

COMPUTER-ASSISTED DIAGNOSIS OF SKIN CANCER

THE DERMATOLOGY POINT OF VIEW



PROF.

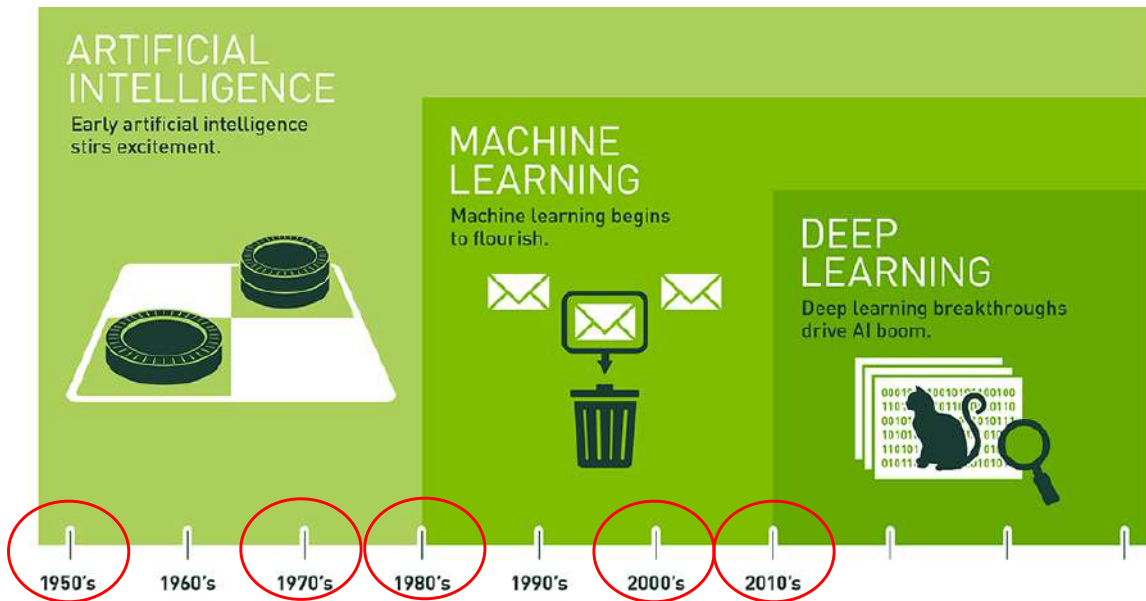
GIOVANNI PELLACANI

1. WHAT ARTIFICIAL INTELLIGENCE IS?

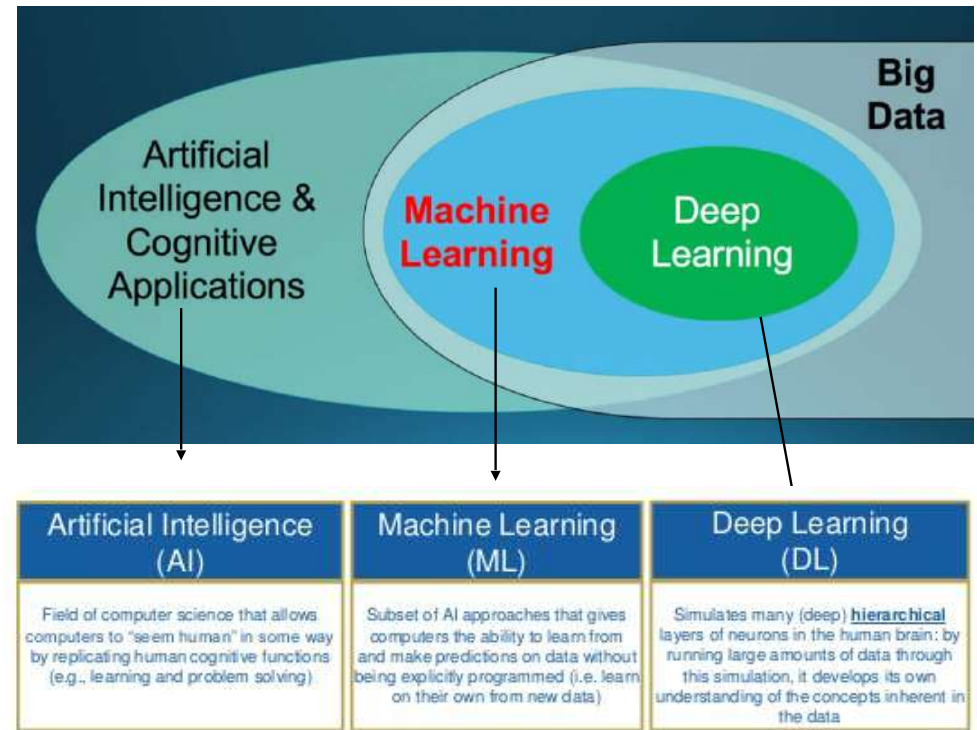
A 3D rendering of a white hand holding a red ribbon that forms a large question mark shape. The ribbon is bright red and glossy, and the hand is white and stylized. The background is white.

WHAT IS ARTIFICIAL INTELLIGENCE?

The theory and development of computer systems able to perform tasks, normally required human intelligence, such as visual perception, speech recognition, decision-making and translation between languages (Oxford Dictionary, 2019)



Since an early flush of optimism in the 1950s, smaller subsets of artificial intelligence – first machine learning, then deep learning, a subset of machine learning – have created ever larger disruptions.



1956: Dartmouth conference: birth of A.I.



1970: medical researches discovered the applicability of AI in life sciences (limited in dermatology)

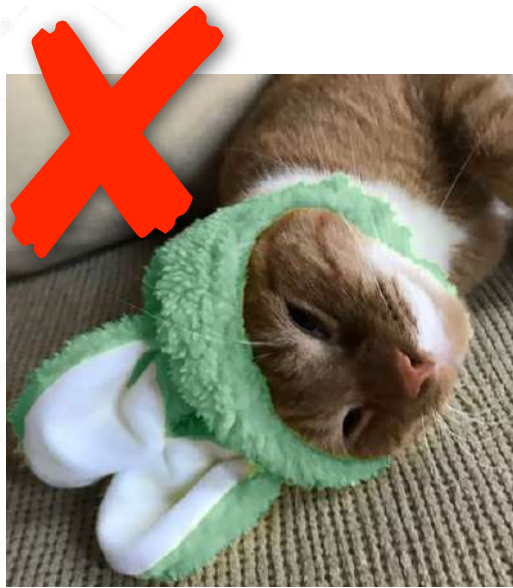


1980: machine learning
2006: "deep learning" (Hinton et al)



2012: "CNN" (convolutional neural network) for image processing, speech recognition, text processing and... for medical sciences **(also dermatology)**

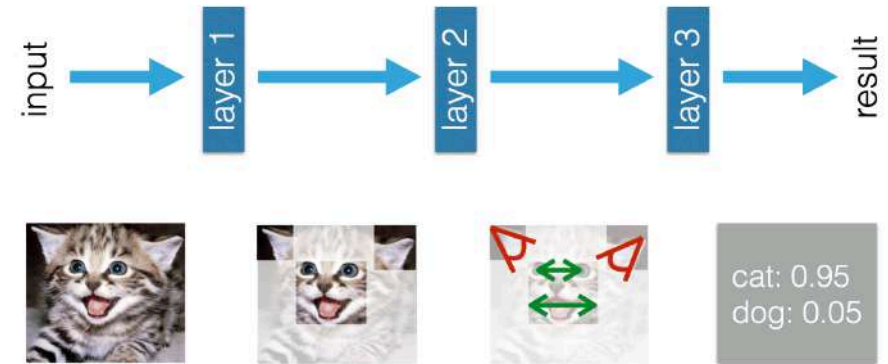
A.I.: classical approach



- Round face
- 2 triangular ears
- 2 eyes
- Tail
- Rectangular body

“CAT”

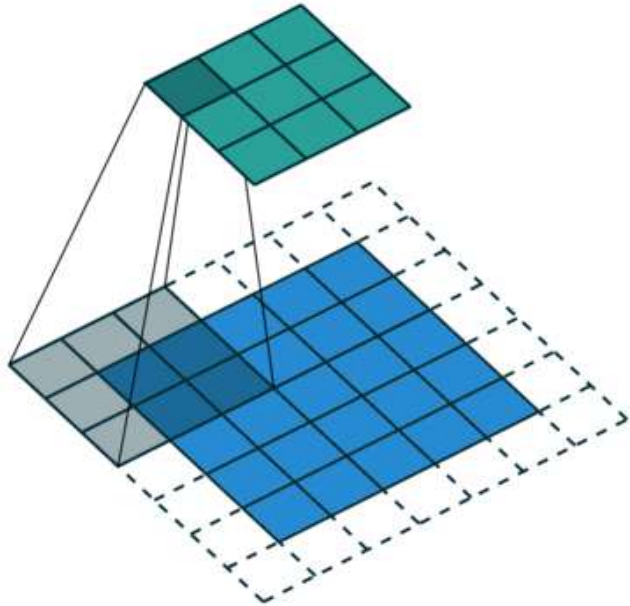
Deep learning (Convolutional Neural Network)



Statistical model based on brain network (neuronal units connected in different layers), to analyze automatically features (from simple features to complex features) → output (probability)

Convolutional Neural Networks

Convolutional Neural Networks are designed by stacking layers of convolutional filters



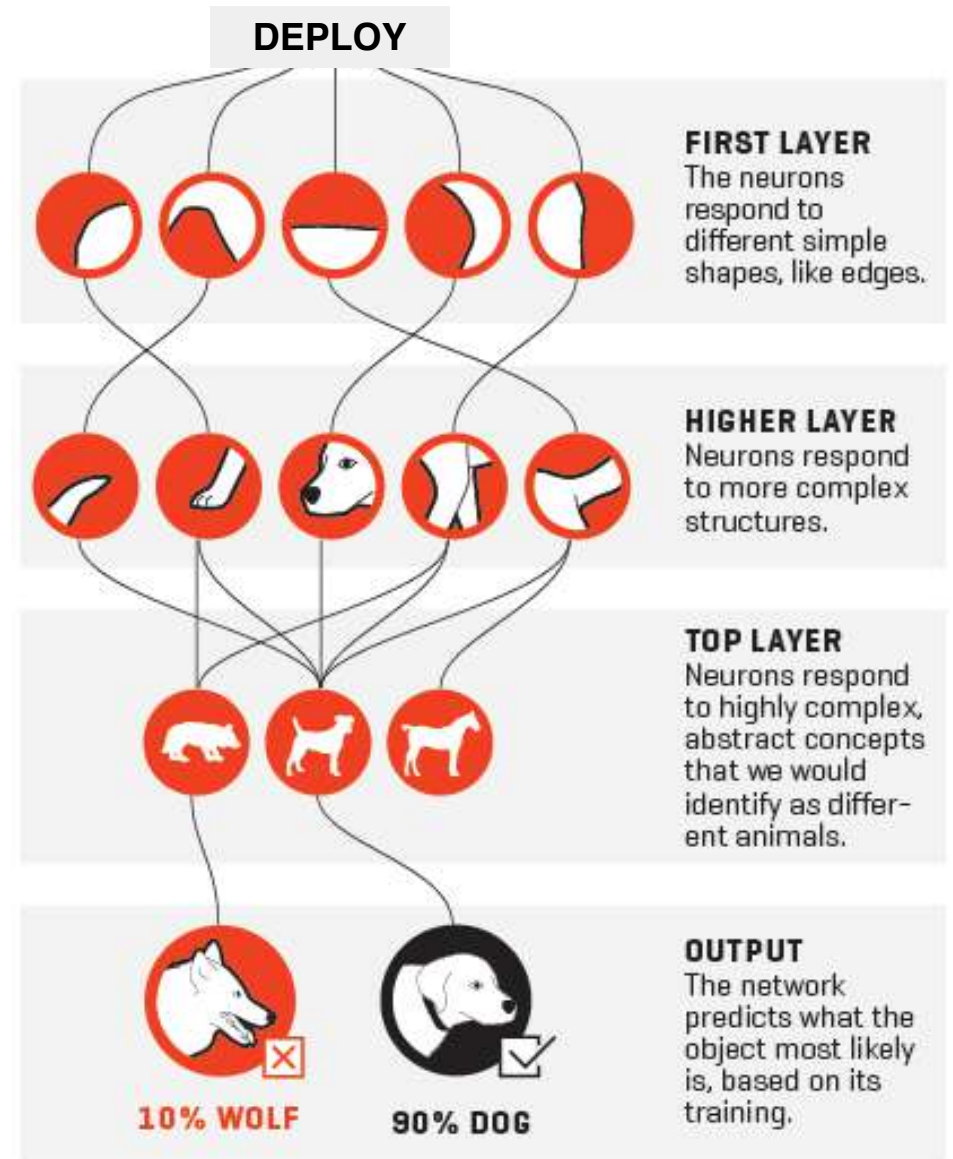
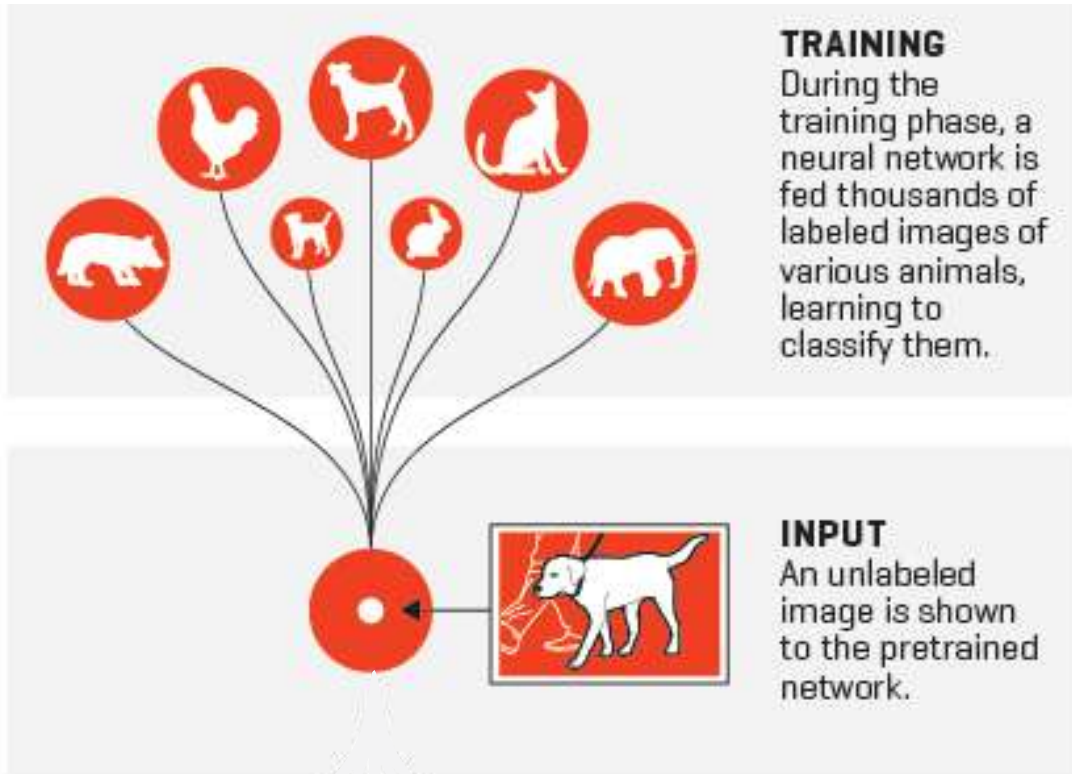
Convolutional Filters can learn to extract features from the input image

