PrimO
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Practical Recommendations in Immuno & Molecular Oncology

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Artificial Intelligence in Cancer Therapeutics:

Fact or Fiction?

Sanjay Juneja, M.D.
Hematologist & Medical Oncologist
***AI In Precision Oncology* Journal, Editorial Board Member**

What is the first action one takes after processing the need for treatment of a cancer diagnosis?

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"We want someone with *experience.*"

What about *experience* makes it so desirable?

1

2

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1

Adequate number of cases (high power) to best optimize pattern recognition.

2

What about *experience* makes it so desirable?

1

Adequate number of cases (high power) to best optimize pattern recognition.

2

To appreciate the number of variables—whether from the chosen intervention, or specific patient characteristics—to achieve the desired outcome.

What are two functions of AI?

1

2

What are two functions of AI?

1

Enormous capability for large data processing and pattern recognition.

2

What are two functions of AI?

1

Enormous capability for large data processing and pattern recognition.

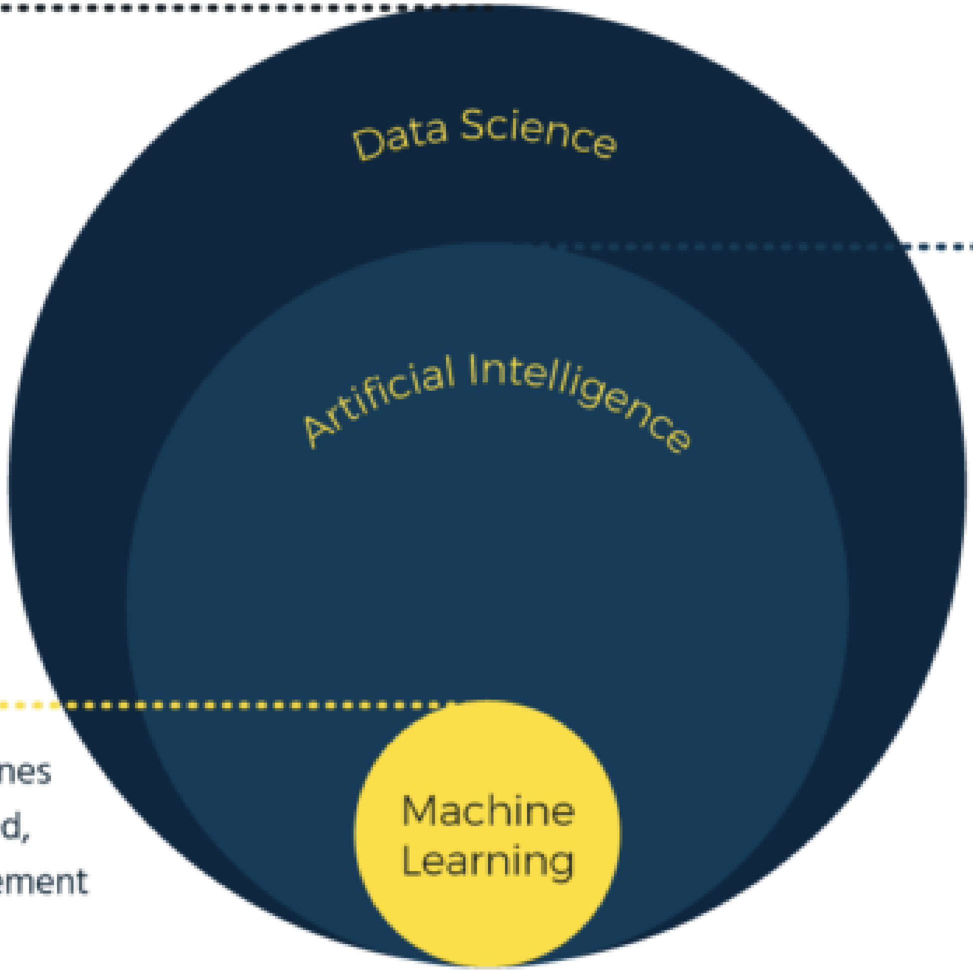
2

To best **predict** outcome. Both in those hoped to achieve, as well as those to avoid.

