

# Intelligenza artificiale in medicina nucleare

Dott. Stelvio Sestini SOC Medicina Nucleare Prato

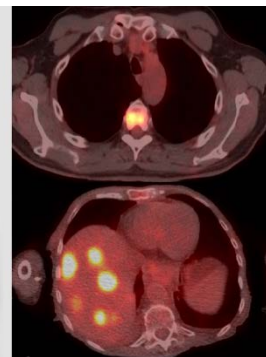
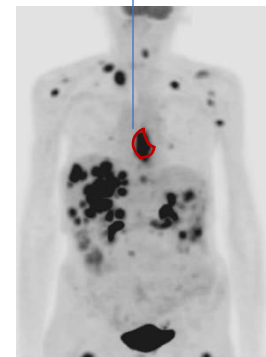
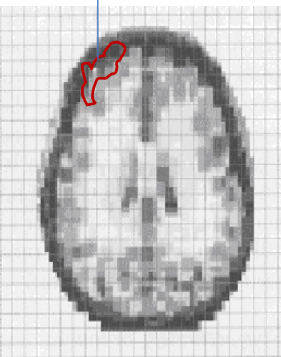
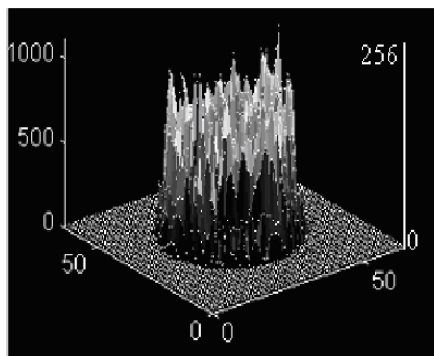
# Artificial Intelligence in Nuclear Medicine

Felix Nensa<sup>1</sup>, Aydin Demircioglu<sup>1</sup>, and Christoph Rischpler<sup>2</sup>

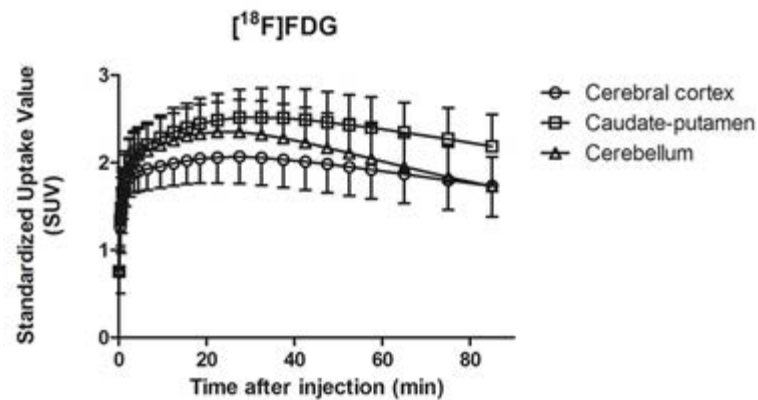
J Nucl Med 2019; 60:295–375

DOI: 10.2967/jnumed.118.220590

1) What do we measure : the 4<sup>th</sup> dimension  $[C_{\text{radioligand}}] / \text{time} [\Delta t_{0 - \text{Equilibrium}}]$  in volume of interest ( $V_{\text{xyz}}$ )



Time Activity Curve



# Artificial Intelligence in Nuclear Medicine

Felix Nensa<sup>1</sup>, Aydin Demircioglu<sup>1</sup>, and Christoph Rischpler<sup>2</sup>

## 2) AI: Symbolic reasoning

We model entities of the real world and their logical relationships in the form of symbols with which arithmetic operations can then be performed.

the only one AI during  
From the 1950s to the  
1980s,

Already using so far !!

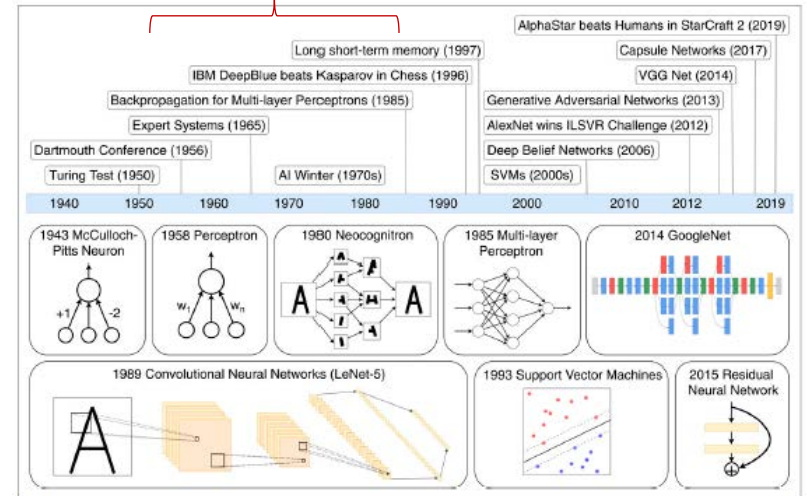


FIGURE 1. Brief time line of major developments in AI and machine learning. Some methods are also depicted symbolically. ILSVR = ImageNet Large Scale Visual Recognition; SVMs = support vector machines; VGG = Visual Geometry Group.

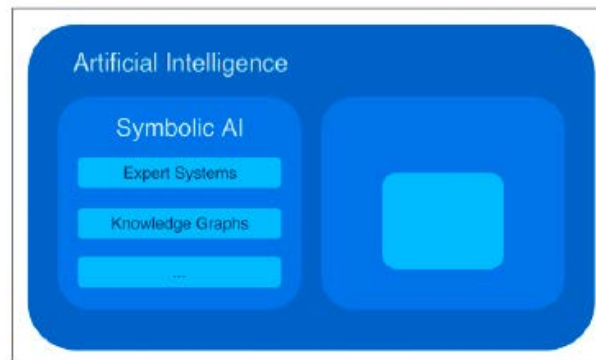
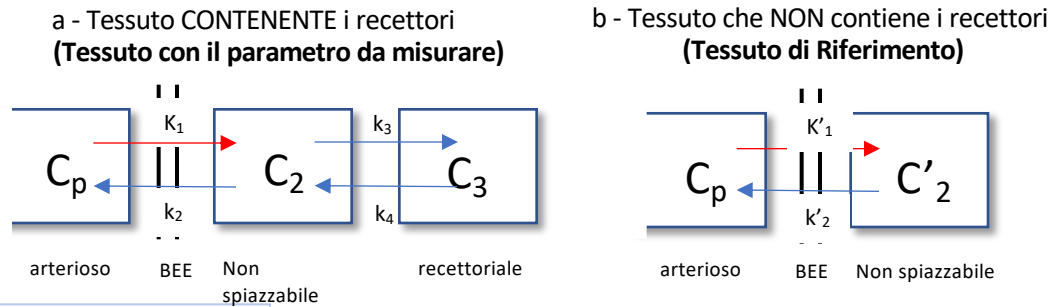
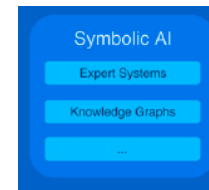


FIGURE 2. Division of field of AI into symbolic AI and machine learning, of which deep learning is a branch.

# AI: Example - Compartmental Modelling in Nuclear Medicine



Le variazioni di  $[C]$  nei singoli compartimenti possono essere descritte con un *set di equazione differenziali* che tiene conto degli input/output nei compartimenti stessi:

a { Eq. 4  $\frac{dC_3(t)}{dt} = k_3C_2(t) - k_4C_3(t)$

Eq. 7  $0 = k_3C_2(t) - k_4C_3(t) \rightarrow$  Eq. 10  $\frac{C_3}{C_2} = \frac{k_3}{k_4}$  e sostituendo  $C_2 = \frac{C_3k_4}{k_3}$  in Eq. 8

a { Eq. 5  $\frac{dC_2(t)}{dt} = K_1C_p(t) - k_2C_2(t) - k_3C_2(t) + k_4C_3(t)$

Eq. 8  $0 = K_1C_p(t) - k_2C_2(t) - k_3C_2(t) + k_4C_3(t) \rightarrow$  Eq. 11  $\frac{C_3}{f_1C_p} = \frac{K_1k_3}{k_2k_4}$  dove  $BP = \frac{C_3}{f_1C_p} \approx \frac{B'_{max}}{K_d}$  in vitro

b { Eq. 6  $\frac{dC'_2(t)}{dt} = K_1C_p(t) - k'_2C'_2(t)$

Eq. 9  $0 = K'_1C_p(t) - k'_2C'_2(t) \rightarrow$  Eq. 12  $\frac{C'_2}{f_1C_p} = \frac{K'_1}{k'_2}$

All'Equilibrio (no trasferimento netto di radiofarmaco tra i comp.), il lato sn delle equazioni = 0