The first convolutional layer is responsible for capturing low-level features such as edges

The following layers adapt to extract high-level features such as object shapes

Convolutional Neural Networks gain a wholesome understanding of images drawn from a certain dataset

HOW NEURAL NETWORKS RECOGNIZE A DOG IN A PHOTO



2. ARTIFICIAL INTELLIGENCE AND SKIN LESIONS

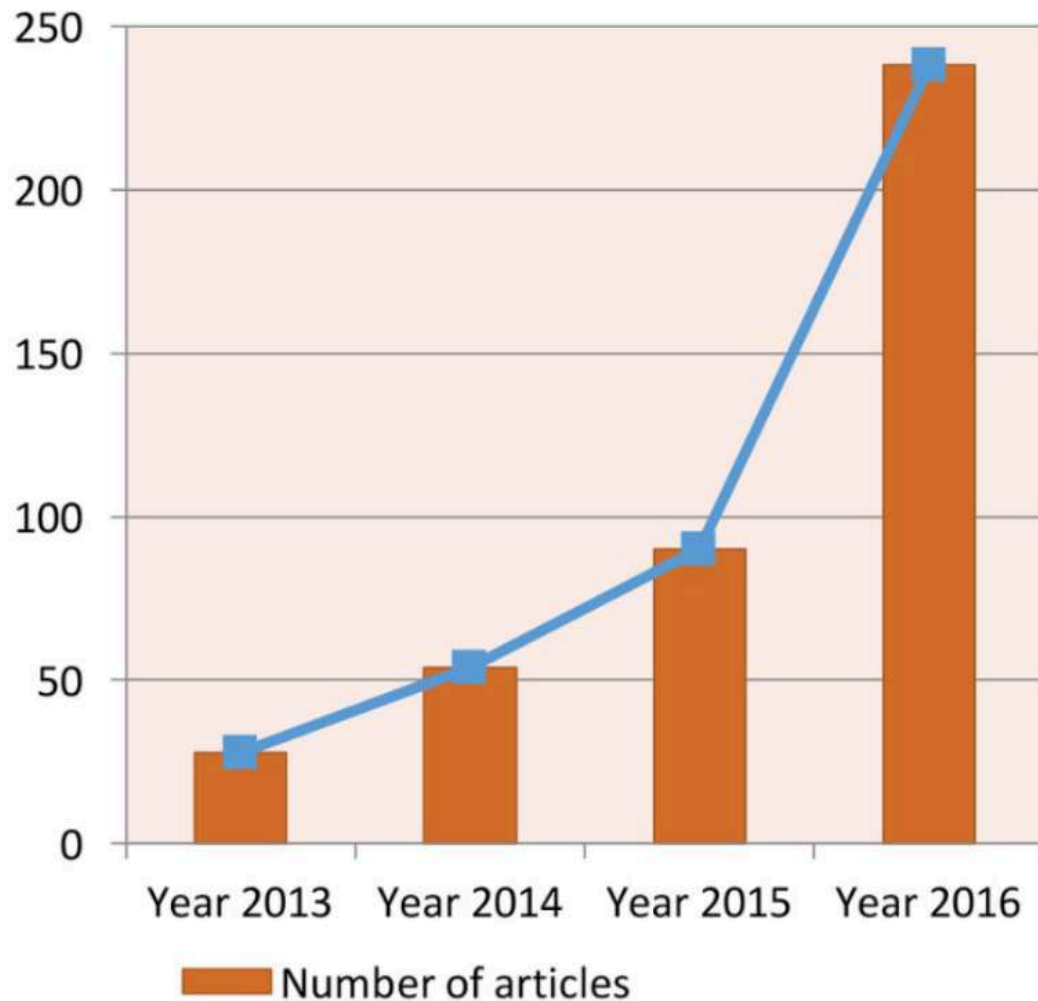
WHY ARTIFICIAL INTELLIGENCE IN DIAGNOSIS OF SKIN LESIONS?



- ❑ In most countries , primary vigilance is maintained through primary care clinics before being referred to dermatologists → primary care doctors are under a heavy burden to correctly screen patients
- ❑ Paucity of experts dermatologists
- ❑ Rising incidence of skin cancer in aging population
- ❑ Early diagnosis of skin cancer



HIGH DEMAND FOR POINT-OF-CARE DECISION **SUPPORT SYSTEMS** TO DIAGNOSE SKIN LESIONS WITHOUT THE NEED OF HUMAN EXPERTISE



[An improved strategy for skin lesion detection and classification using uniform segmentation and feature selection based approach.](#)

Nasir M, Attique Khan M, Sharif M, Lali IU, Saba T, Iqbal T.
 Microsc Res Tech. 2018 Jun;81(6):528-543. doi: 10.1002/jemt.23009. Epub 2018 Feb 21.
 PMID: 29464868
[Similar articles](#)

[A Review of Denoising Medical Images Using Machine Learning Approaches.](#)

Kaur P, Singh G, Kaur P.
 Curr Med Imaging Rev. 2018 Oct;14(5):675-685. doi: 10.2174/1573405613666170428154156. Review.
 PMID: 30532667 [Free PMC Article](#)
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[Risk-Aware Machine Learning Classifier for Skin Lesion Diagnosis.](#)

Mobiny A, Singh A, Van Nguyen H.
 J Clin Med. 2019 Aug 17;8(8). pii: E1241. doi: 10.3390/jcm8081241.
 PMID: 31426482 [Free PMC Article](#)
[Similar articles](#)

[Rethinking Skin Lesion Segmentation in a Convolutional Classifier.](#)

Burdick J, Marques O, Weinthal J, Furht B.
 J Digit Imaging. 2018 Aug;31(4):435-440. doi: 10.1007/s10278-017-0026-y. Review.
 PMID: 29047032 [Free PMC Article](#)
[Similar articles](#)

[Rapid and accurate intraoperative pathological diagnosis by artificial intelligence with deep learning technology.](#)

Zhang J, Song Y, Xia F, Zhu C, Zhang Y, Song W, Xu J, Ma X.
 Med Hypotheses. 2017 Sep;107:98-99. doi: 10.1016/j.mehy.2017.08.021. Epub 2017 Sep 1.
 PMID: 28915974
[Similar articles](#)

[A novel cumulative level difference mean based GLDM and modified ABCD features ranked using eigenvector centrality approach for four skin lesion types classification.](#)

Wahba MA, Ashour AS, Guo Y, Napoleon SA, Elnaby MMA.
 Comput Methods Programs Biomed. 2018 Oct;165:163-174. doi: 10.1016/j.cmpb.2018.08.009. Epub 2018 Aug 24.
 PMID: 30337071
[Similar articles](#)

[Automatic discrimination of actinic keratoses from clinical photographs.](#)

Spyridonos P, Gaitanis G, Likas A, Bassukas ID.
 Comput Biol Med. 2017 Sep 1;88:50-59. doi: 10.1016/j.compbiomed.2017.07.001. Epub 2017 Jul 3.
 PMID: 28692931
[Similar articles](#)



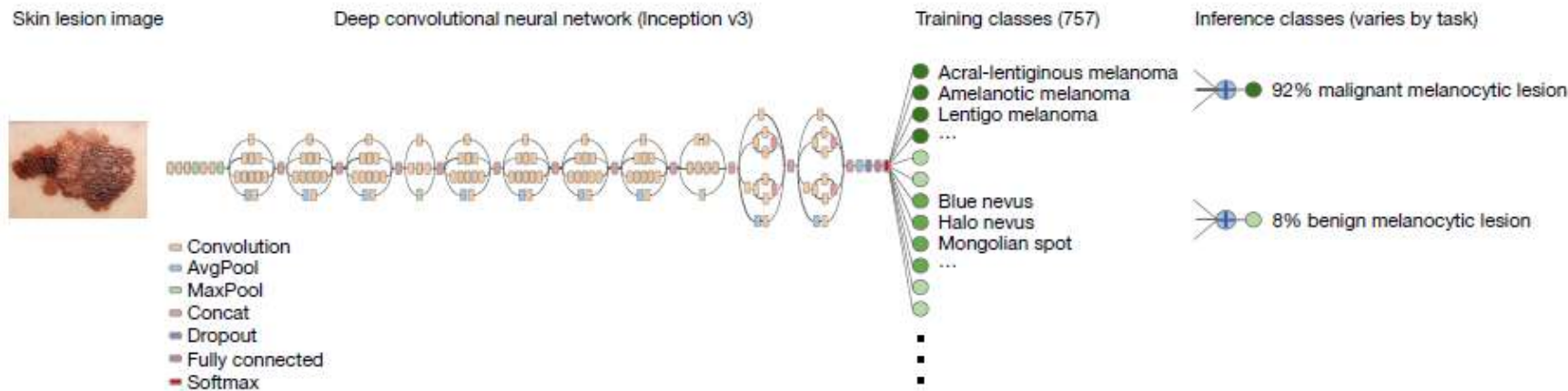
LIGHTS...



...AND
SHADOWS

Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteva^{1*}, Brett Kuprel^{1*}, Roberto A. Novoa^{2,3}, Justin Ko², Susan M. Swetter^{2,4}, Helen M. Blau⁵ & Sebastian Thrun⁶



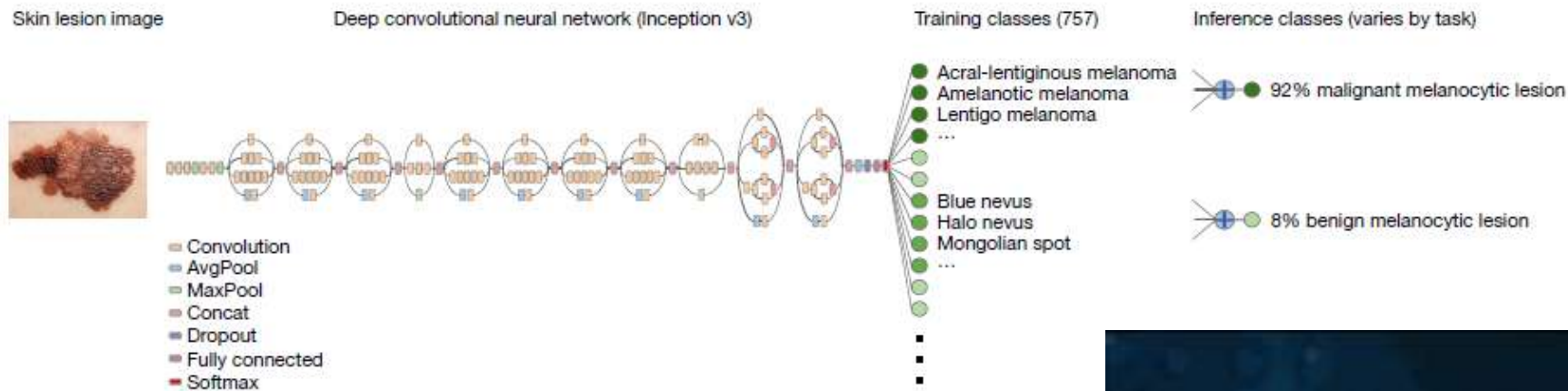
and disease labels as inputs. We train a CNN using a dataset of 129,450 clinical images—two orders of magnitude larger than previous datasets¹²—

The CNN achieves performance on par with all tested experts across both tasks, demonstrating an artificial intelligence capable of classifying skin cancer with a level of competence comparable to dermatologists.



Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteva^{1*}, Brett Kuprel^{1*}, Roberto A. Novoa^{2,3}, Justin Ko², Susan M. Swetter^{2,4}, Helen M. Blau⁵ & Sebastian Thrun⁶



and disease labels as inputs. We train a CNN using a dataset of 129,450 clinical images—two orders of magnitude larger than previous datasets¹²—consisting of 2,032 different diseases.

