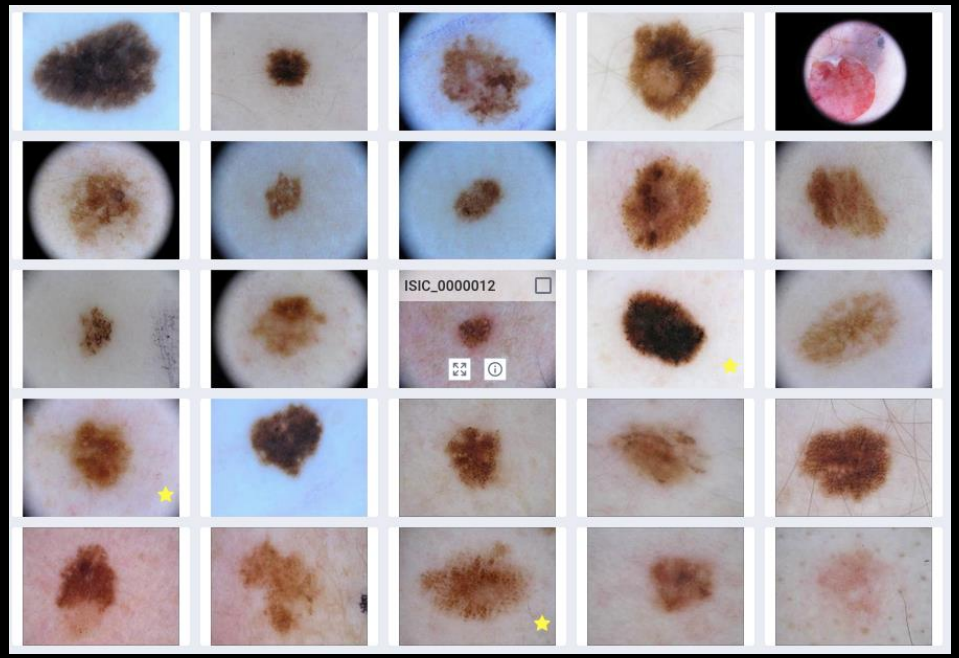
Artificial intelligence (AI) has the potential to help clinicians care for patients and treat disease — from improving the screening process for breast cancer to helping detect tuberculosis more efficiently. When we combine these advances in AI with other technologies, like smartphone cameras, we can unlock new ways for people to stay better informed about their health, too.

Derm Challenges: Absence of Datasets

- Deep learning is data hungry
- Giant derm datasets lacking
- Many systems don’t talk to one another

Solutions: Open source databases

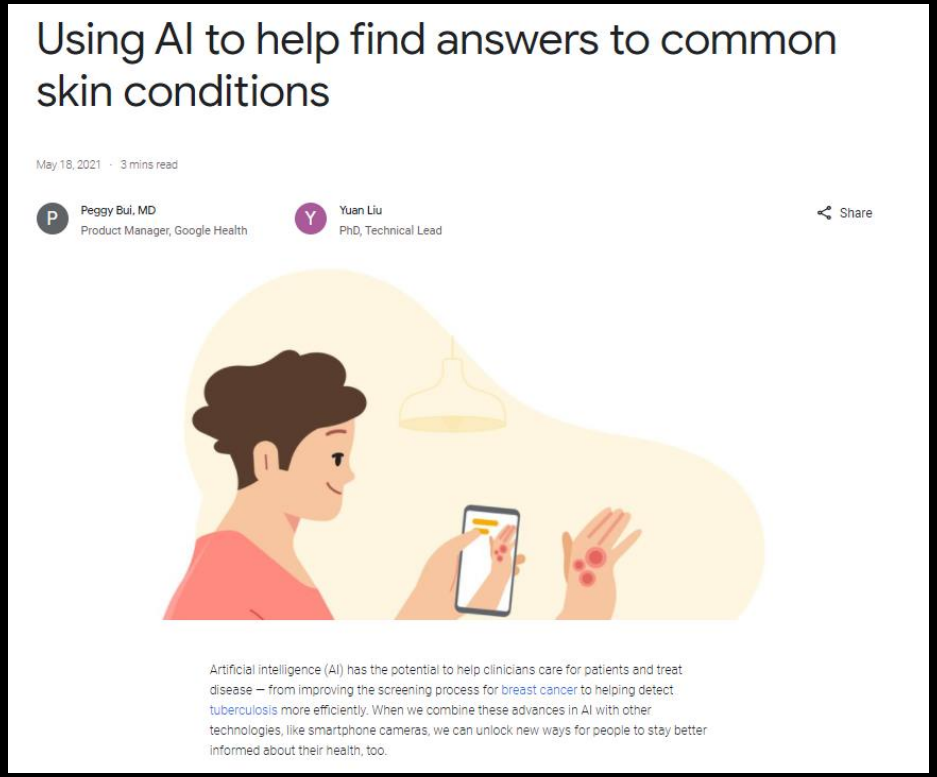
- Publicly available
- Standards around images?
- What kinds of images?
- Data collection



ISIC dataset

Challenge: Proper Assessment

- In-silico vs In-vivo
- Parameters (picture quality, lighting, focus, camera type)
- Does it improve care?
- How does it work *with* clinicians?