## Legenda

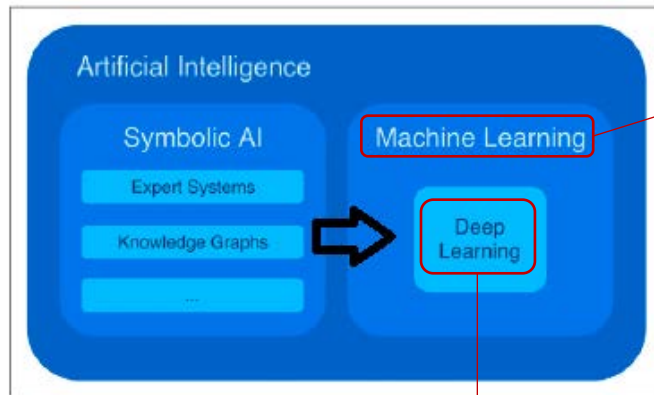
$C_p(t)$  = [plasmatica] del radiofarmaco non metabolizzato (Bq/mL)  
 $C_2(t)$  = [radiofarmaco] nel comp. non spiazzabile del tessuto con i recettori (Bq/mL)  
 $C'_2(t)$  = [radiofarmaco] nel comp. non spiazzabile del tessuto di riferimento (Bq/mL)  
 $C_3(t)$  = [radiofarmaco] nel comp. recettoriale specifico (Bq/mL)

$f_1C_p(t)$  = frazione di  $C_p$  che può diffondere verso  $C_2$  o  $C'_2$   
 $f_1C_2(t)$  = frazione di  $C_p$  che può diffondere verso  $C_3$   
 $K_1$  e  $K'_1$  = Delivery Rate Constant dal plasma al comp. non spiazzabile (mL/g/min)  
 $k_2$  e  $k'_2$  = rate di retro-diffusione dal comp. non spiazzabile al comp. plasmatico ( $\text{min}^{-1}$ )  
 $K_3$  e  $k_4$  = rate di trasferimento dal comp. non spiazzabile al comp. Recettoriale e viceversa ( $\text{min}^{-1}$ )

# Artificial Intelligence in Nuclear Medicine

Felix Nensa<sup>1</sup>, Aydin Demircioglu<sup>1</sup>, and Christoph Rischpler<sup>2</sup>

## 3) AI: MACHINE LEARNING – DEEP LEARNING



**FIGURE 2.** Division of field of AI into symbolic AI and machine learning, of which deep learning is a branch.

In “conventional machine learning” computer systems learn to accomplish a task independently—that is, without explicit instructions—and thus perform observational learning from large amounts of data.

Warning

... big data are necessary to learn

... the internal representation of the investigated system is very complex as “black boxes,” and the corresponding output of such systems can no longer be reliable

Warning

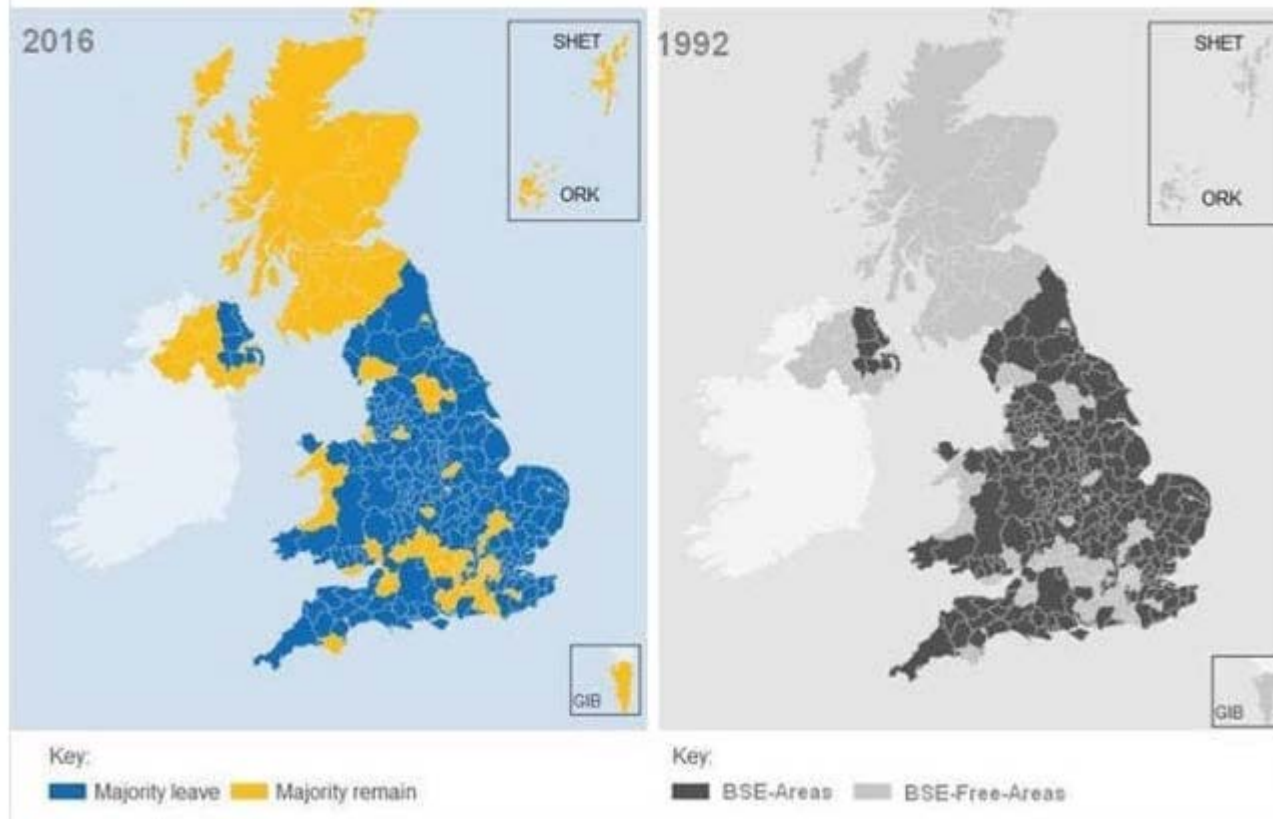
... to be aware of question in input

deep learning is based on artificial neural networks (ANNs). Because of a multitude of layers (so-called hidden layers) between the input and output layers, these neural networks have a much larger space for free parameters and thus allow much more complex abstractions than conventional machine learning methods.

Warning

... to be aware of question in input ...

## EU Referendum Results 2016 vs. Mad Cow Disease Outbreak Areas 1992

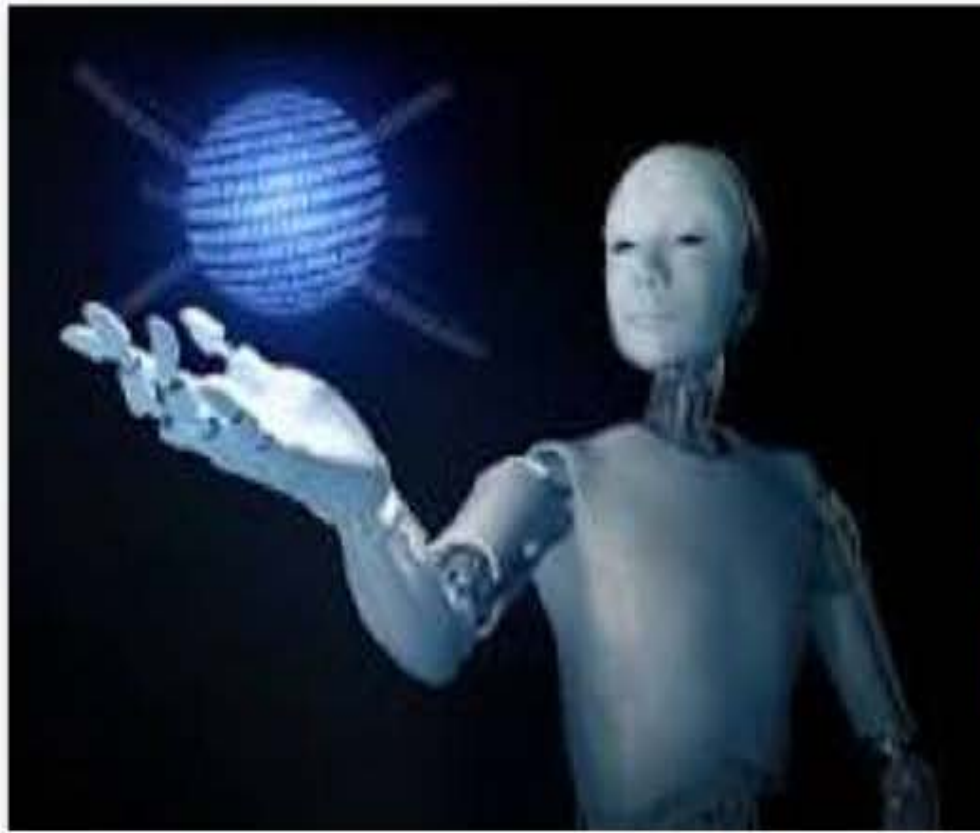




# Intelligenza Artificiale in Medicina Nucleare



**Fisica Sanitaria PO - PT**



Artificial intelligence (AI) is intelligence exhibited by machines.