AI vs. Data Science vs. Machine Learning

Data Science

- Collection, preparation, and analysis of data
- Leverages AI/ML, research, industry expertise, and statistics to make business decisions



Artificial Intelligence

- Technology for machines to understand/interpret, learn, and make 'intelligent' decisions
- Includes Machine Learning among many other fields

Machine Learning

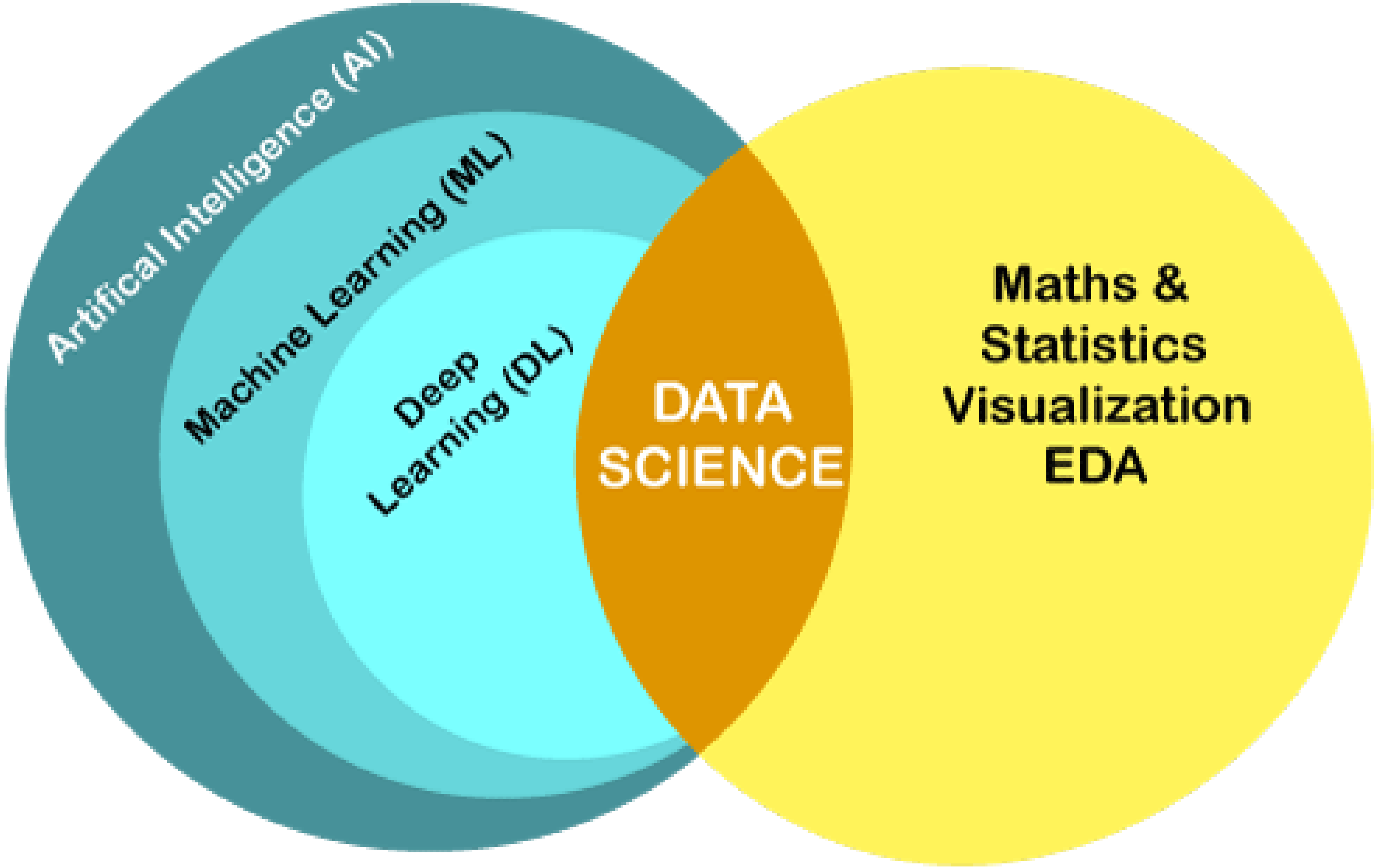
- Algorithms that help machines improve through supervised, unsupervised, and reinforcement learning
- Subset of AI and Data Science tool

Deep Learning

Whereas older machine learning algorithms classically *plateaued* as data sets grow larger, with *deep learning,* algorithms continue to *improve* with the more data they receive.