The CNN = average **63.7 images per diagnosis!!!** ts
across both tasks, demonstrating an artificial intelligence capable of classifying skin cancer with a level of competence comparable to dermatologists.



Comparison of the accuracy of human readers versus machine-learning algorithms for pigmented skin lesion classification: an open, web-based, international, diagnostic study

Philipp Tschandl, PhD · Noel Codella, PhD · Bengü Nisa Akay, MD · Prof Giuseppe Argenziano, PhD · Ralph P Braun, MD · Prof Horacio Cabo, MD · et al. [Show all authors](#)

Published: June 11, 2019 · DOI: [https://doi.org/10.1016/S1470-2045\(19\)30333-X](https://doi.org/10.1016/S1470-2045(19)30333-X) ·  Check for updates



STRENGTH ...

When comparing all human readers with all machine-learning algorithms, the algorithms achieved a mean of 2.01 (95% CI 1.97 to 2.04; $p < 0.0001$) more correct diagnoses (17.91 [SD 3.42] vs 19.92 [4.27]).

Comparison of the accuracy of human readers versus machine-learning algorithms for pigmented skin lesion classification: an open, web-based, international, diagnostic study

Philipp Tschandl, PhD · Noel Codella, PhD · Bengü Nisa Akay, MD · Prof Giuseppe Argenziano, PhD · Ralph P Braun, MD · Prof Horacio Cabo, MD · et al. [Show all authors](#)

Published: June 11, 2019 · DOI: [https://doi.org/10.1016/S1470-2045\(19\)30333-X](https://doi.org/10.1016/S1470-2045(19)30333-X) [Check for updates](#)



STRENGTH ...



LIMITATIONS

When comparing all human readers with all machine-learning algorithms, the algorithms achieved a mean of 2·01 (95% CI 1·97 to 2·04; $p < 0·0001$) more correct diagnoses (17·91 [SD 3·42] vs 19·92 [4·27]).

- The metrics **treated all diagnoses equally** (the algorithms did not consider that it is more detrimental to mistake a malignant for a benign lesion than viceversa)
- **Lesions** in the test set and training set were not standardized
- **Absence of additional data** (anatomical site, age, and sex)
- **Low sensitivity** if used image from source different than training data (**test set**)

Accuracy of Computer-Aided Diagnosis of Melanoma A Meta-analysis

Vincent Dick, CandMed; Christoph Sinz, MD; Martina Mittlböck, PhD; Harald Kittler, MD; Philipp Tschandl, MD, PhD

RESULTS The literature search yielded 1694 potentially eligible studies, of which 132 were included and 70 offered sufficient information for a quantitative analysis. Most studies came from the field of computer science. Prospective clinical studies were rare. Combining the results for automated systems gave a melanoma sensitivity of 0.74 (95% CI, 0.66-0.80) and a specificity of 0.84 (95% CI, 0.79-0.88). Sensitivity was lower in studies that used independent test sets than in those that did not (0.51; 95% CI, 0.34-0.69 vs 0.82; 95% CI, 0.77-0.86; $P < .001$); however, the specificity was similar (0.83; 95% CI, 0.71-0.91 vs 0.85; 95% CI, 0.80-0.88; $P = .67$). In comparison with dermatologists' diagnosis, computer-aided diagnosis showed similar sensitivities and a 10 percentage points lower specificity, but the difference was not statistically significant. Studies were heterogeneous and substantial risk of bias was found in all but 4 of the 70 studies included in the quantitative analysis.

CONCLUSIONS AND RELEVANCE Although the accuracy of computer-aided diagnosis for melanoma detection is comparable to that of experts, the real-world applicability of these systems is unknown and potentially limited owing to overfitting and the risk of bias of the studies at hand.

Accuracy of Computer-Aided Diagnosis of Melanoma A Meta-analysis

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LIMITATIONS...

- **Etherogeneous studies** with high risk for **bias**
- **Experimental setting** (smarthpone, pc, tablet...)
- **Low sensitivity WHEN** used images **from different sources** than the training dataset
- Referral centers for melanoma
- Skin lesion images not standardized
- Often use limited to melanocytic lesions **ONLY**
- Lack of data for unusual presentations and rare skin tumors

Accuracy of Computer-Aided Diagnosis of Melanoma A Meta-analysis

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“There is a fear that less-skilled physicians or even non-medical personnel will use such systems to deliver a service that should be restricted to dermatologists. Therefore, a successful CAD would most probably enhance and support dermatologists rather than replace them.”



Artificial intelligence and melanoma diagnosis: ignoring human nature may lead to false predictions

Aimilios Lallas¹, Giuseppe Argenziano²

“We are convinced that AI has the potential....to become an additional precious tool in the hand of doctors... the main obstacles of this goal are the misconceptions about our role as doctors”



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3. WHAT WE DID IN THE PAST

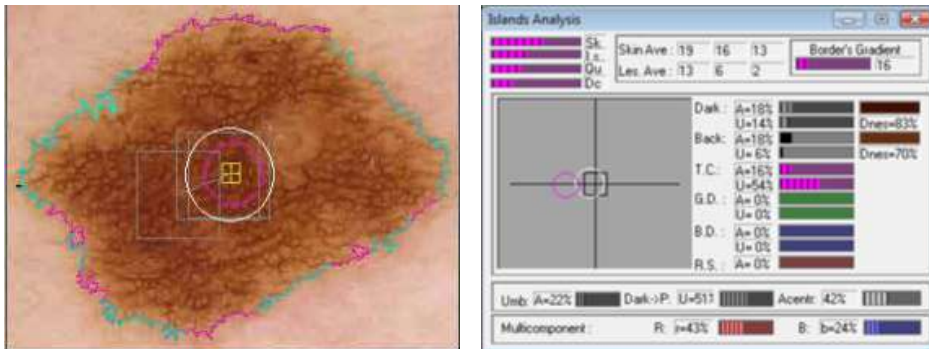
WE STARTED 20 YEARS OLD...

Melanoma Research 1999, 9, pp. 163–171

Digital videomicroscopy and image analysis with automatic classification for detection of thin melanomas

S. Seidenari*, G. Pellacani and A. Giannetti

Department of Dermatology, University of Modena,
41100 Modena, Italy. Tel: (+39) 59 422464; Fax: (+39)
59 424271; Email: seidenar@unimo.it



ARTIFICIAL INTELLIGENCE APPROACH



AND CONTINUED WITH...

Collaboration with:
Prof Costantino Grana
Dept. of Informatic Engineering, Unimore

[IEEE Trans Med Imaging](#), 2003 Aug;22(8):959-64.

A new algorithm for border description of polarized light surface microscopic images of pigmented skin lesions.

Grana C¹, Pellacani G, Cucchiara R, Seidenari S.

[Br J Dermatol](#), 2003 Sep;149(3):523-9.

Computer description of colours in dermoscopic melanocytic lesion images reproducing clinical assessment.

Seidenari S¹, Pellacani G, Grana C.

[Melanoma Res](#), 2004 Apr;14(2):125-30.

Automated description of colours in polarized-light surface microscopy images of melanocytic lesions.

Pellacani G¹, Grana C, Seidenari S.



ARTIFICIAL INTELLIGENCE APPROACH

AND CONTINUED WITH...

[Skin Res Technol.](#) 2005 Nov;11(4):236-41.

Pigment distribution in melanocytic lesion images: a digital parameter to be employed for computer-aided diagnosis.

[Seidenari S¹](#), [Pellacani G](#), [Grana C](#).

[Acta Derm Venereol.](#) 2006;86(2):123-8.

Asymmetry in dermoscopic melanocytic lesion images: a computer description based on colour distribution.

[Seidenari S¹](#), [Pellacani G](#), [Grana C](#).

[J Eur Acad Dermatol Venereol.](#) 2006 Nov;20(10):1214-9.

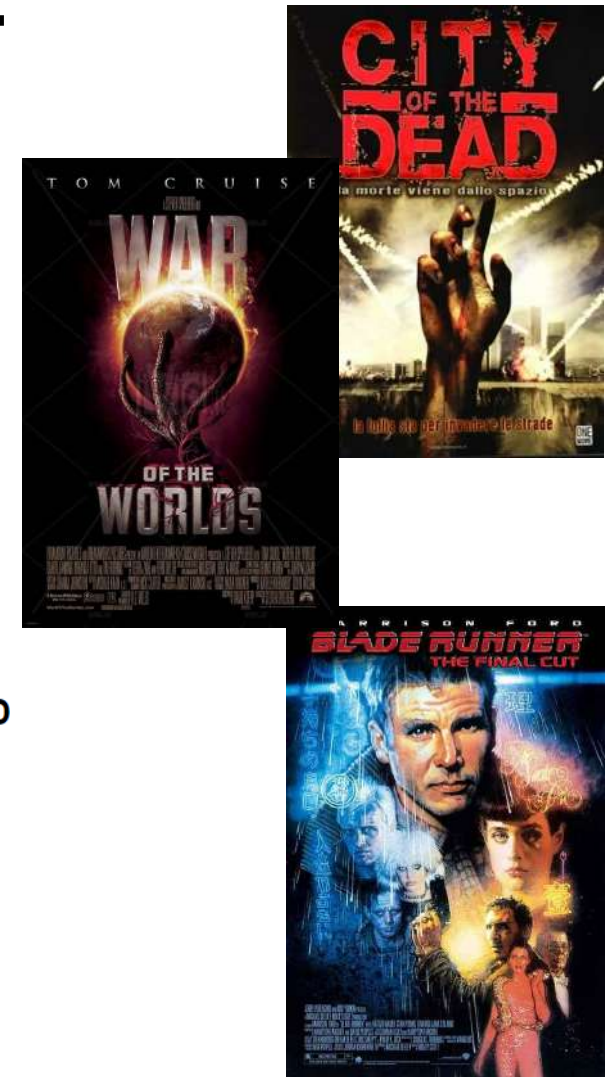
Algorithmic reproduction of asymmetry and border cut-off parameters according to the ABCD rule for dermoscopy.

[Pellacani G¹](#), [Grana C](#), [Seidenari S](#).

[Dermatology.](#) 2007;214(2):137-43.

Colour clusters for computer diagnosis of melanocytic lesions.

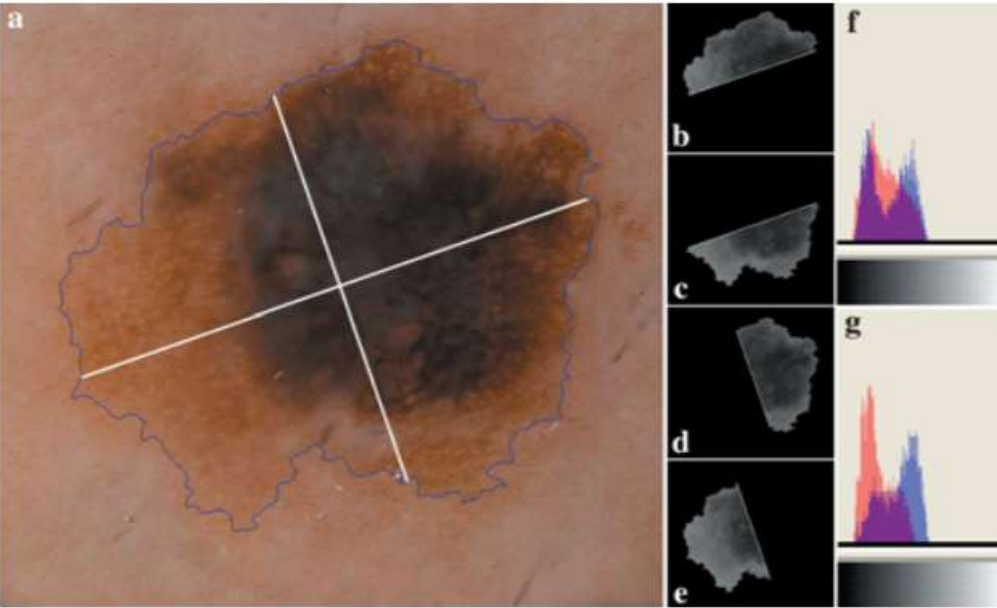
[Seidenari S¹](#), [Grana C](#), [Pellacani G](#).