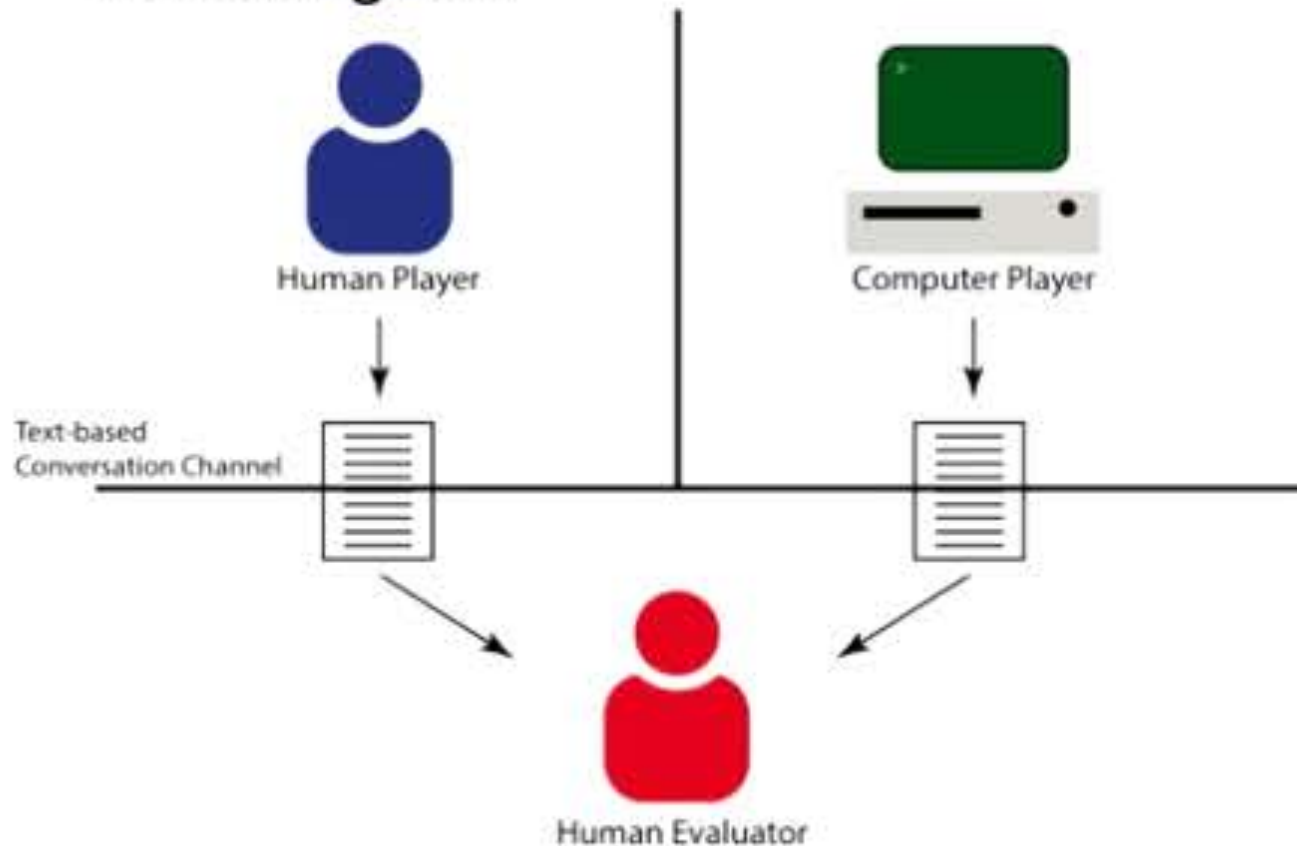
...

Colloquially, the term "artificial intelligence" is applied when a machine mimics "cognitive" functions that humans associate with other human minds, such as "learning" and "problem solving".



# Can Machines Think?

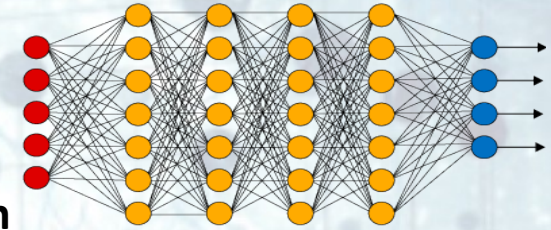
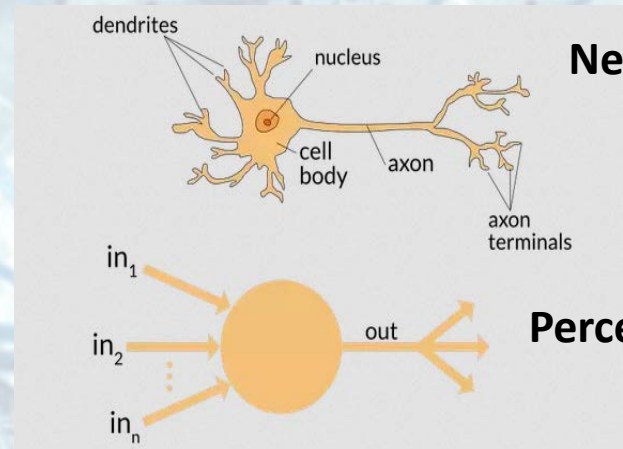
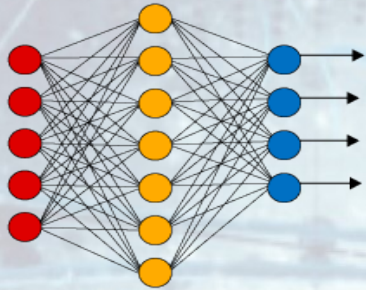
- The Turing Test



Turing AM. *Mind*. 1950;59:433-460.

Warwick K and Shah H. *J Exp Theor Artif Intell*. 2016;28:989-1007.

# From Neural Network to Deep Learning



## Application Areas

system identification, natural resource management, process control, vehicle control, quantum chemistry, [decision making](#), game playing, face identification, pattern recognition, signal classification, sequence recognition, object recognition, finance, **medical diagnosis**, [visualization](#), [data mining](#), machine translation, email spam filtering, [social network](#) filtering

Automatic speech recognition, Image recognition, visual art processing, Natural language processing, drug discovery and toxicology, customer relationship management, recommendation engines, Mobile advertising, **medical prognosis**, bioinformatics, Image restoration etc.

# From Neural Network to Deep Learning

## Supervised Machine Learning

e.g. a comprehensive symptom-diagnoses dataset identified in the Partners' medical record

Training Set  
 $\{(x^{(i)}, y^{(i)}); i=1, \dots, m\}$



Machine learning  
algorithm



New Data  
 $\{x'\}$



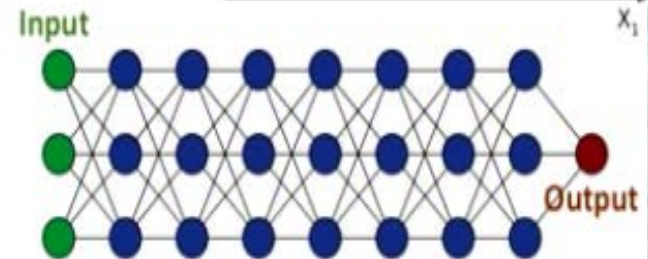
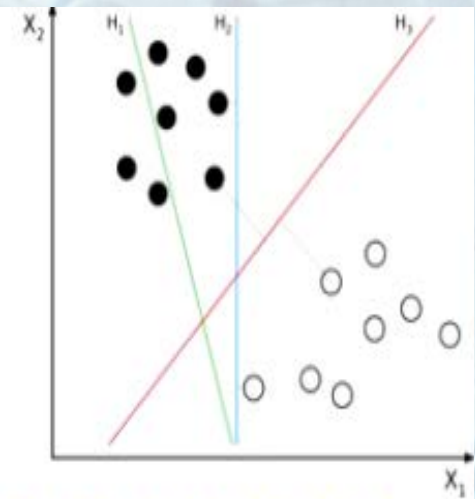
Machine learning  
model