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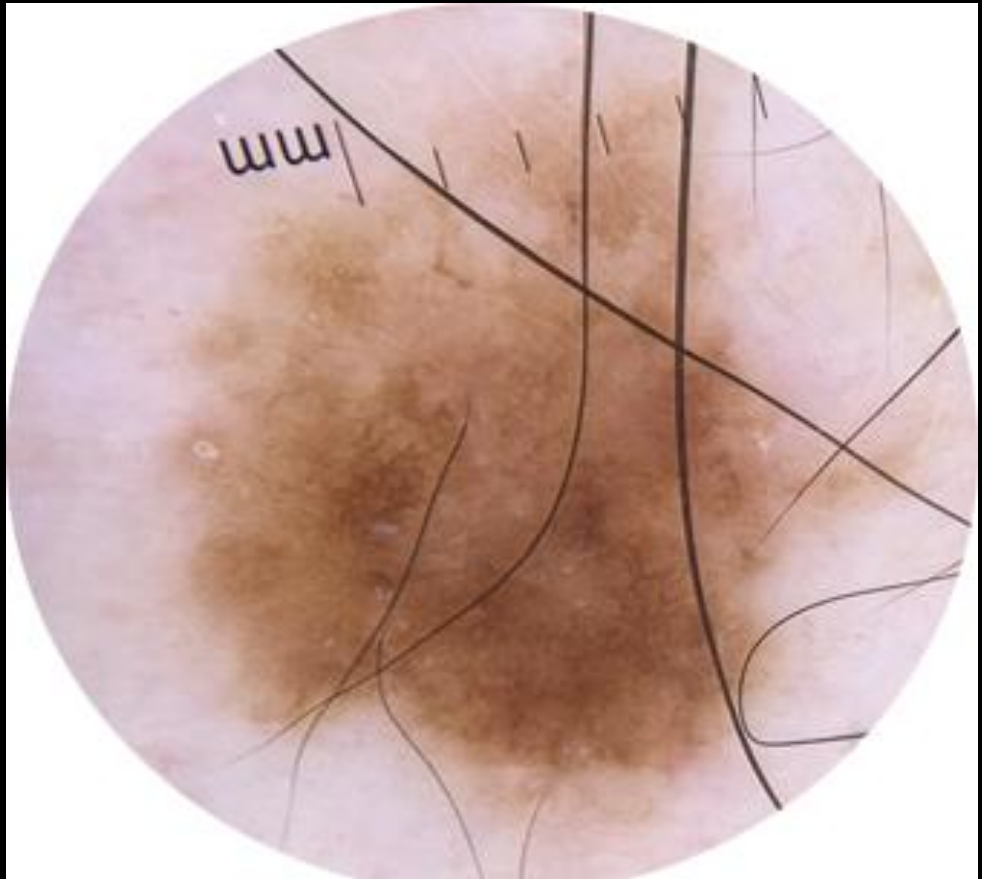
Derm Challenges: The Gold Standard (?)

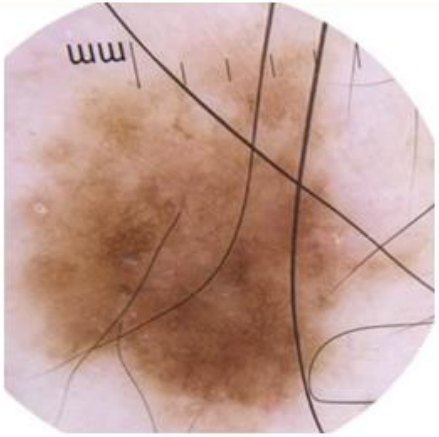
- Histopathology is traditional gold standard
- Elmore et al (BMJ, 2017)
  - Intraobserver agreement of 67% for melanocytic neoplasms (35% for moderate atypia, 63% for melanomas)
- 187 pathologists, 240 lesions

Pop Quiz

- 52 yo male from Argentina
- No prior history of skin cancer



ModelDerm in action



[beta] Please check focus and composition :

Low (0.00); Nonspecific skin lesion

Melanoma : Probably Not;
Observation and follow-up (1,2)