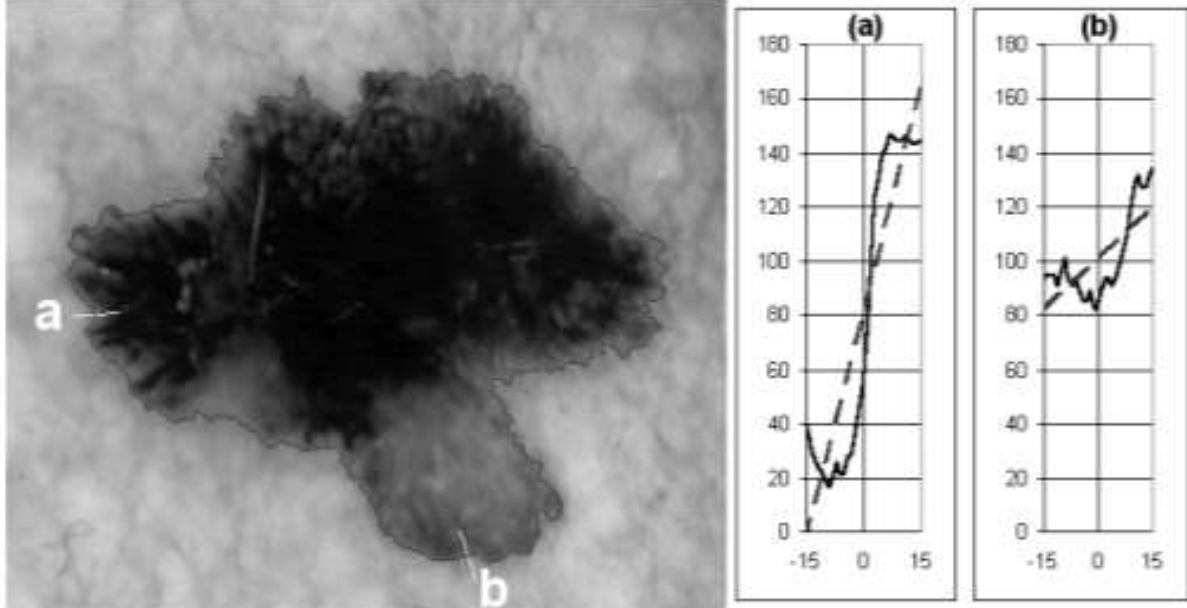
ARTIFICIAL INTELLIGENCE APPROACH

THE MAIN GOAL WAS TO IDENTIFY THE DERMOSCOPIC FEATURES AND TO REPRODUCE THE ABCD RULE

Asymmetry

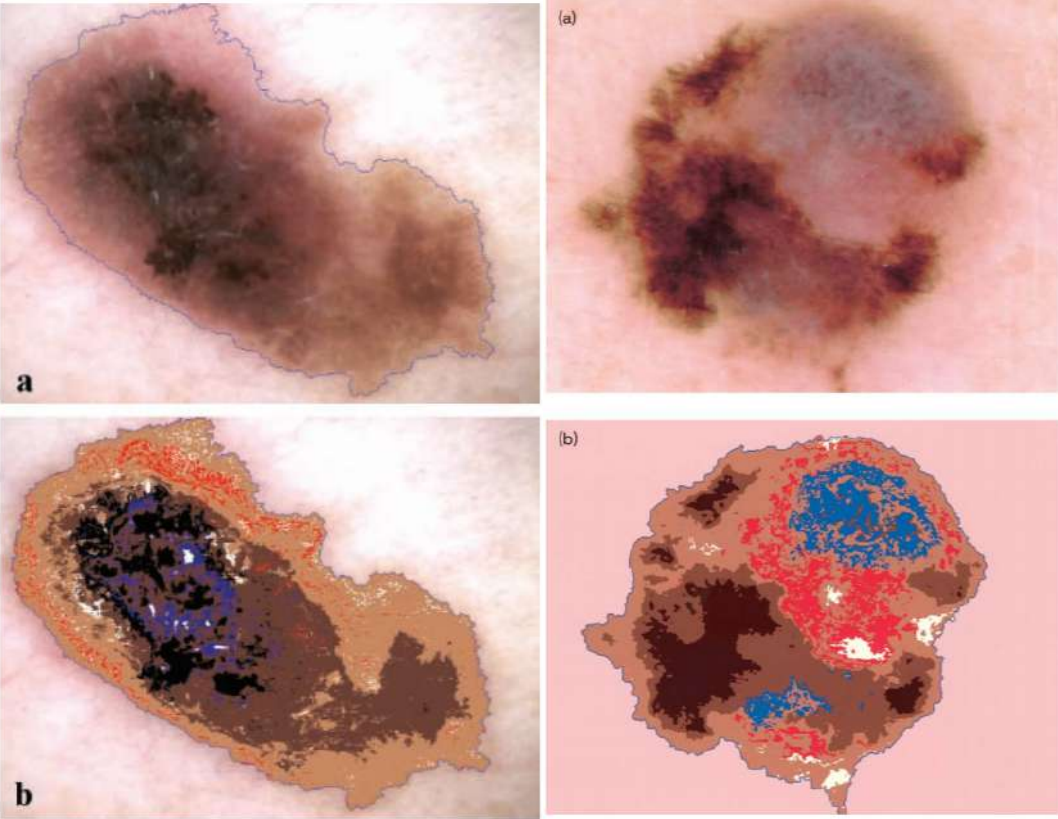


Border

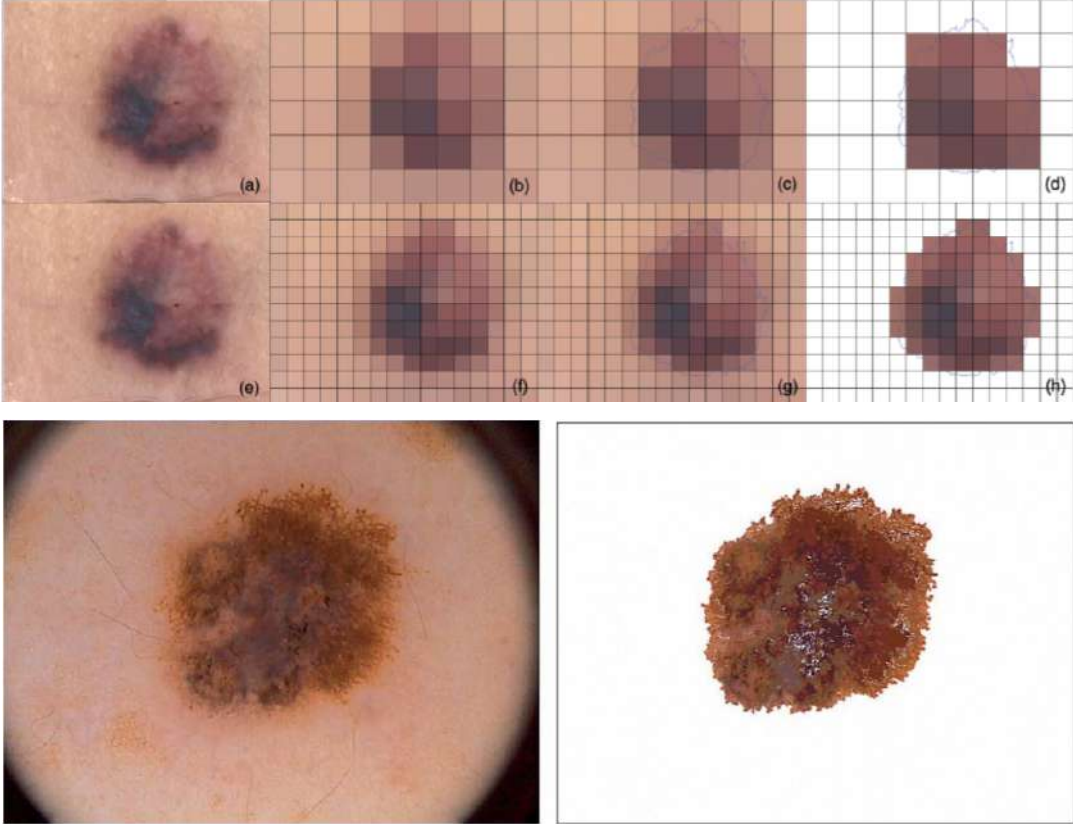


THE MAIN GOAL WAS TO IDENTIFY THE DERMOSCOPIC FEATURES AND TO REPRODUCE THE ABCD RULE

Colours



Dermoscopic structures



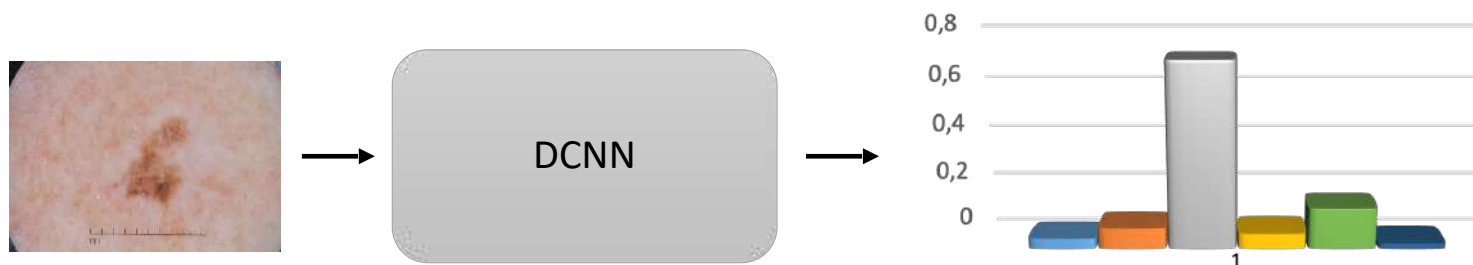
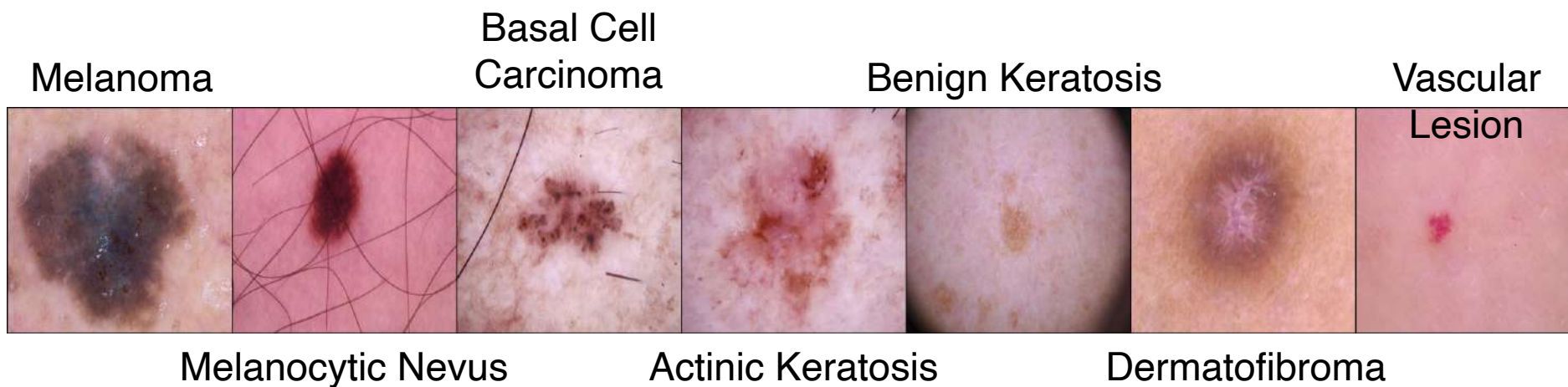


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4. WHAT'S GOING ON

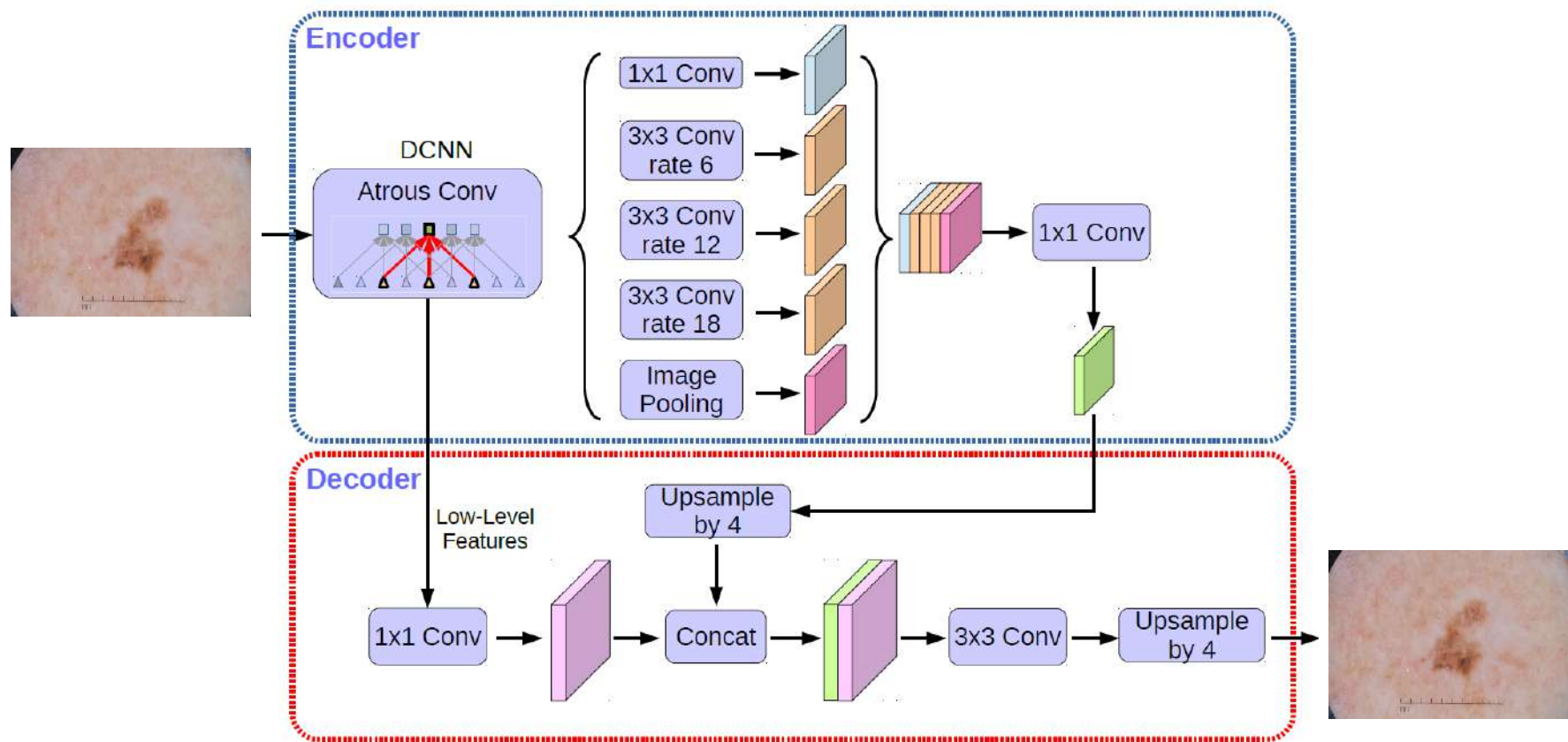
CONVOLUTED NEURAL NETWORK APPROACH

FEATURE EXTRACTION: CLASSIFICATION



CONVOLUTED NEURAL NETWORK APPROACH

FEATURE EXTRACTION: AUTO-ENCODER















ISIC Challenge 2019

ISIC 2019

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LESION DIAGNOSIS: IMAGES ONLY