Predicted Outcome  
 $\{y'\}$

e.g. the symptoms  
of a new patient

e.g. diagnoses

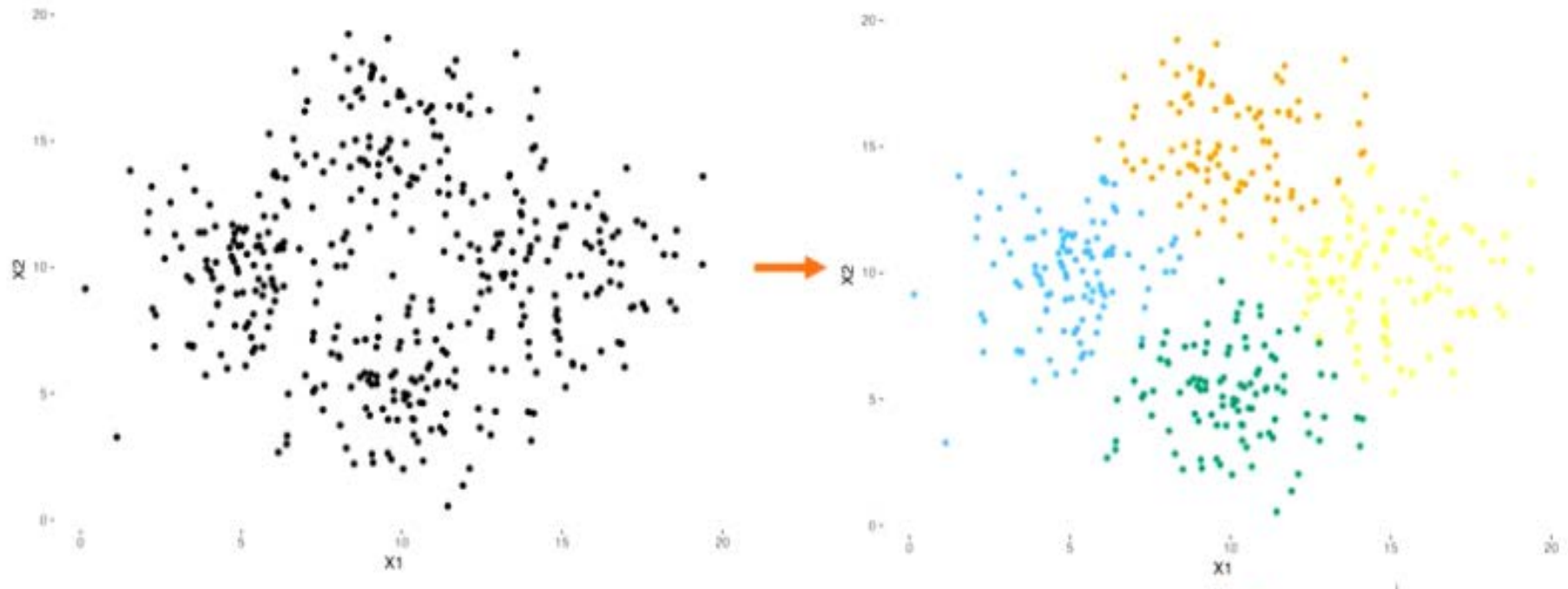




# From Neural Network to Deep Learning

## Unsupervised Machine Learning

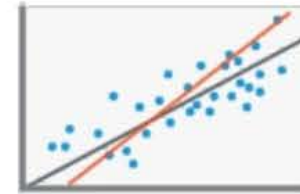
- e.g. Clustering



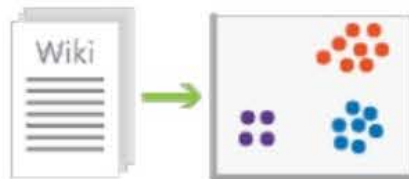
# From Neural Network to Deep Learning



Classification  
(supervised – predictive)



Regression  
(supervised – predictive)



Clustering  
(unsupervised – descriptive)



Anomaly Detection  
(unsupervised – descriptive)



# Artificial Intelligence

- The field of study that attempts to both understand and build intelligent entities
- Fueled by
  - Availability of the big data
  - Advanced machine learning algorithms
  - Growth in computation power



2018

=



2006



# From Neural Network to Deep Learning



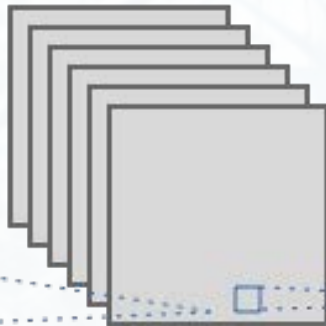
What We See

00 00 22 97 38 15 00 40 00 70 04 00 07 78 02 12 00 77 81 00  
49 49 39 40 17 81 18 07 80 07 17 40 00 40 40 40 04 08 40 00  
81 49 81 78 00 78 14 28 40 71 40 47 00 00 00 00 00 10 04 40  
60 70 00 20 04 40 11 42 40 24 40 04 01 02 00 71 07 00 04 00  
22 91 14 71 11 47 40 00 01 00 04 04 22 40 00 00 00 10 00  
28 47 00 00 00 00 40 02 44 70 00 00 78 04 04 20 00 17 12 00  
02 00 01 20 44 20 07 10 20 00 40 07 00 04 70 00 10 00 04 70  
47 24 20 40 02 42 12 20 00 40 04 00 00 00 40 01 00 00 00 20  
24 00 00 00 40 70 00 24 07 17 70 70 04 00 14 00 04 00 70  
21 04 20 00 70 00 74 44 20 40 00 14 00 00 00 07 04 00 00 00  
78 17 00 20 22 70 01 47 10 04 00 00 04 42 14 14 00 00 04 00  
14 00 00 42 04 00 01 47 00 00 00 24 00 17 04 04 00 00 07  
04 04 00 40 00 71 00 07 00 44 44 07 04 40 20 00 01 04 17 00  
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04 42 00 00 07 00 00 14 07 07 07 00 14 04 14 70 00 07 00 00  
00 04 00 07 07 42 20 70 00 40 00 47 04 00 12 00 40 00 00 40  
04 42 14 70 00 20 00 11 24 04 70 10 00 40 20 00 40 74 04  
20 49 04 41 72 00 20 00 44 42 00 40 02 47 00 00 74 00 04 04  
20 78 00 20 70 01 00 01 74 01 40 71 40 04 01 14 20 07 00 04  
01 70 04 71 00 01 04 40 14 00 00 40 01 40 02 01 00 10 47 00

What Computers See



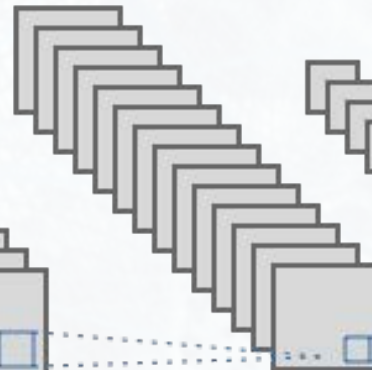
Input



Convolution + ReLU



Pooling



Convolution + ReLU

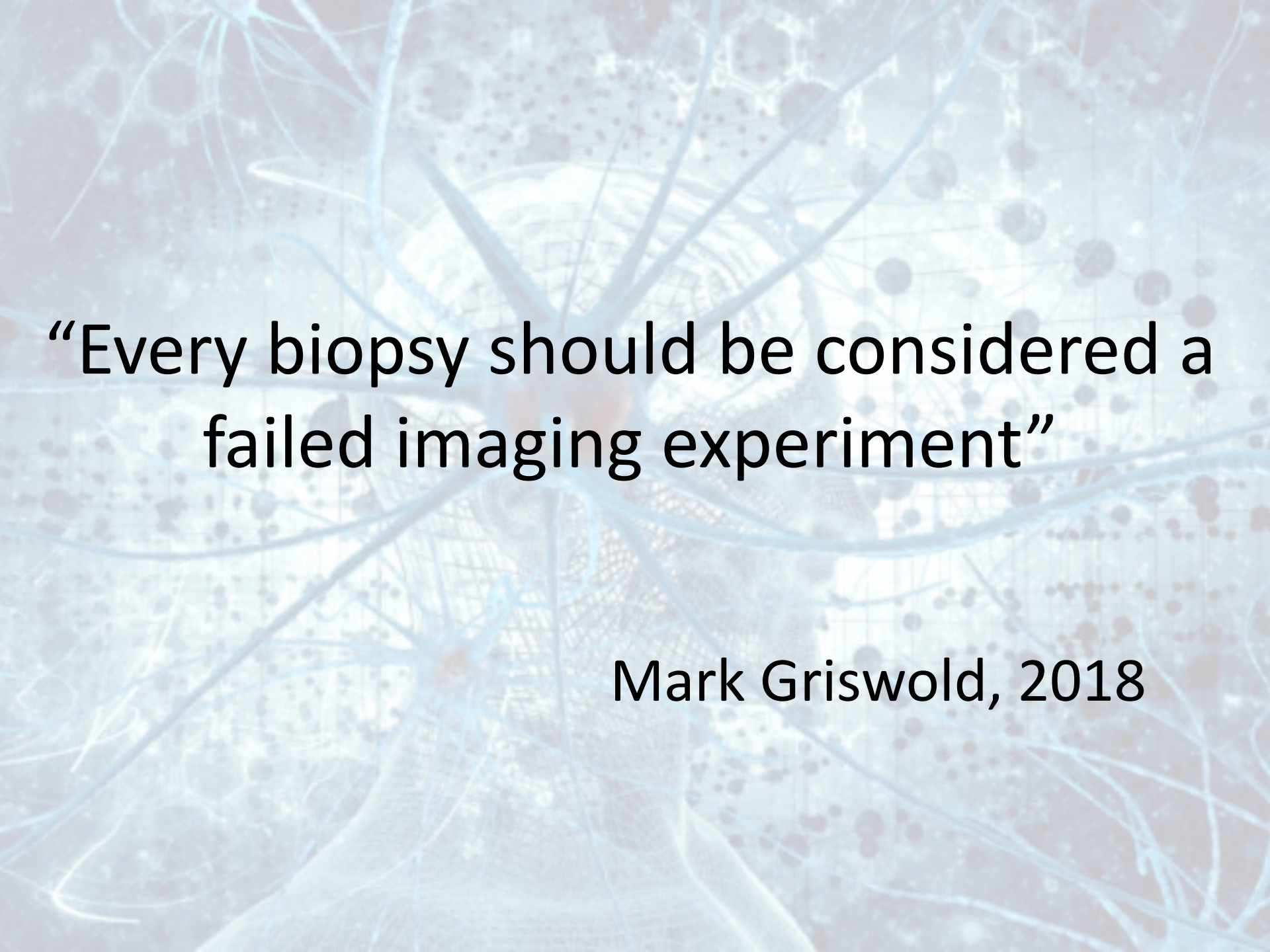


Pooling



Fully Connected



The background of the slide is an abstract composition of thin, light blue lines and small, semi-transparent dots of various shades of blue and white. These elements are scattered across the entire frame, creating a sense of depth and complexity, reminiscent of a neural network or a microscopic view of tissue.