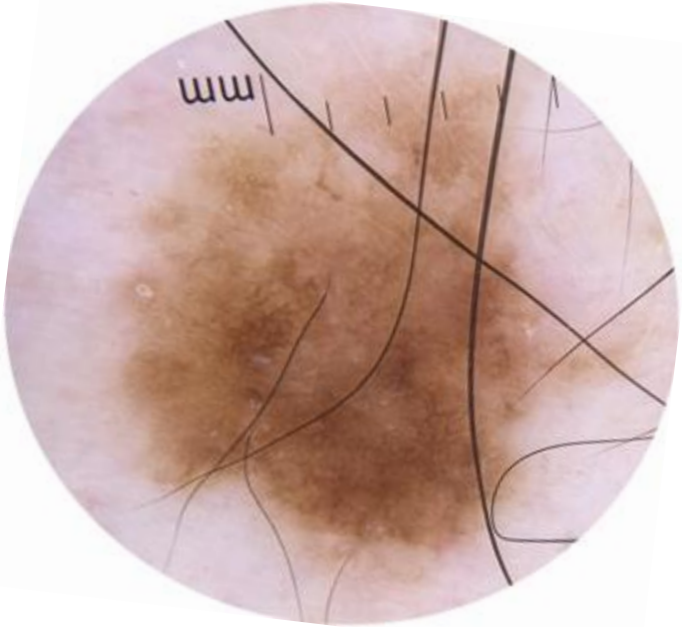
Malignancy prediction : Low (1,0)