Ie. Self driving cars, language translation, image captions

Multiple layers of processing—generated outputs get handed off as new inputs, etc

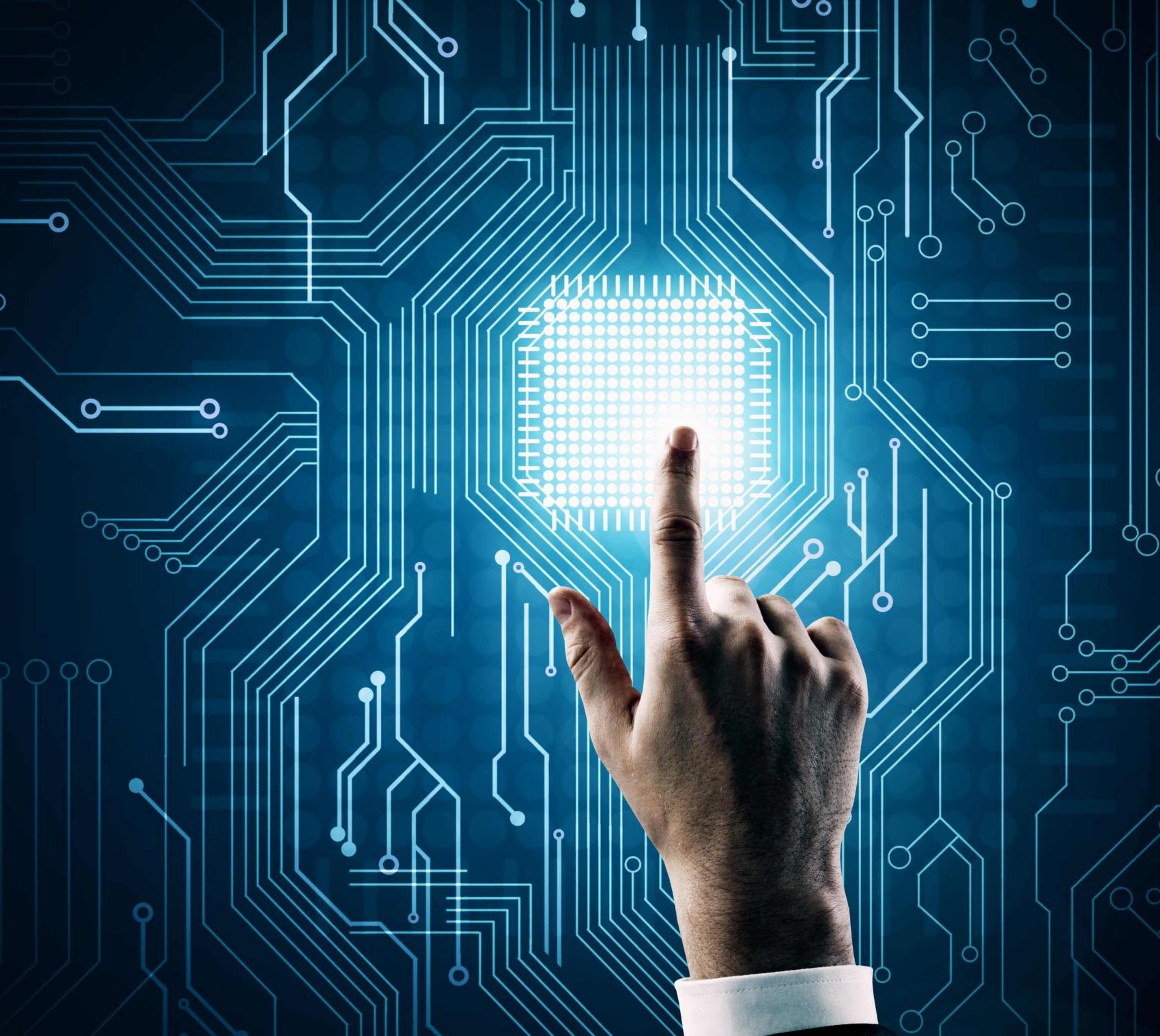

Artifical Intelligence (AI)
Machine Learning (ML)
Deep Learning (DL)
DATA SCIENCE
Maths &
Statistics
Visualization
EDA

The Infamous “Move 37”

Historic match of Go in 2016 between AlphaGo and legend Lee Sedol

AlphaGo makes a move so unconventional the entire crowd of onlookers gasp, suspecting it surely made an error.