**“Every biopsy should be considered a failed imaging experiment”**

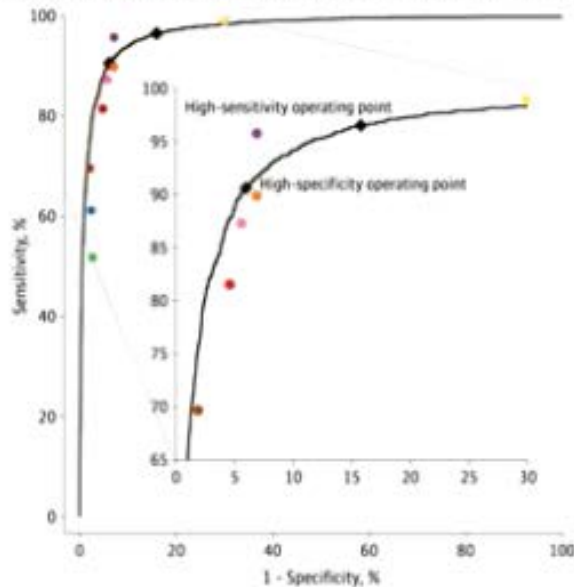
**Mark Griswold, 2018**

# DL in Medicine

JAMA | Original Investigation | INNOVATIONS IN HEALTH CARE DELIVERY

## Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs

Varun Gulshan, PhD; Lily Peng, MD, PhD; Marc Coram, PhD; Martin C. Stumpe, PhD; Derek Wu, BS; Arunachalam Narayanaswamy, PhD; Subhashini Venugopalan, MS; Kasumi Widner, MS; Tom Madams, MEng; Jorge Cuadros, OD, PhD; Ramasamy Kim, OD, DNB; Rajiv Raman, MS, DNB; Philip C. Nelson, BS; Jessica L. Mega, MD, MPH; Dale R. Webster, PhD

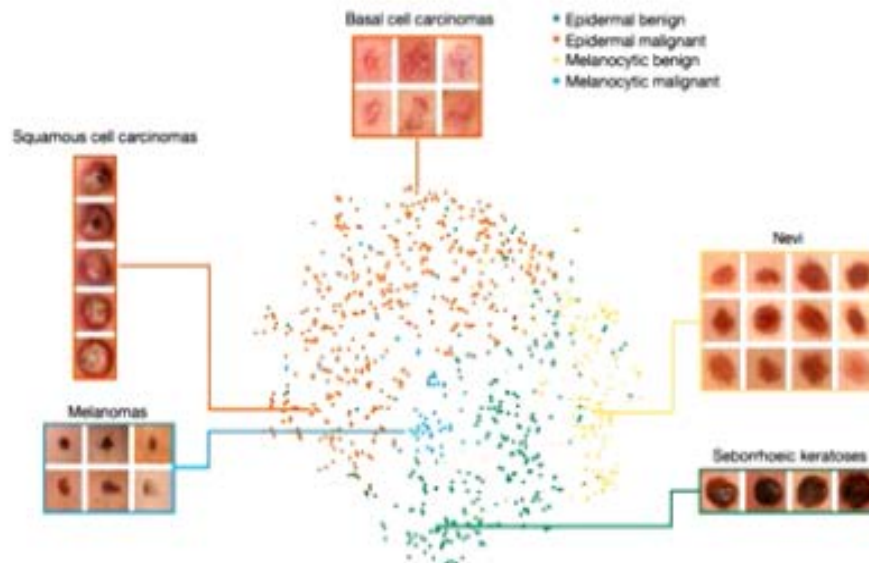


- A deep neural network model detects referable diabetic retinopathy with expert-level performance
- A similar system by another group is approved by the U.S. FDA

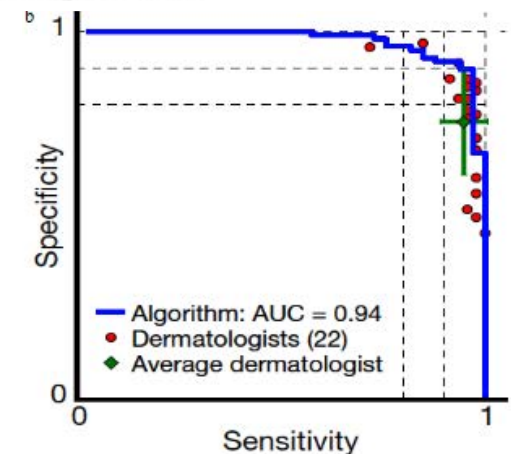
# DL in Medicine

## Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteve<sup>1\*</sup>, Brett Kuper<sup>1\*</sup>, Roberto A. Nova<sup>2,3</sup>, Justin Ko<sup>2</sup>, Susan M. Swetter<sup>2,4</sup>, Helen M. Blau<sup>5</sup> & Sebastian Thrun<sup>6</sup>



- Machine learning models accurately classified skin lesion images into 2,032 diagnoses





# DL in Medicine

## A Recurrent CNN for Automatic Detection and Classification of Coronary Artery Plaque and Stenosis in Coronary CT Angiography

Majd Zreik, Robbert W. van Hamersvelt, Jelmer M. Wolterink,  
Tim Leiner, Max A. Viergever, Ivana Išgum

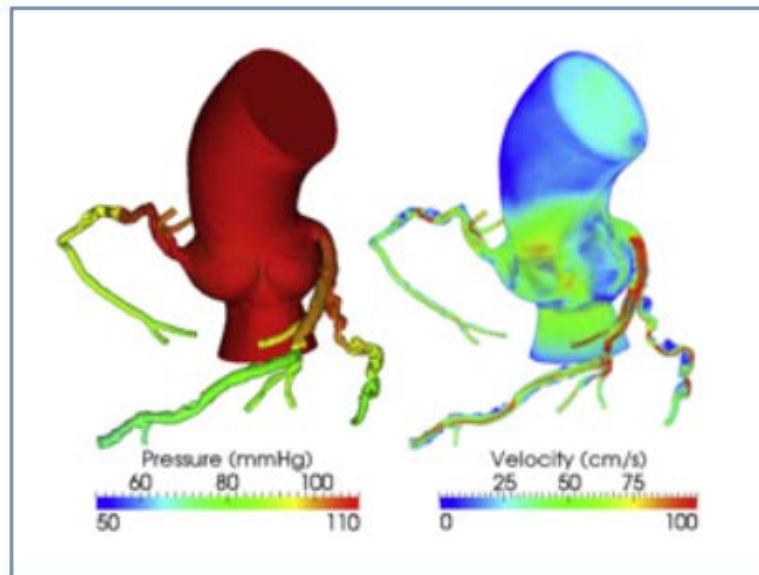
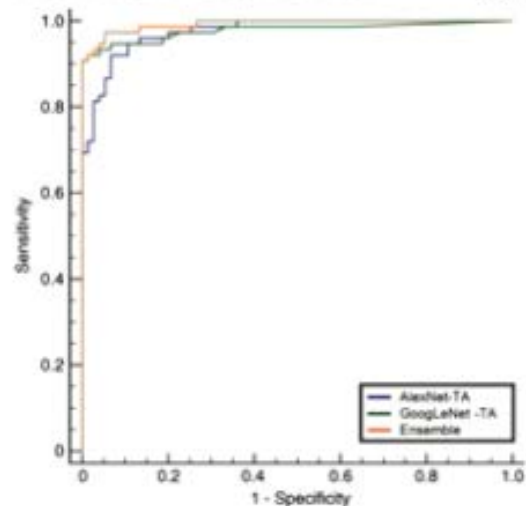


Figure 4: Three-dimensional pressure and velocity fields at one point in the cardiac cycle using FFR- based on CTA imaging ( $\text{FFR}_{\text{CT}}$ ). The computation is repeated throughout the cardiac cycle. *Source:* Images have been taken from Taylor et al 2013 [34].