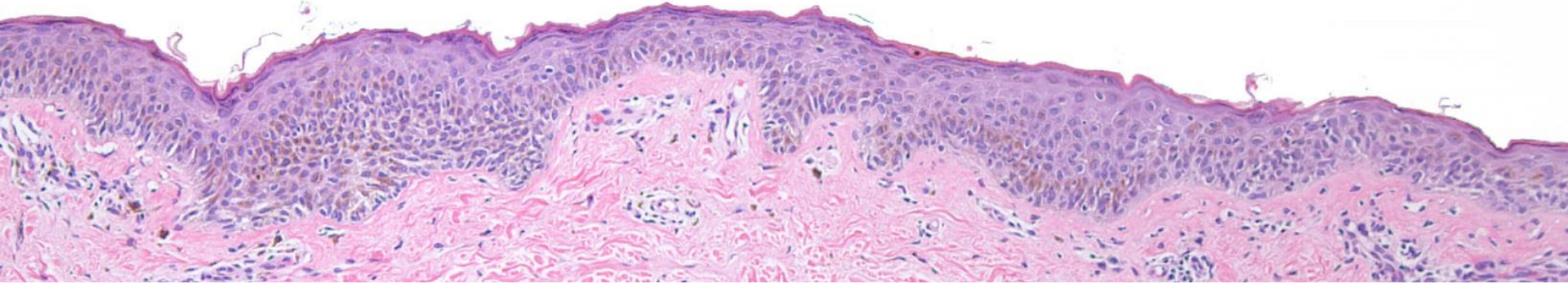
q0.00 0.93

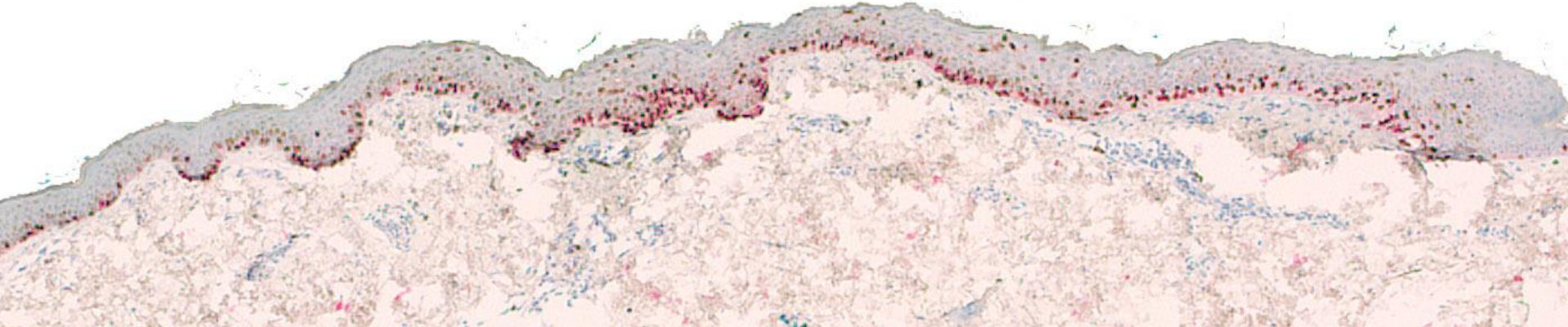
0.07n1.00M0.00N0.15;v.20180623

MANUAL CROP

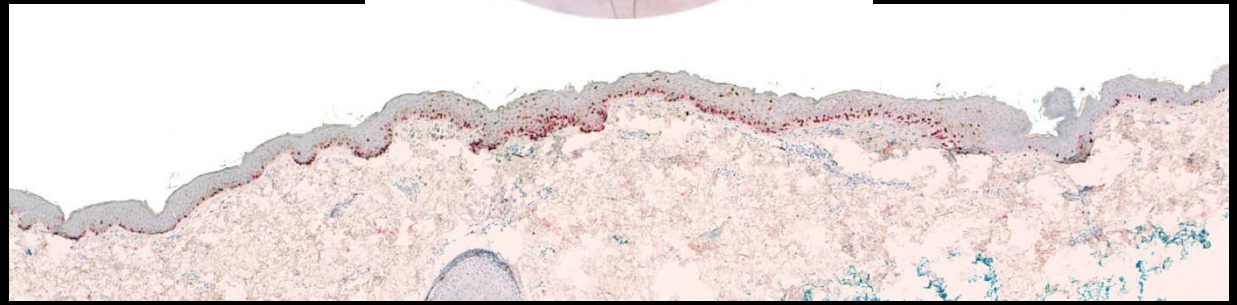
Screenshot Close





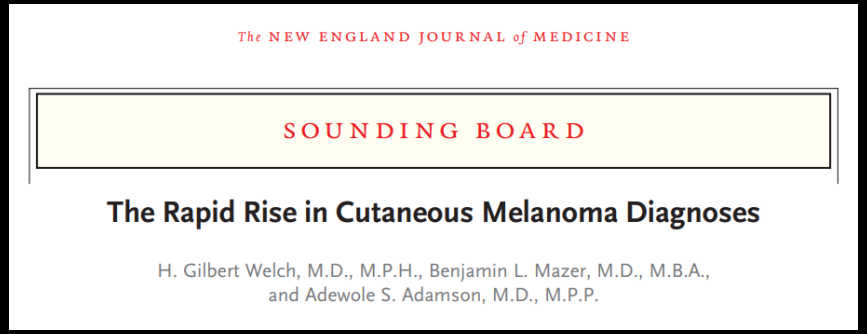


Challenge: Is this melanoma?



Are we over-diagnosing melanoma?

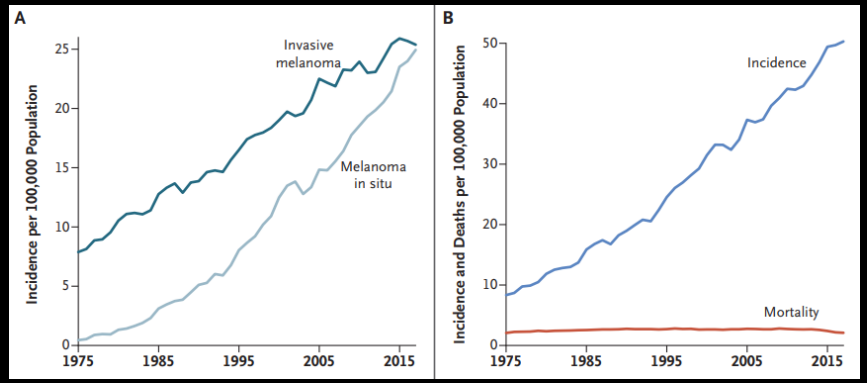
- Rapid increase in melanoma over past 5 decades


The NEW ENGLAND JOURNAL of MEDICINE

SOUNDING BOARD

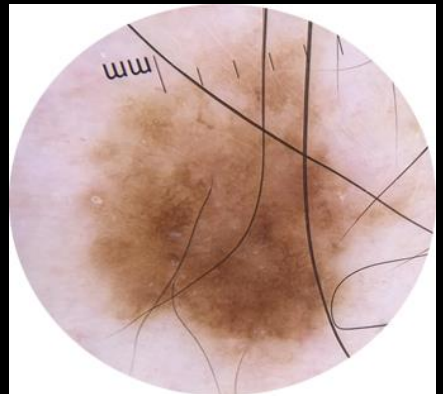
The Rapid Rise in Cutaneous Melanoma Diagnoses

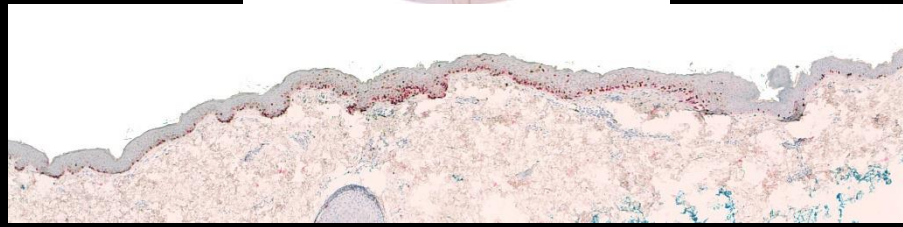
H. Gilbert Welch, M.D., M.P.H., Benjamin L. Mazer, M.D., M.B.A., and Adewole S. Adamson, M.D., M.P.P.