LESION DIAGNOSIS: IMAGES AND METADATA

Rank <64 total>	Team <64 unique teams>	Approach Name	Manuscript	Used External Data <19 yes>	Primary Metric Value <Balanced Multiclass Accuracy>	
1	DAISYLab Hamburg University of Technology/University Medical Center Hamburg-Eppendorf	Ensemble of Multi-Res EfficientNets + SEN154 2		 Yes	0.636	▼
2	DysionAI DYSION AI, Inc, Beijing, China	Ensemble of EfficienetB3-B4-Seresnext101		 No	0.607	▼
3	AlmageLab & PRHLT Unimore & UPV	ensemble, ood threshold 100%		 No	0.593	▼
4	DermaCode	13 models + hierarchical approach to select outliers		 No	0.578	▼
5	Nurithm Labs Nurithm Labs	Densenet-161 with heavy use of random crops		 Yes	0.569	▼
6	Torus Actions Torus Actions	Simple test approach		 No	0.563	▼

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Aggregate Metrics

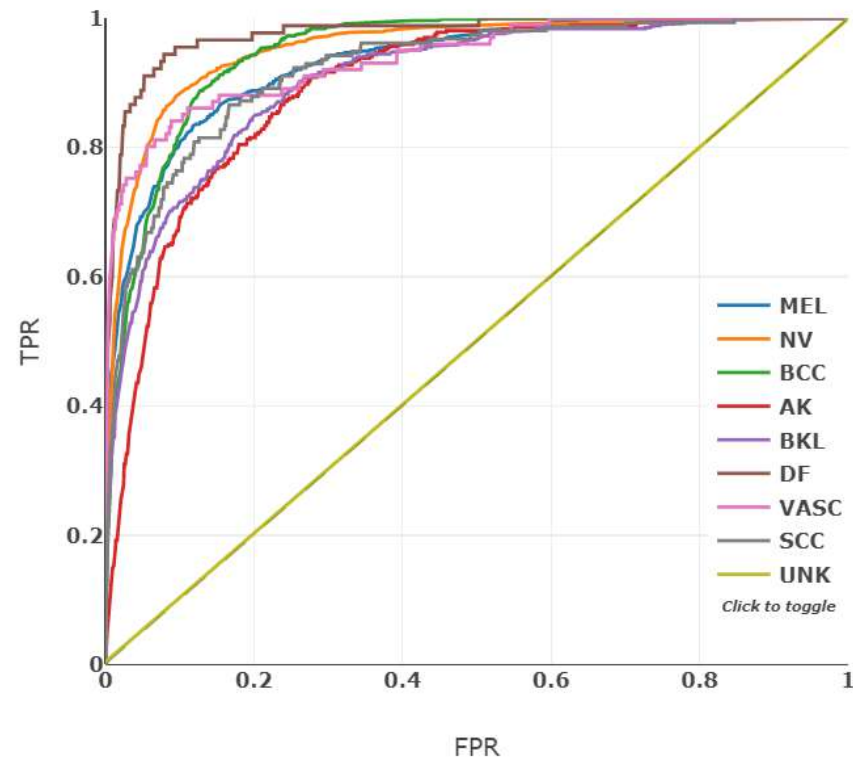
Value ⓘ

Balanced Multiclass Accuracy ⓘ

0.593

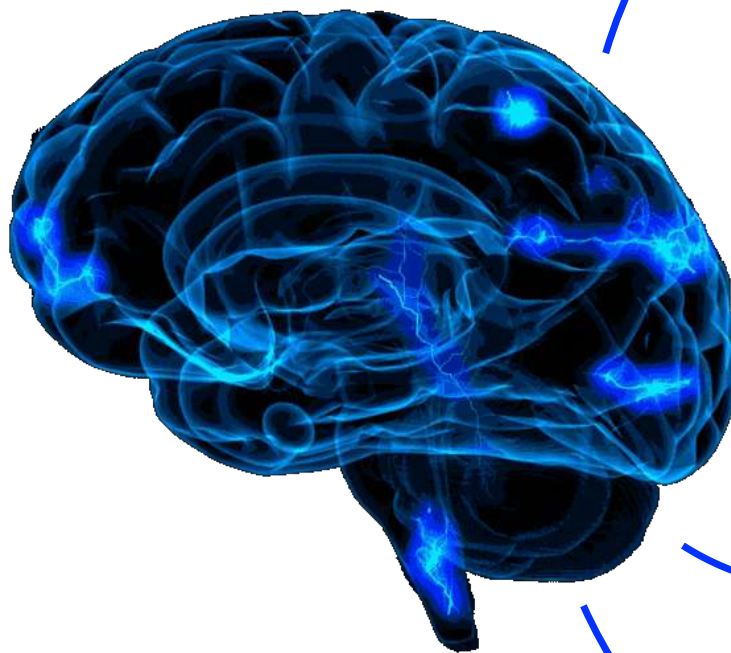
The greatest diagnosis category score determines the category prediction for each image; the mean recall of this multiclass confusion matrix (i.e. the mean of the diagonal element-wise divided by the positive incidences) is the balanced multiclass accuracy

ROC
ensemble, ood threshold 100%





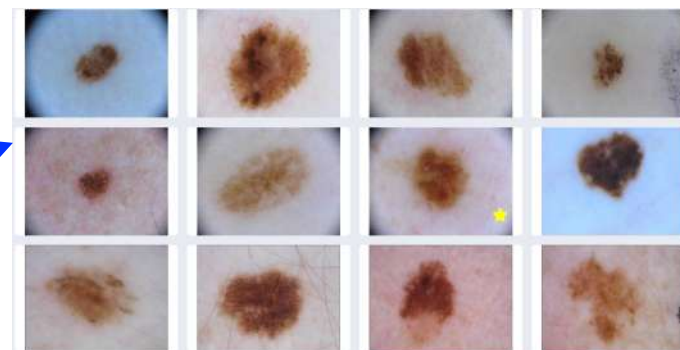
CNN



Melanoma



Melanocytic Nevus



Basal Cell Carcinoma



Dermatofibroma



THE QUESTION IS:



to formulate a diagnosis,
what a machine is looking at?

what a machine is looking at?

Artificial Intelligence

Neural Network

what a machine is looking at?

Artificial Intelligence



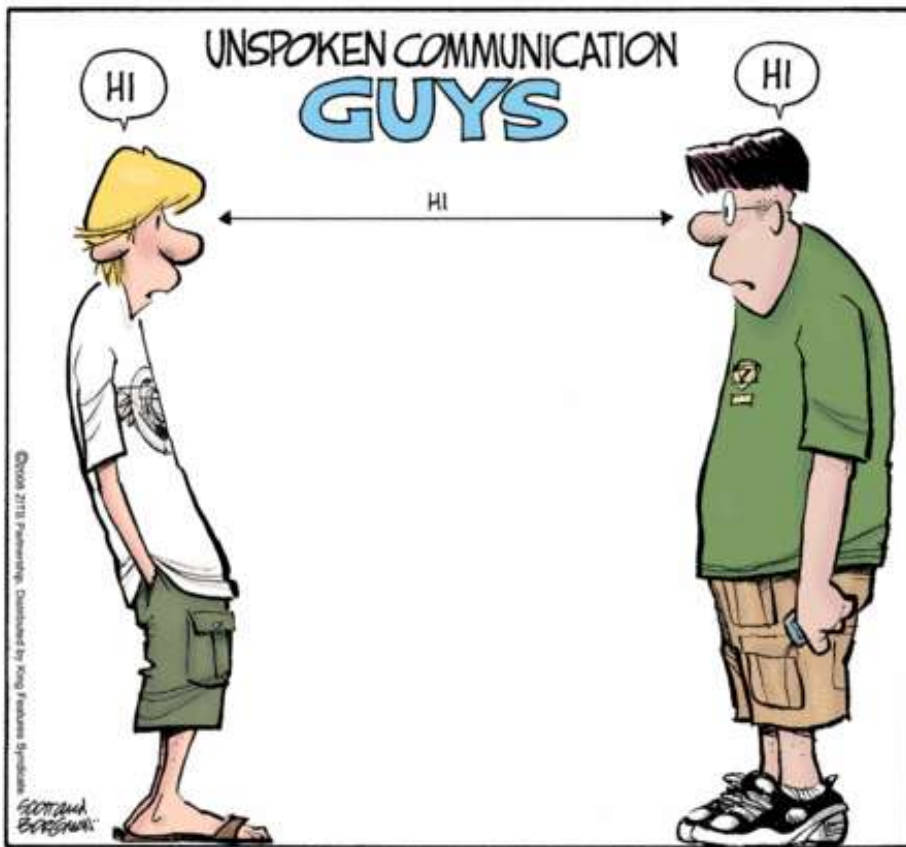
Neural Network



what a machine is looking at?

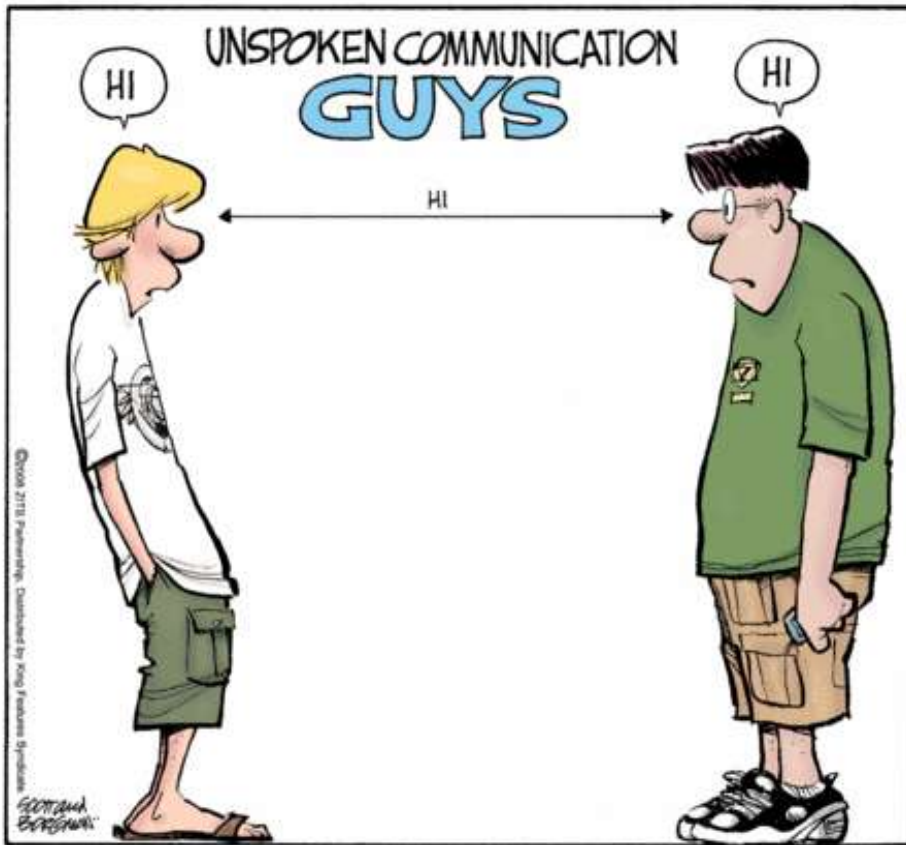
Artificial Intelligence

Neural Network

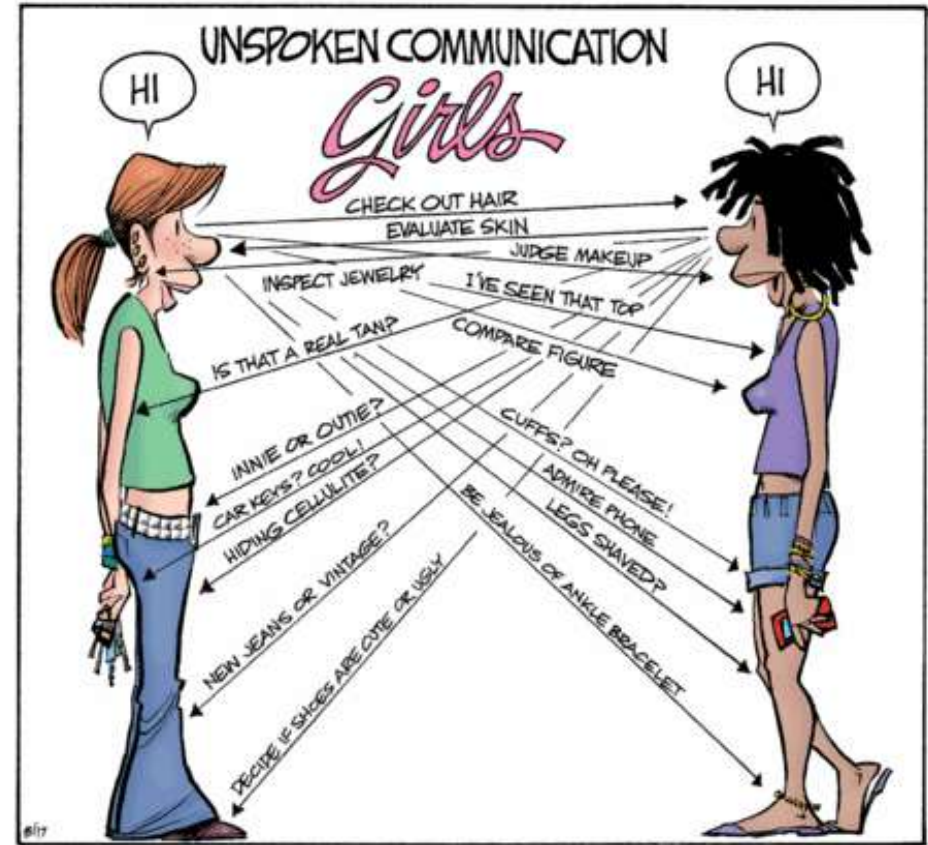


what a machine is looking at?