# DL in Medicine

## Deep Learning at Chest Radiography: Automated Classification of Pulmonary Tuberculosis by Using Convolutional Neural Networks<sup>1</sup>

Paras Lakhani, MD  
Baskaran Sundaram, MD

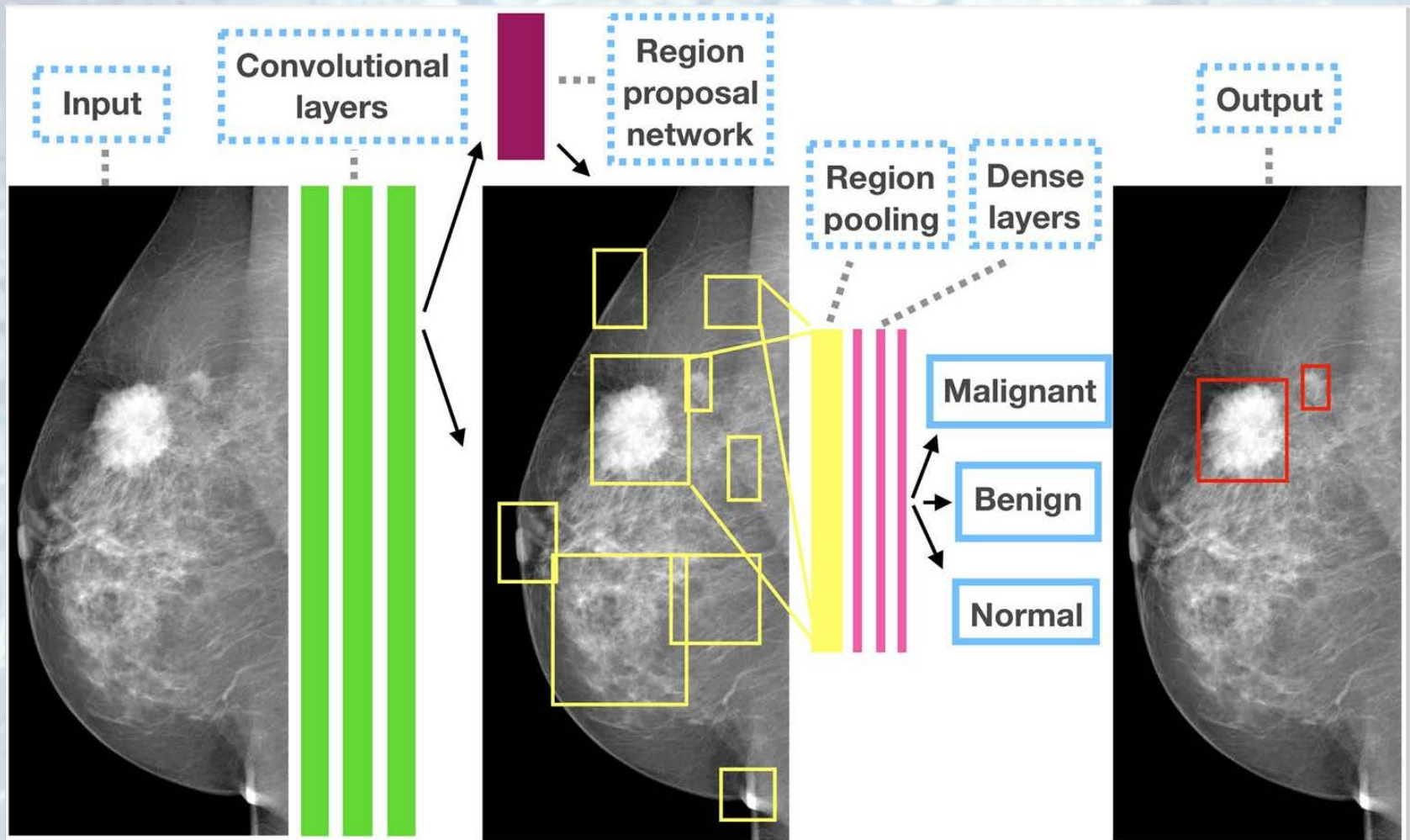


Radiology

- Similar approaches detected tuberculosis on chest radiographs with 99% accuracy

# DL in Medicine

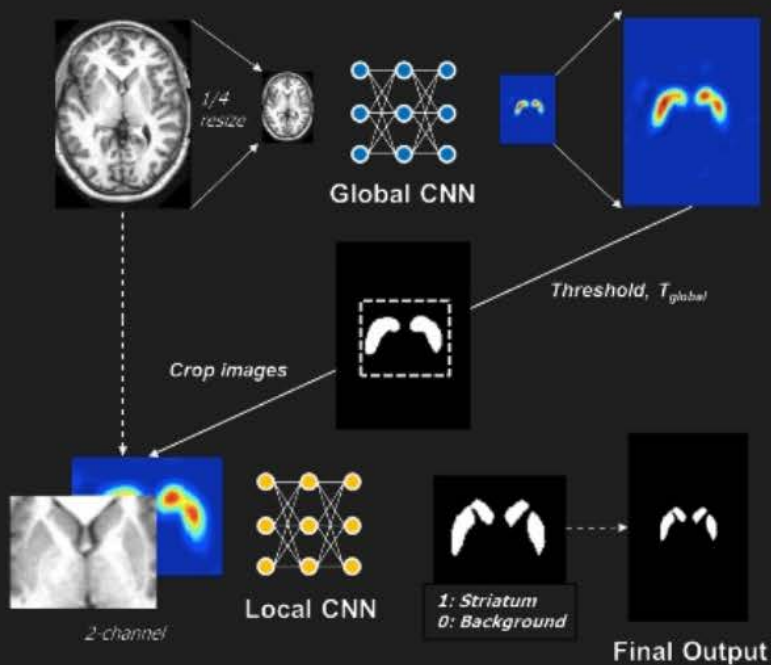
MIT Deploys Deep Learning Tool for Analyzing Mammograms



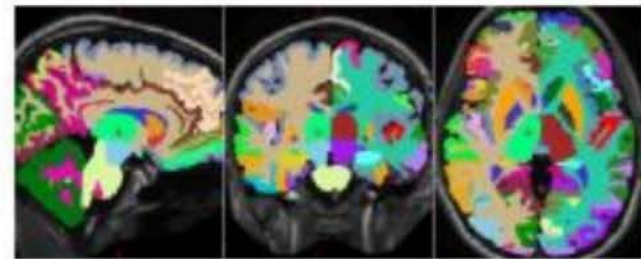


# DL in Medicine

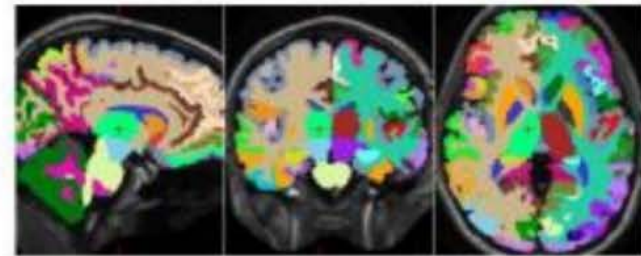
## Segmentation



Choi, H., & Jin, K. H. J Neurosci Methods 2016



(a) Manual segmentation.

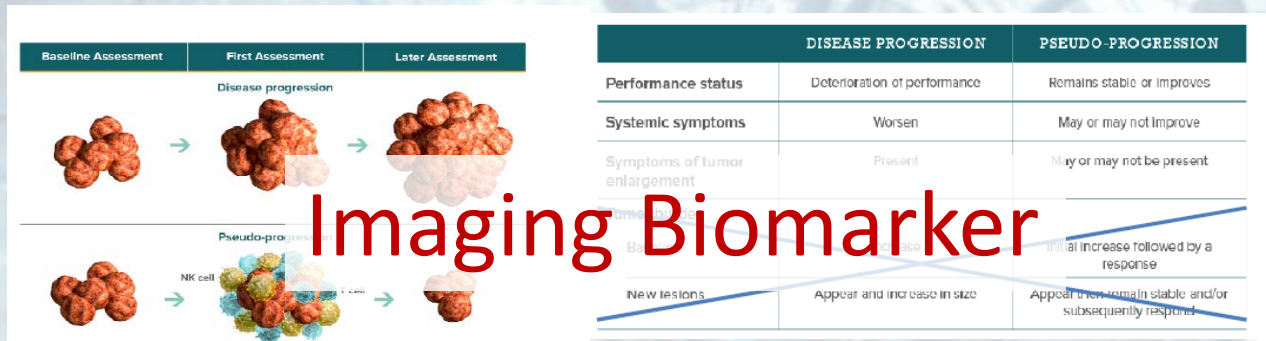


(b) Predicted segmentation.

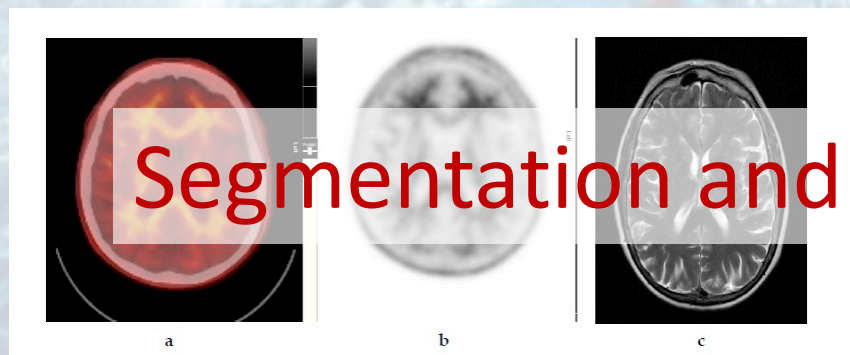
de Brebisson, et al. CVPR 2015.