Solutions?

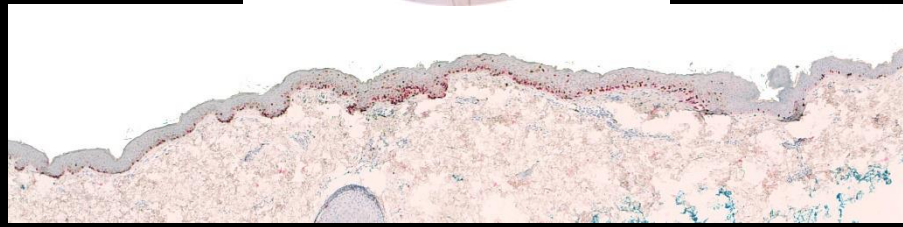
- Molecular data
- Multi-pathologist concordance
- AI?
- Clinical outcomes





Challenge: Would this have become a life-threatening tumor?

- Analogies: thyroid cancer, prostate cancer
- Will we detect life-threatening tumors?
- Will mortality decrease?



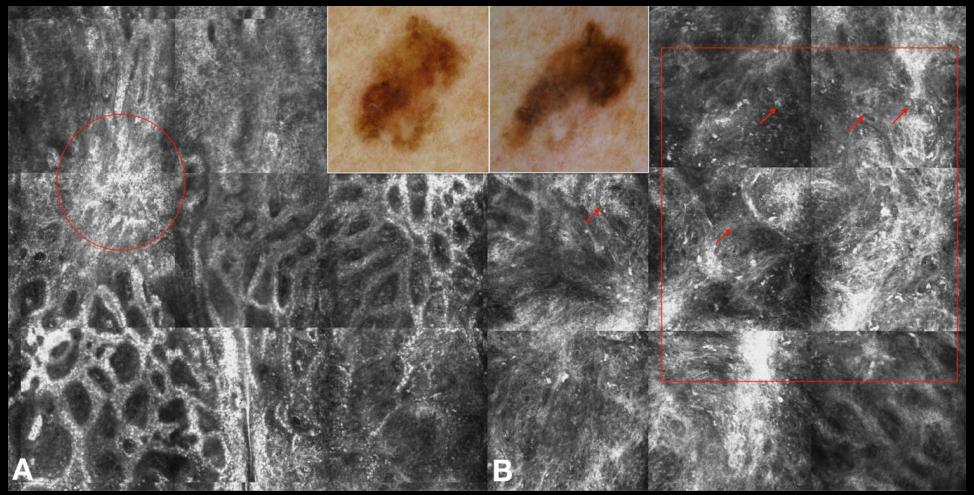
Challenges: low prevalence→ low positive predictive value

- 90% specificity, 2% prevalence→ 16% PPV

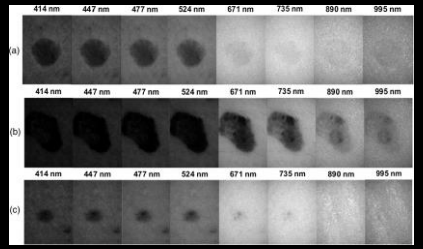
	Melanoma	Melanocytic nevus
Algorithm positive	19	98
Algorithm negative	1	882