Artificial Intelligence

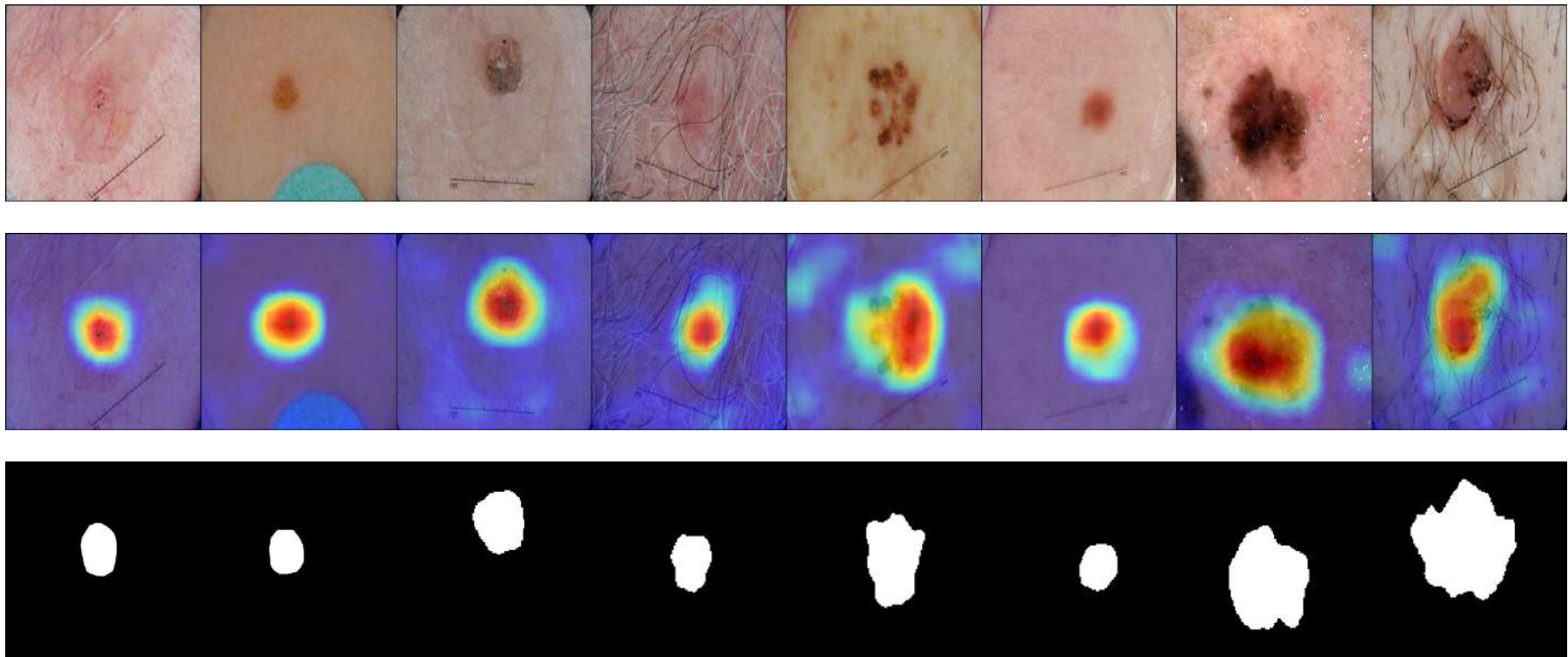


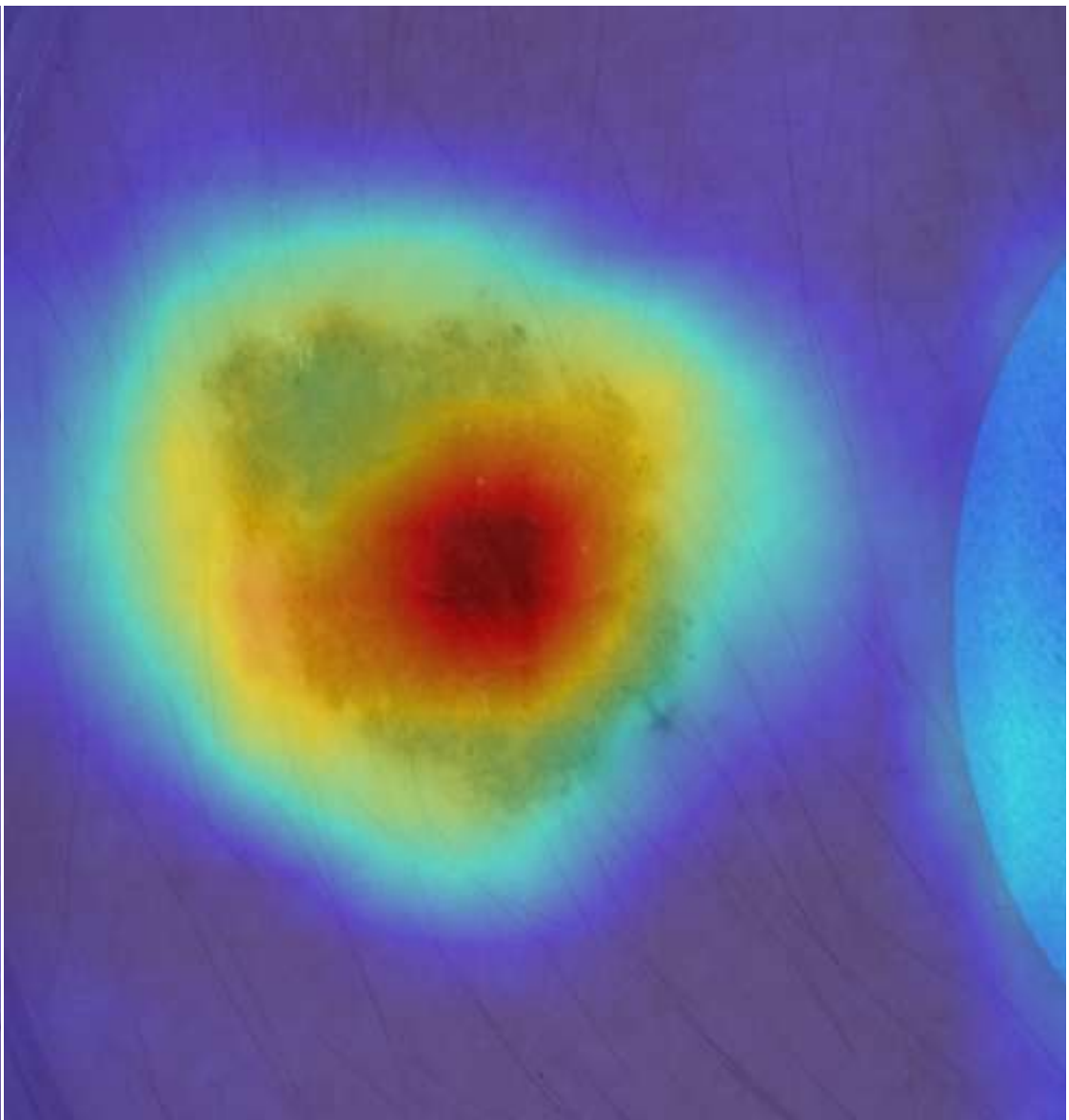
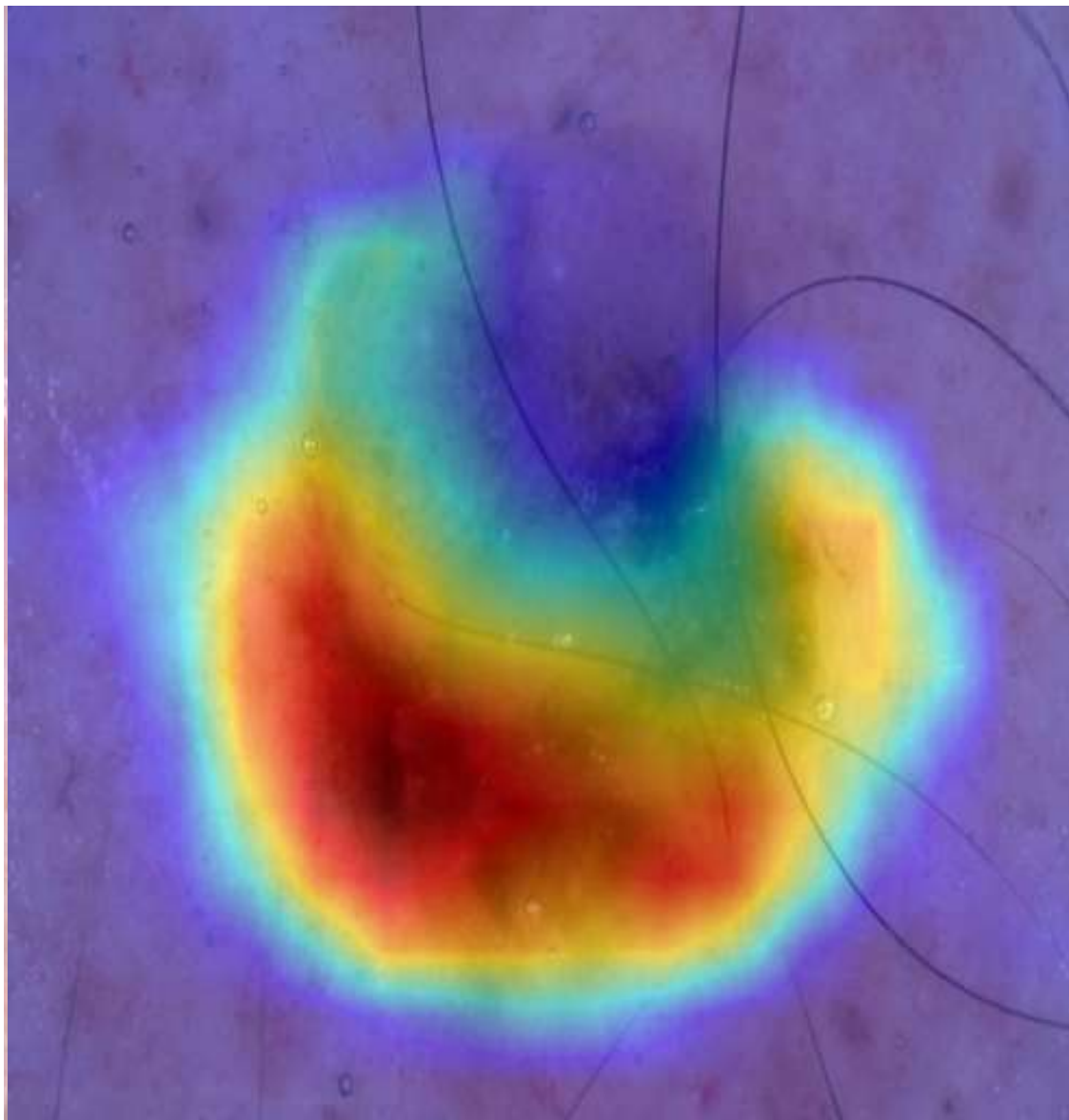
Neural Network