# Moving toward DL...

**Radiomics Immuno-Lung:** Correlate CT quantitative parameters to progression of clinical and / or radiological disease



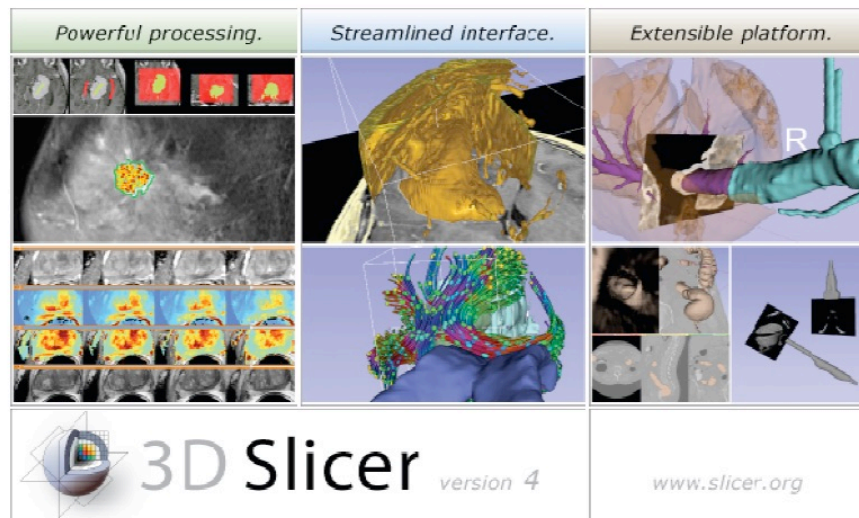
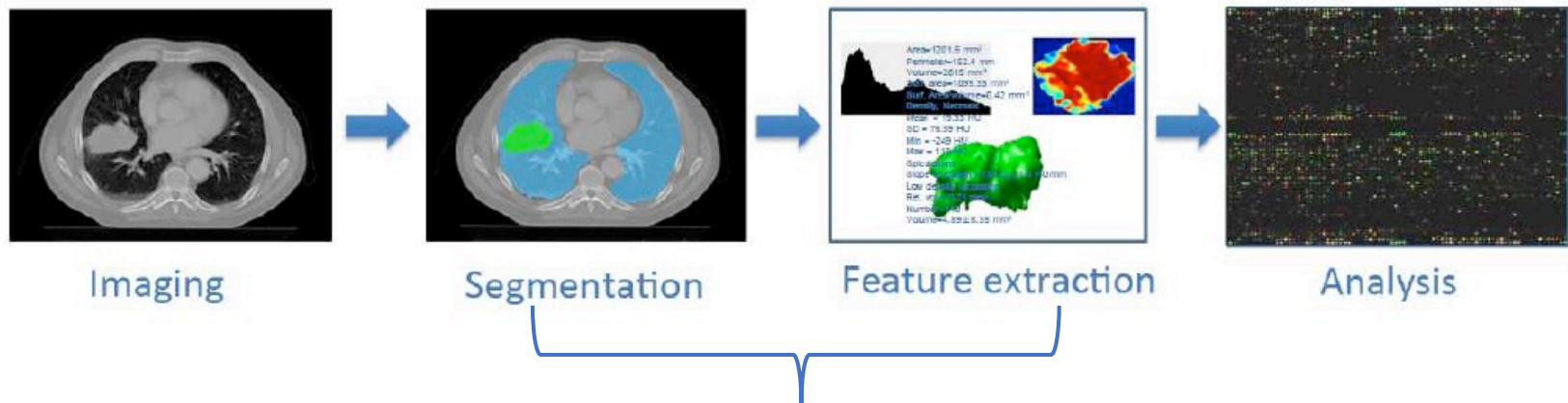
**Objective imaging in Amyloid PET neuroimaging:** Automatic quantitative analysis of PET amyloid images



Segmentation and Imaging Biomarker



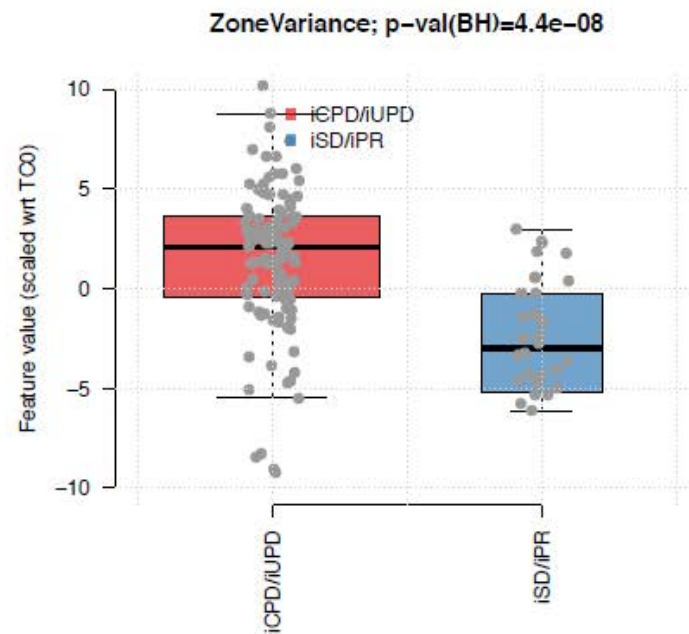
# Radiomics Immuno-Lung: Correlate CT quantitative parameters to progression of clinical and / or radiological disease



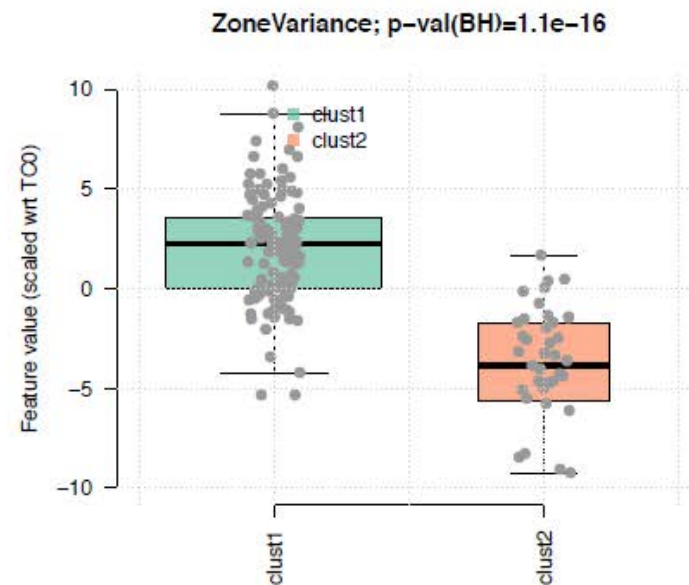
# Radiomics Immuno-Lung: Correlate CT quantitative parameters to progression of clinical and / or radiological disease

Nivolumab only, TCs > TC0 (n=161)

## By clinical



## By cluster membership

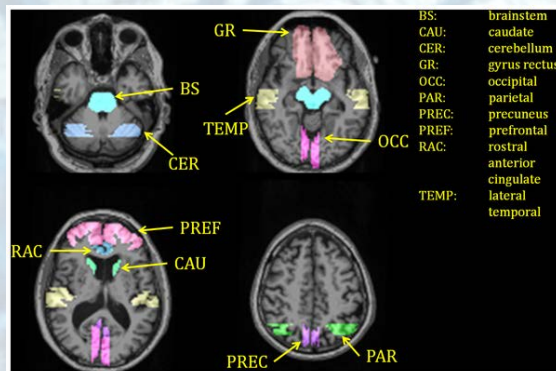
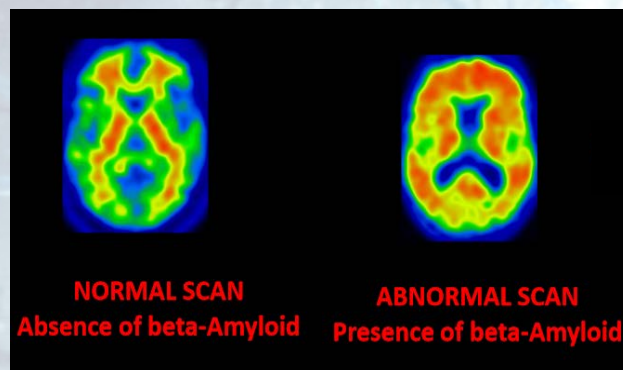




# Objective imaging in Amyloid PET neuroimaging: Automatic quantitative analysis of PET amyloid images

## Segmentation

From Fusion and manual contouring



To AutoSegmentation...

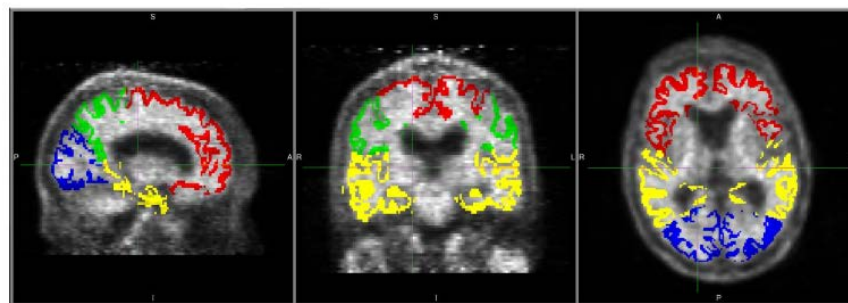


Figure 3.3: Example of image processing outcome in sagittal, coronal and transversal views. The original PET data is overlaid with the masks for the four lobes. These masks are obtained by applying atlas base masks on the grey-matter-only PET. Frontal lobe is depicted in red, parietal lobe in green, occipital lobe in blue and temporal lobe in yellow.