Solutions: high risk population

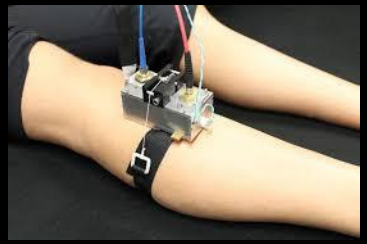
Solutions: Better imaging modalities



Condorelli AG et al, 2021



Delpueyo X et al, 2017



Sanchez G. et al, 2015

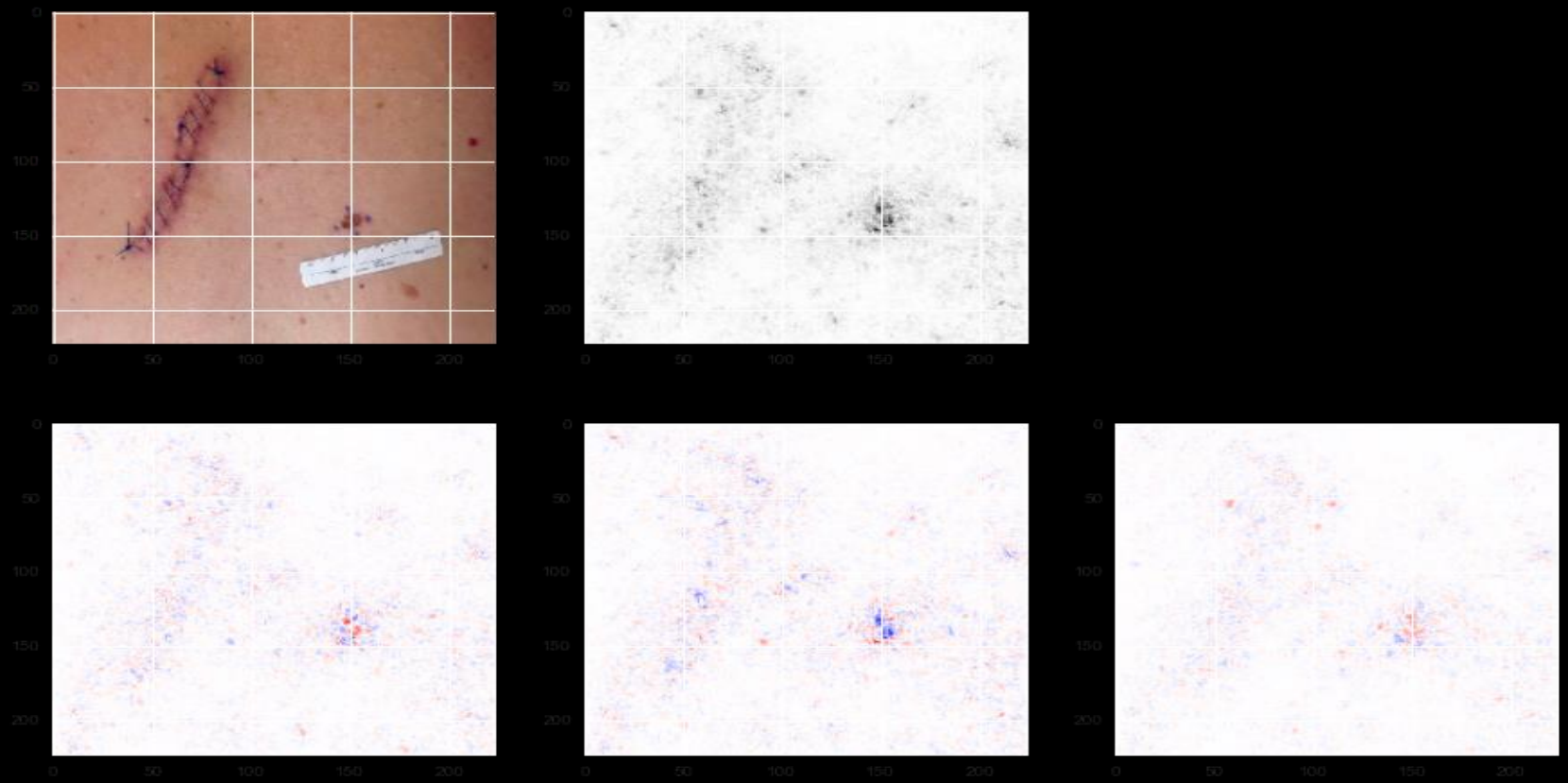
General challenges in AI: Bias and Confounding

- Factors that lead to systematically incorrect answers
- Present in:
  - Initial datasets
  - Study design
  - Statistical analysis
  - Outcomes

Challenge: Bias

- Example: Rulers

Pitfalls of AI: Bias and Confounding

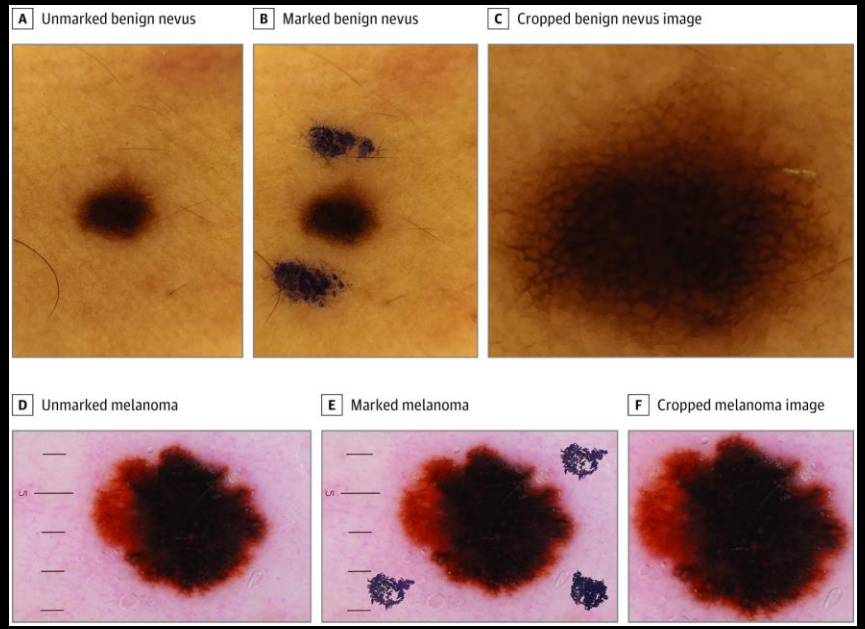


JAMA Dermatology | Original Investigation

Association Between Surgical Skin Markings in Dermoscopic Images and Diagnostic Performance of a Deep Learning Convolutional Neural Network for Melanoma Recognition