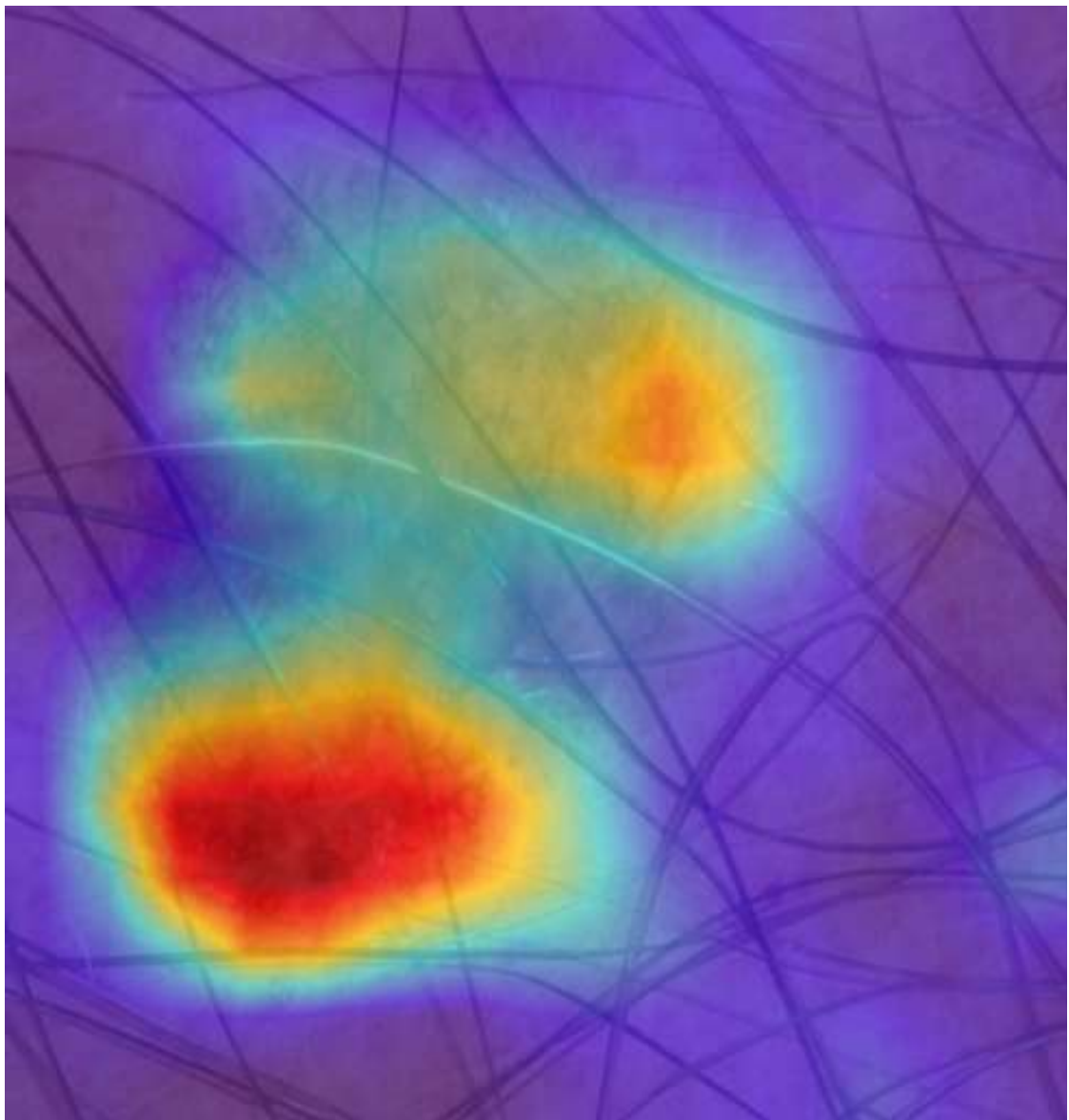
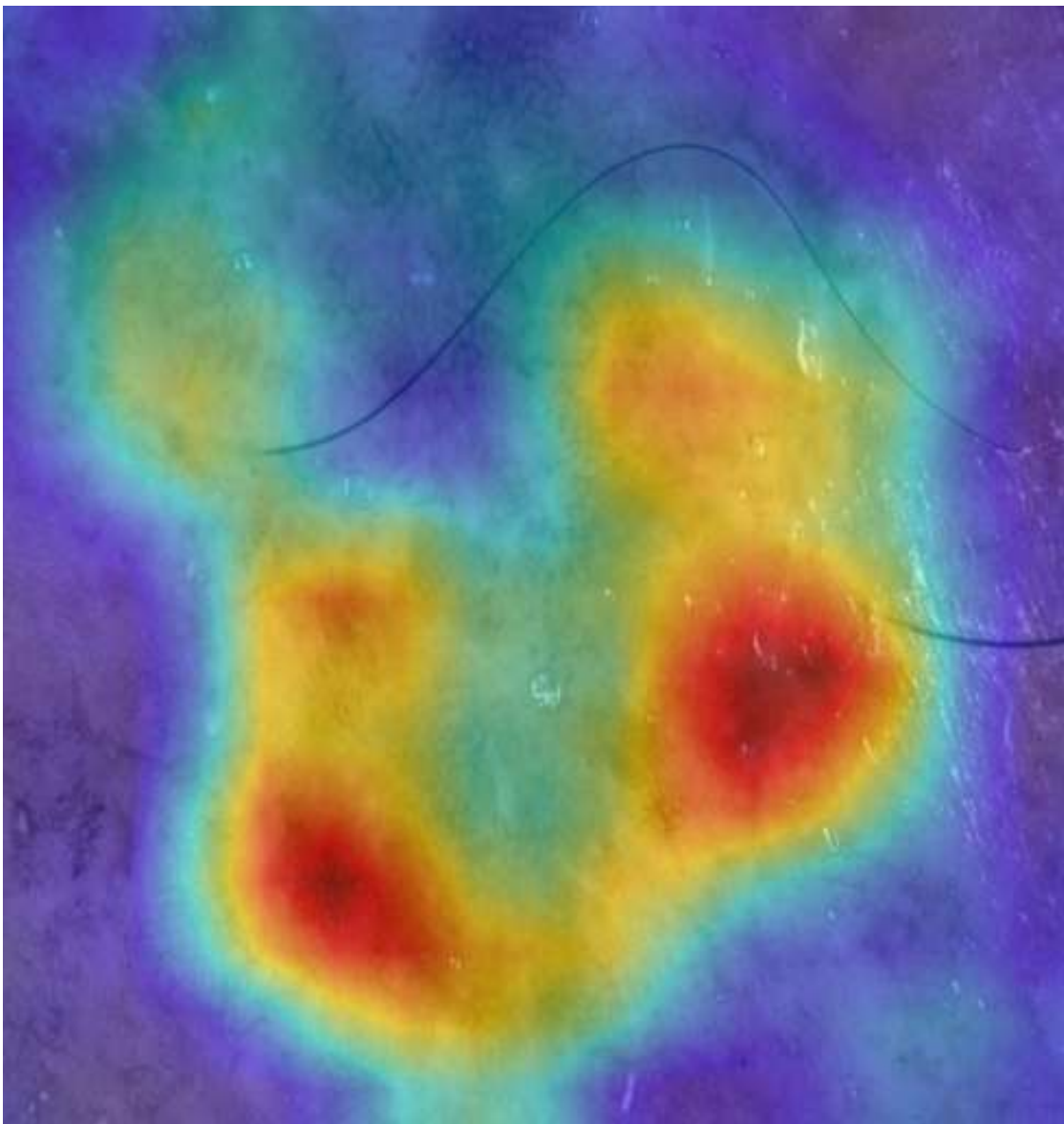


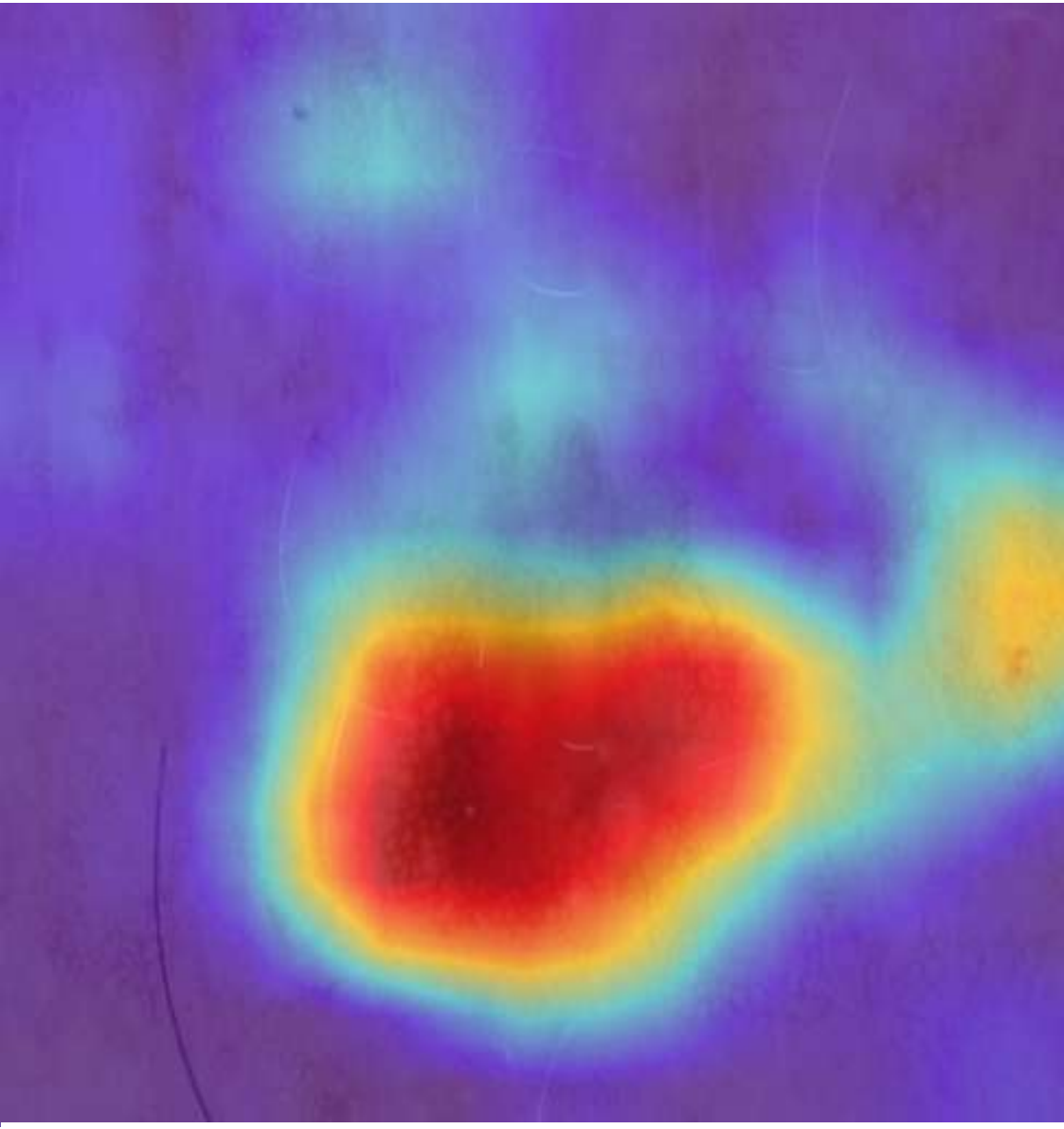
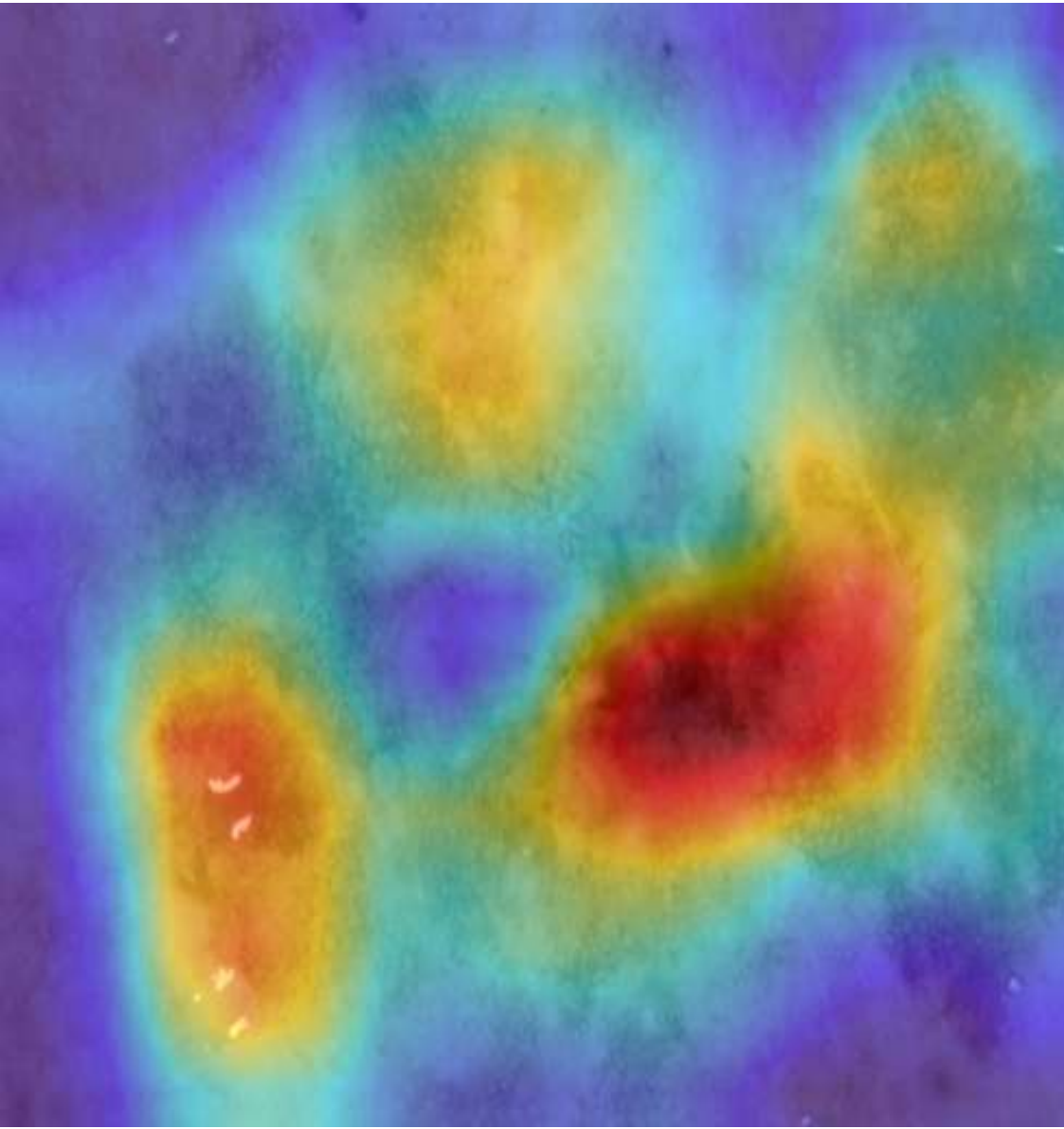
FEATURE EXTRACTION: HEATMAP