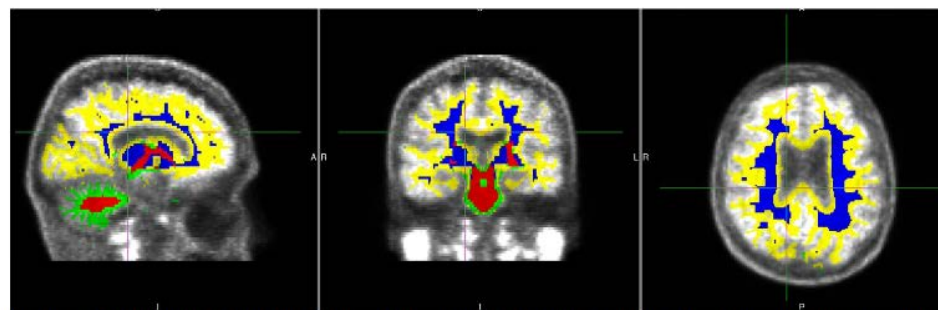


Figure 3.4: Visualization of four white matter based reference regions. All colours summed show the original whole brain white matter region, eroded white matter is represented by red and blue areas together. The white matter region without cerebellum is composed of yellow and blue area and blue alone depicts the smallest option which is eroded and cerebellum stripped of.

# Objective imaging in Amyloid PET neuroimaging: Automatic quantitative analysis of PET amyloid images

## Imaging Biomarkers

From One Parameter

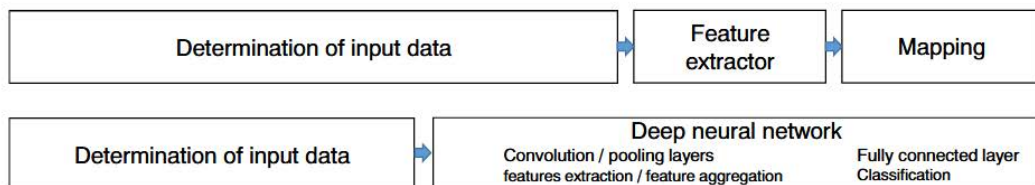
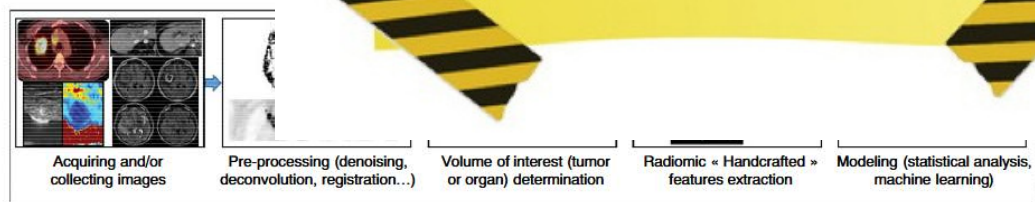
Image features

...to



al data

ics  
ne




**Fig. 1** The radiomics pipeline, in comparison with the usual machine learning workflow, and the deep learning workflow



# DL in Nuclear Medicine...coming out

## Full-Dose PET Image Estimation from Low-Dose PET Image Using Deep Learning: a Pilot Study

Sydney Kaplan<sup>1,2</sup> · Yang-Ming Zhu<sup>1,3</sup> 

© Society for Imaging Informatics in Medicine 2018

### Abstract

Positron emission tomography (PET) imaging is an effective tool used in determining disease stage and lesion malignancy; however, radiation exposure to patients and technicians during PET scans continues to draw concern. One way to minimize radiation exposure is to reduce the dose of radioactive tracer administered in order to obtain the scan. Yet, low-dose images are inherently noisy and have poor image quality making them difficult to use. This paper proposes the use of a deep learning model that takes specific image features into account in the loss function to enhance low-dose PET image slices and estimate their full-dose image quality equivalent. Testing on low-dose PET images indicates a significant improvement in image quality that is comparable to the ground truth full-dose images. Additionally, this approach can lower the cost of conducting a PET scan since less radioactive material is required, which may promote the usage of PET scans for medical diagnosis.

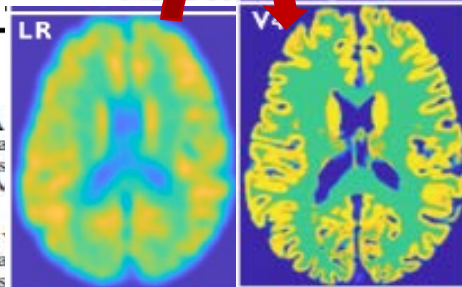
**Keywords** Deep learning · Denoising · Image estimation · Low-dose · PET

1/5 of Dose  
Administration

## SUPER-RESOLUTION PET IMAGING USING CONVOLUTIONAL NEURAL NETWORKS

**Tzu-A**  
Department of Electrical and  
Computer Engineering  
University of Massachusetts Lowell, MA 01854

**Fan**  
Department of Electrical and  
Computer Engineering  
University of Massachusetts Lowell, MA 01854

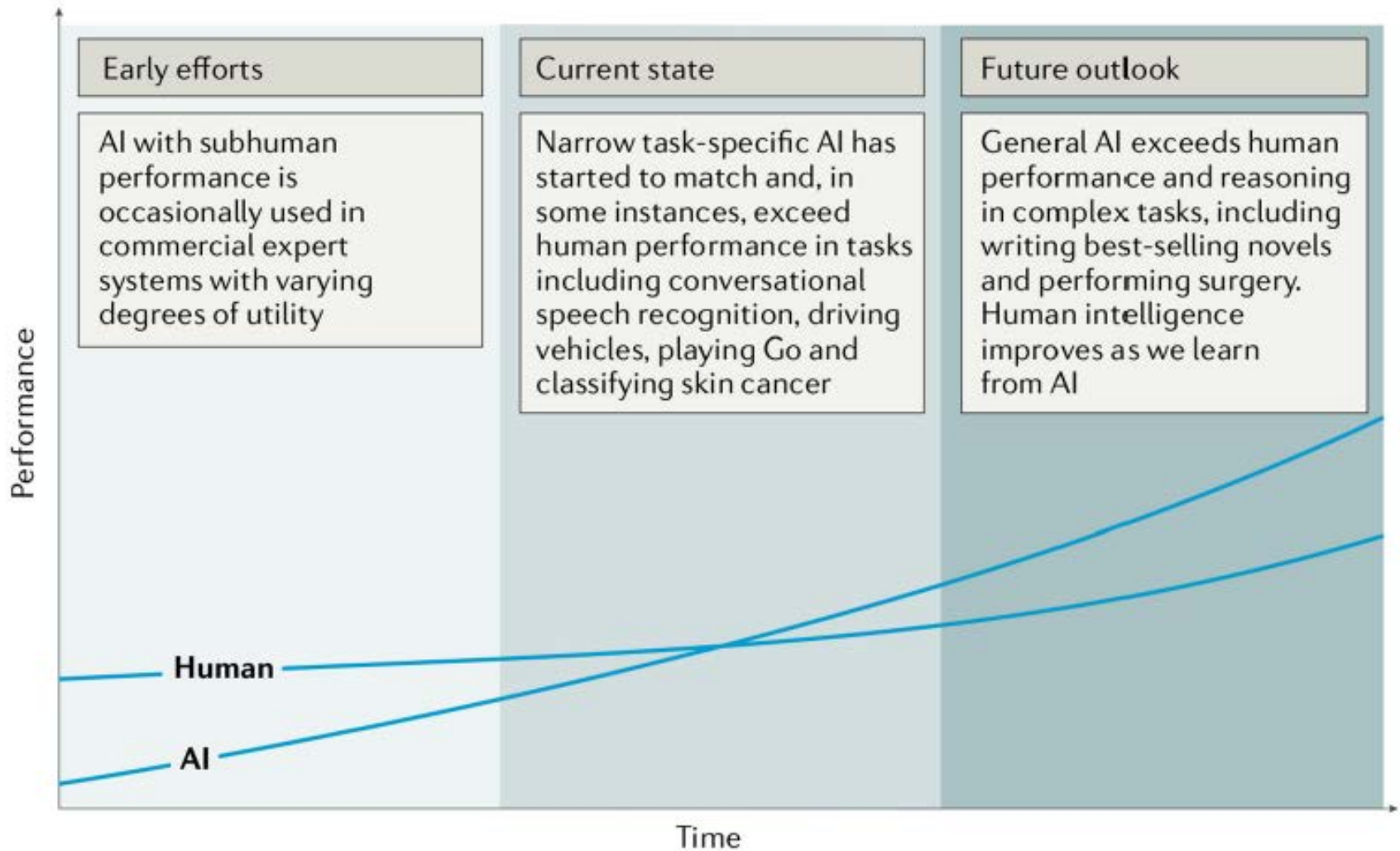


**Samadrita R. Chowdhury**  
Department of Electrical and Computer Engineering  
University of Massachusetts Lowell  
Lowell, MA 01854

**Joyita Dutta**  
Department of Electrical and Computer Engineering  
University of Massachusetts Lowell  
Lowell, MA 01854  
Gordon Center for Medical Imaging  
Massachusetts General Hospital  
Boston, MA 01720



# AI in future outlook....





Radiologists and nuclear doctors will  
be replace by AI?

Probably the ones who will not use it !!