Julia K. Winkler, MD; Christine Fink, MD; Ferdinand Toberer, MD; Alexander Enk, MD; Teresa Deinlein, MD; Rainer Hofmann-Wellenhof, MD; Luc Thomas, MD; Aimilios Lallas, MD; Andreas Blum, MD; Wilhelm Stolz, MD; Holger A. Haenssle, MD

- Winkler et al (2019) demonstrated in rigorous fashion
- Markings decreased specificity (45%)
- Cropping boosted sensitivity and specificity



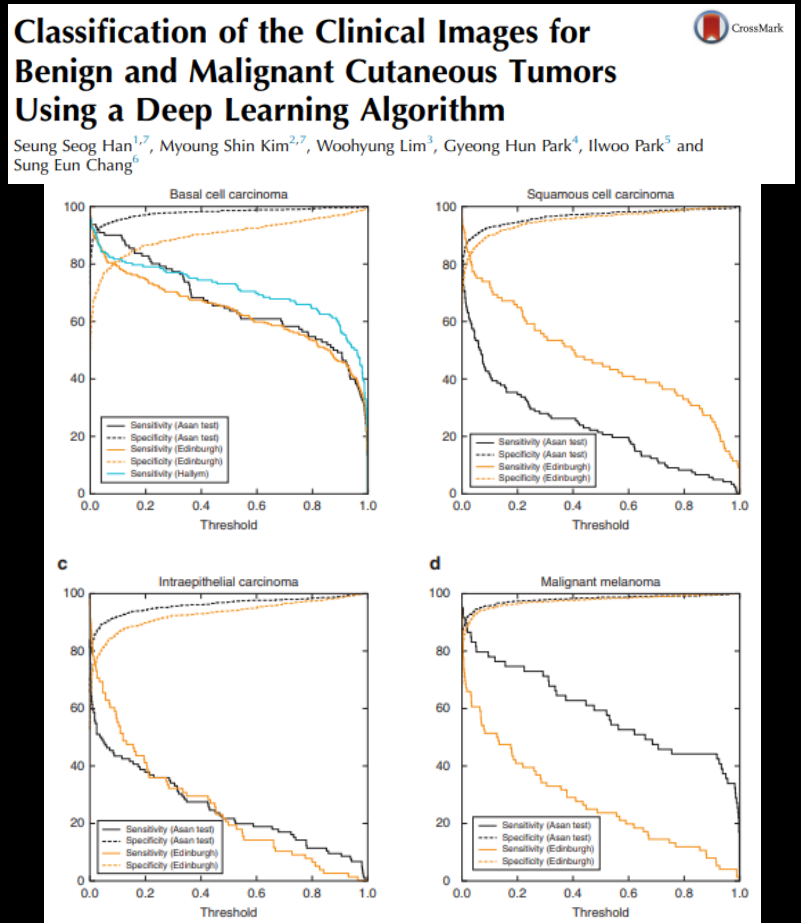
Dataset bias examples: racial/ethnic composition

- Need to ensure extensive representation by varied skin types
- Extensive additional work is needed
- Companies have already encountered BIG problems here

http://www.bbc.com/news/technology-33347866

Dataset bias examples: racial/ethnic composition

- Released dataset
- Differential performance based on dataset/ skin type
- https://modelderm.com



Classification of the Clinical Images for Benign and Malignant Cutaneous Tumors Using a Deep Learning Algorithm

Seung Seog Han[1,7], Myoung Shin Kim[2,7], Woohyung Lim[3], Gyeong Hun Park[4], Ilwoo Park[5] and Sung Eun Chang[6]

Bias, AI, and Equity

- POC can develop skin cancer
  - Different location distribution, different appearance
- Decreased detection→ advanced presentation
- Advanced presentation→Dataset bias→ Algorithmic bias→ Decreased detection

https://www.wect.com/story/38133492/plaid-pack-bob-marleys-cause-of-death-used-to-dispel-myth-about-skin-cancer/
https://www.onlinetruesformer-beauty-queen-dayanara-torrestories.com/2020/10/.html

Challenge: Regulatory and Cultural Frameworks

- Different countries, different standards
- When is a test “good enough”?
- Rapid dissemination of information technology
- Different cultural values around beneficence, avoidance of harm
- “First do no harm” vs “Move fast and break things”