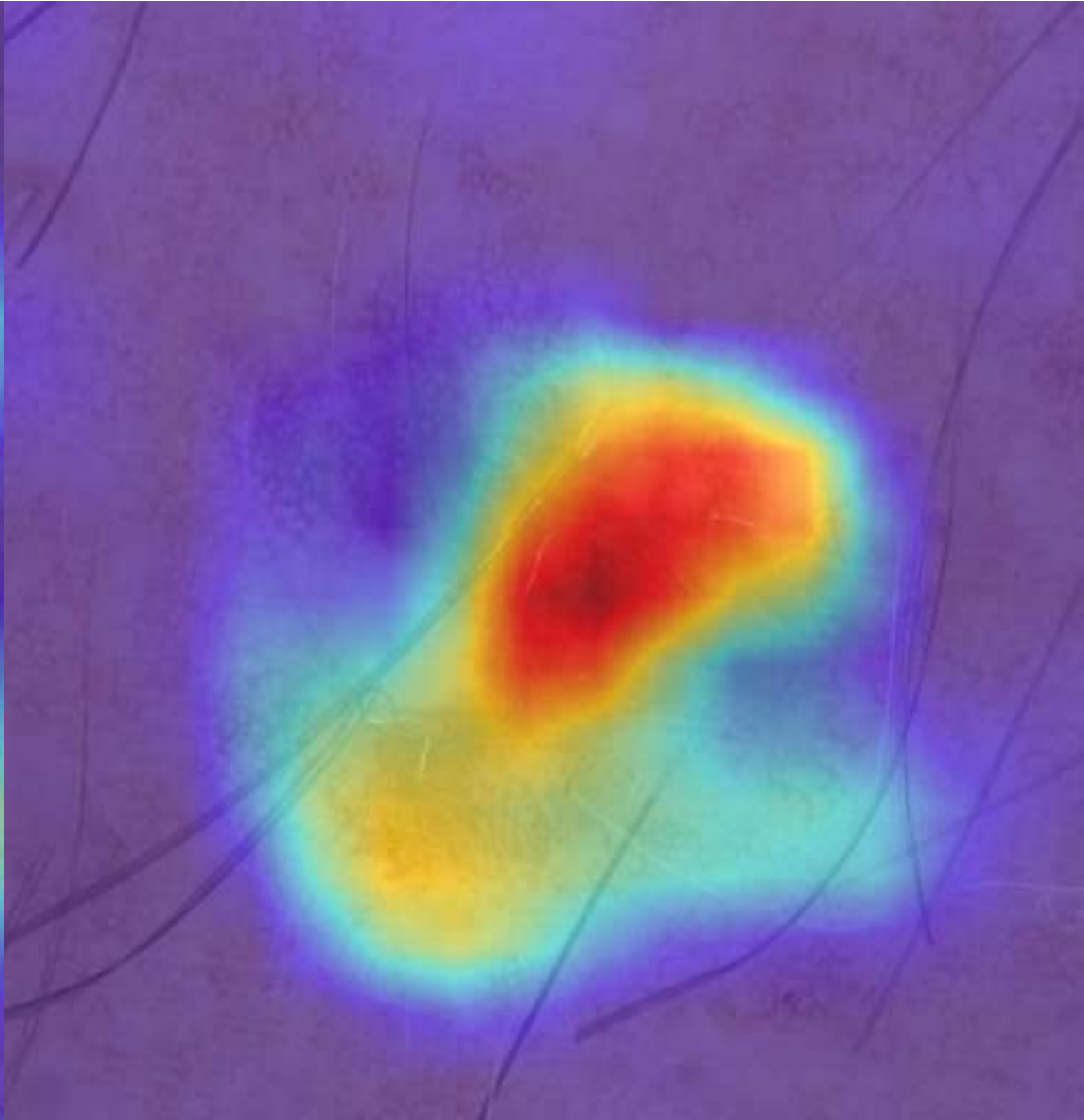
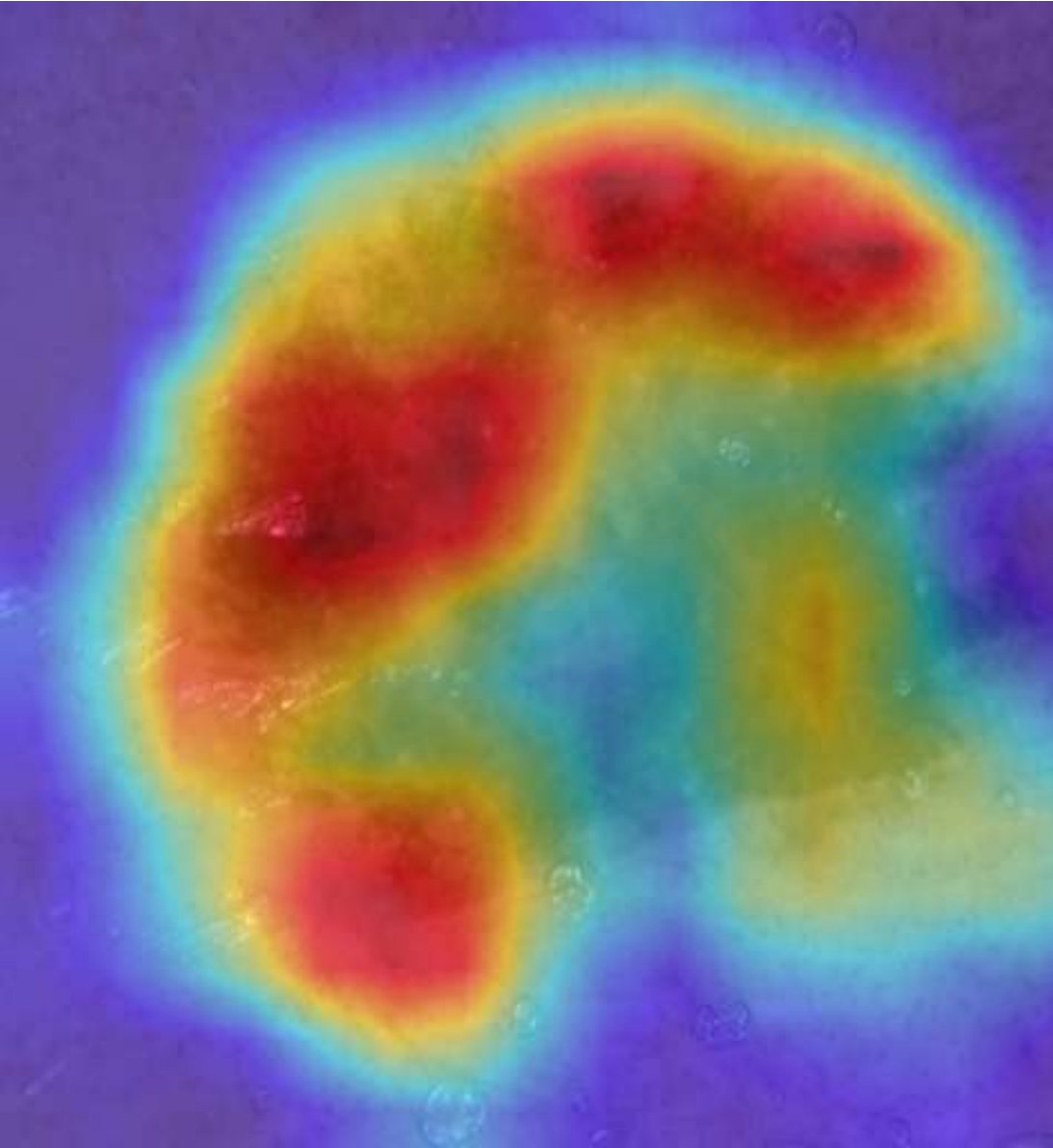
what a machine is looking at?





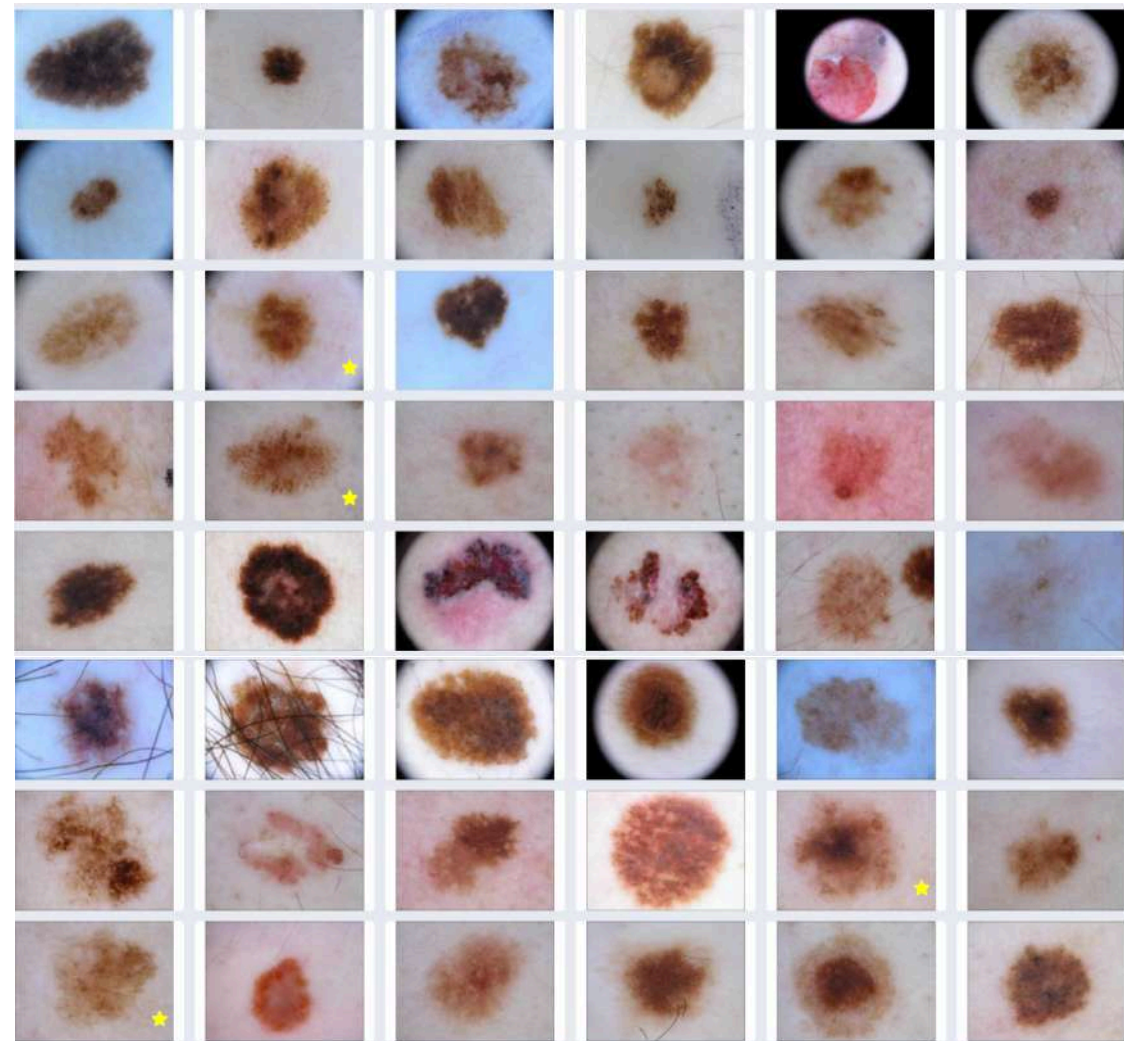






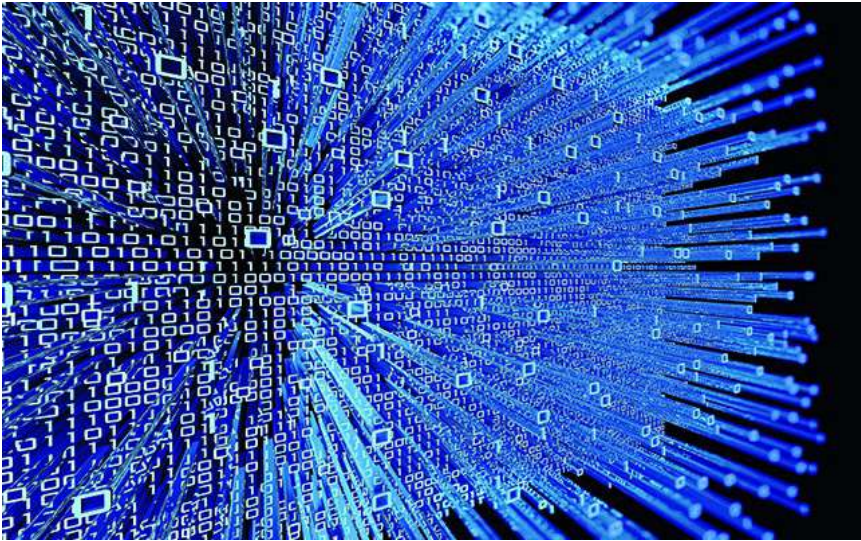
5. MAIN LIMITATION IN CNN

Today facial recognition is not “utopia” ...



.. does melanoma have more faces than human faces?

WHICH IS THE LIMIT IN MELANOMA RECOGNITION BY CNN?



**LACK OF AN ADEQUATE AMOUNT OF GOOD
QUALITY DATA!!!!**

6. FUTURE PERSPECTIVES

POSSIBLE FUTURE PROSPECTIVE

1. Open-access, standardized data (including also medical information)
2. Big data
3. Not only diagnosis (mobile app to digital monitoring skin lesions?)
4. Independent evaluation methodologies to accurately measure system efficacy



Thanks

To Prof Costantino Grana, Informatic Engineer - UNIMORE