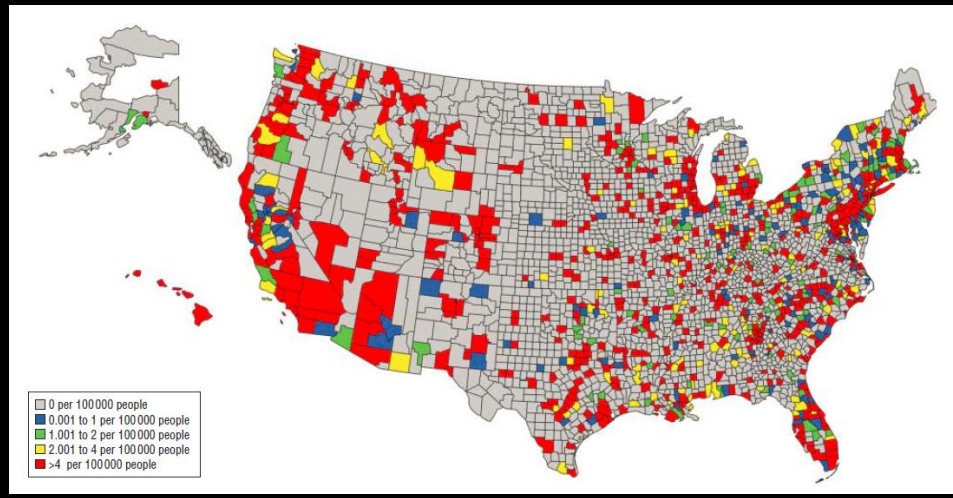
https://en.wikipedia.org/w/index.php?curid=48438689

Transformation: marked productivity increases

- Decrease superfluous visits
- Improve diagnosis and management

Transformation: Democratizing access

- Data collection at scale
- Diagnostics at scale
- Diminish health disparities



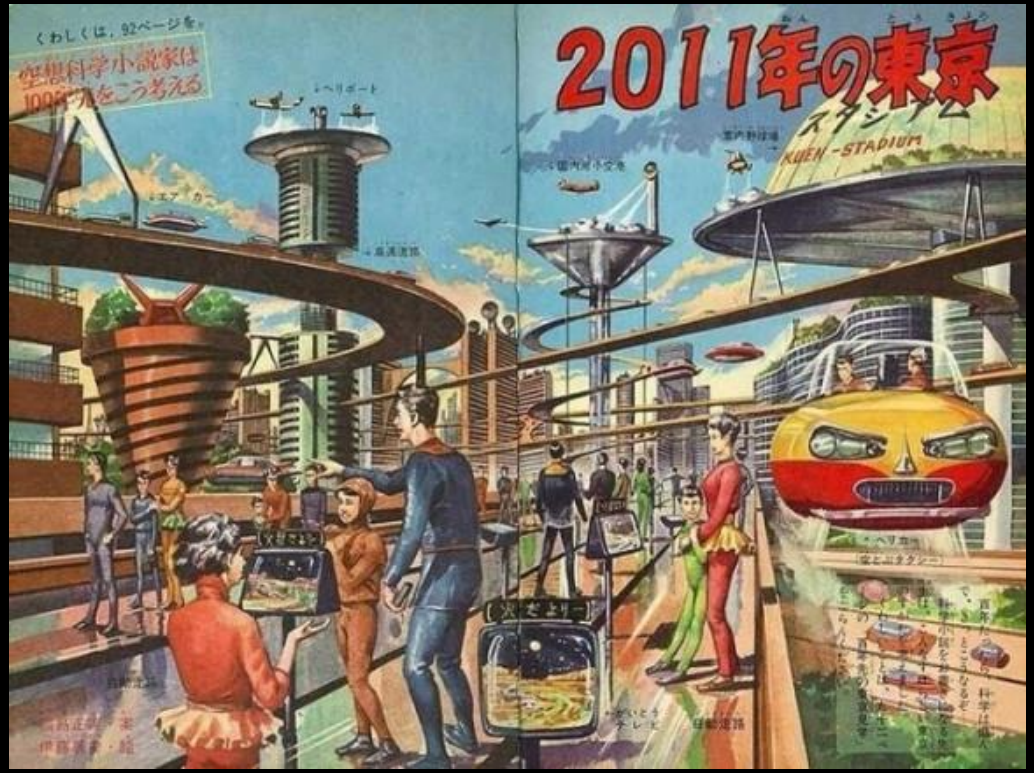
Bordeaux et al, 2012

Near Future

- Prospective clinical trials
- Likely focus: dermoscopy
- Tools for skin cancer experts

Long term?

- Data collection at scale
- Difficult to predict



http://www.escapistmagazine.com/forums/read/7.410037-This-is-What-The-1940s-Thought-2011-Would-Look-Like#&gid=gallery_1542&pid=1

Acknowledgements

- Amazing colleagues in the dermatology, pathology, and computer science departments at Stanford
- ISDIS
- ISBI challenge