Later became known as ‘Move 37’, so far removed from any human player’s intuition, demonstrating AI’s ability to recognize patterns and predict in a manner simply out of the box of the



- **<u>88% accuracy</u> in predicting EGFR mutations from CT scans alone!**

Cancers (Basel). 2024 Mar 12;16(6):1130. doi: 10.3390/cancers16061130

Deep-Learning-Based Predictive Imaging Biomarker Model for EGFR Mutation Status in Non-Small Cell Lung Cancer from CT Imaging

Abhishek Mahajan [1,2,*], Vatsal Kania [3], Ujjwal Agarwal [3], Renuka Ashtekar [3], Shreya Shukla [3], Vijay Maruti Patil [4], Vanita Noronha [4], Amit Joshi [4], Nandini Menon [4], Rajiv Kumar Kaushal [5], Swapnil Rane [5], Anuradha Chougule [4], Suthirth Vaidya [6], Krishna Kaluva [6], Kumar Prabhash [4]

Editor: Andreas Stadlbauer

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PMCID: PMC10968632 PMID: 38539465

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- **<u>88% accuracy</u> in predicting EGFR mutations from CT scans alone**

- **990 patients from two NSCLC trials**
  - employed an end-to-end pipeline analyzing CT images without precise segmentation
  - Two 3D convolutional neural networks segmented lung masses and nodules

- **Semantic features**
  - pure solid tumours with no associated ground glass component ($p < 0.03$)
  - the absence of peripheral emphysema ($p < 0.03$)
  - presence of pleural retraction ($p = 0.004$)
  - presence of fissure attachment ($p = 0.001$)
  - presence of metastatic nodules in both tumour-containing & non-tumour-containing lobes ($p = 0.001$)
  - the presence of ipsilateral pleural effusion ($p = 0.04$)
  - average enhancement of the tumour mass above 54 HU (**$p < 0.001$**)

https://www.mdpi.com/2072-6694/16/6/1130

Expert Review of Molecular Diagnostics ›
Volume 24, 2024 - Issue 5

Review

Artificial intelligence in digital histopathology for predicting patient prognosis and treatment efficacy in breast cancer

Christine McCaffrey, Chowdhury Jahangir, Clodagh Murphy, Caoimbhe Burke, **William M. Gallagher** & Arman Rahman

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Cite this article https://doi.org/10.1080/14737159.2024.2346545 Check for updates

Tumor-Infiltrating Lymphocytes (TILs):

- **Quantification and Spatial Analysis**
  - AI algorithms excelled at accurately quantifying TILs within the tumor microenvironment (TME) from digitized H&E images.
  - Went beyond simple counting: AI could analyze the spatial distribution and density of TILs, which proved crucial for predicting response to both chemotherapy and immunotherapy.

- **TIL Subsets:**
  - Some studies explored the prognostic and predictive value of different TIL subsets (e.g., CD8+ T cells, CD4+ T cells). AI could potentially identify these subsets based on morphological features or by integrating data from multiplex IHC staining.

Other Histological Features:

- **Nuclear Features:** AI algorithms to analyze size, shape, texture, and chromatin organization—reflecting the genetic instability and aggressiveness of the tumor, which can influence treatment response.
- **Tumor-Stroma Ratio (TSR):** The ratio of tumor cells to stromal cells in the TME was also found to be predictive of treatment response. AI could accurately quantify the TSR, which provided insights into the tumor's microenvironment and its potential to respond to therapy.
- **Mitotic Count:** AI algorithms could identify and count mitotic figures, which are indicative of cell proliferation and tumor aggressiveness. This information could be used to predict response to chemotherapy.
- **Large-Scale DNA Organization (LDO):** AI could analyze the organization of DNA within the nucleus, which can be correlated with disease states and used to predict prognosis and potentially treatment response.

Integration of Multi-Modal Data

- **Combining Histological and Clinical Data**
  - Some studies demonstrated the potential of integrating histological features extracted by AI with clinical data (e.g., age, tumor stage, hormone receptor status) to improve the accuracy of treatment response prediction.

- **Inferring Genomic and Proteomic Data:**
  - Emerging research suggests that AI algorithms may be able to infer genomic and proteomic information directly from H&E images. This could provide a more comprehensive understanding of the tumor's molecular profile and its potential response to targeted therapies.

Springer

Eur Radiol. 2021 Oct 15;32(5):3131–3141. doi: 10.1007/s00330-021-08306-w

Analysis of mammograms using artificial intelligence to predict response to neoadjuvant chemotherapy in breast cancer patients: proof of concept

I Skarping [1,2,✉], M Larsson [3], D Förnvik [4]

Author information   Article notes   Copyright and License information

PMCID: PMC9038782 PMID: 34652522

For training and validation, 1485 images obtained from 400 patients were used, and the model was ultimately applied to a test set consisting of 53 patients.

The artificial intelligence (AI) model predicted the pCR as represented by the area under the curve of 0.71 (95% confidence interval 0.53–0.90; $p = 0.035$). The sensitivity was 46% at a fixed **specificity of 90%.**

Neural Networks

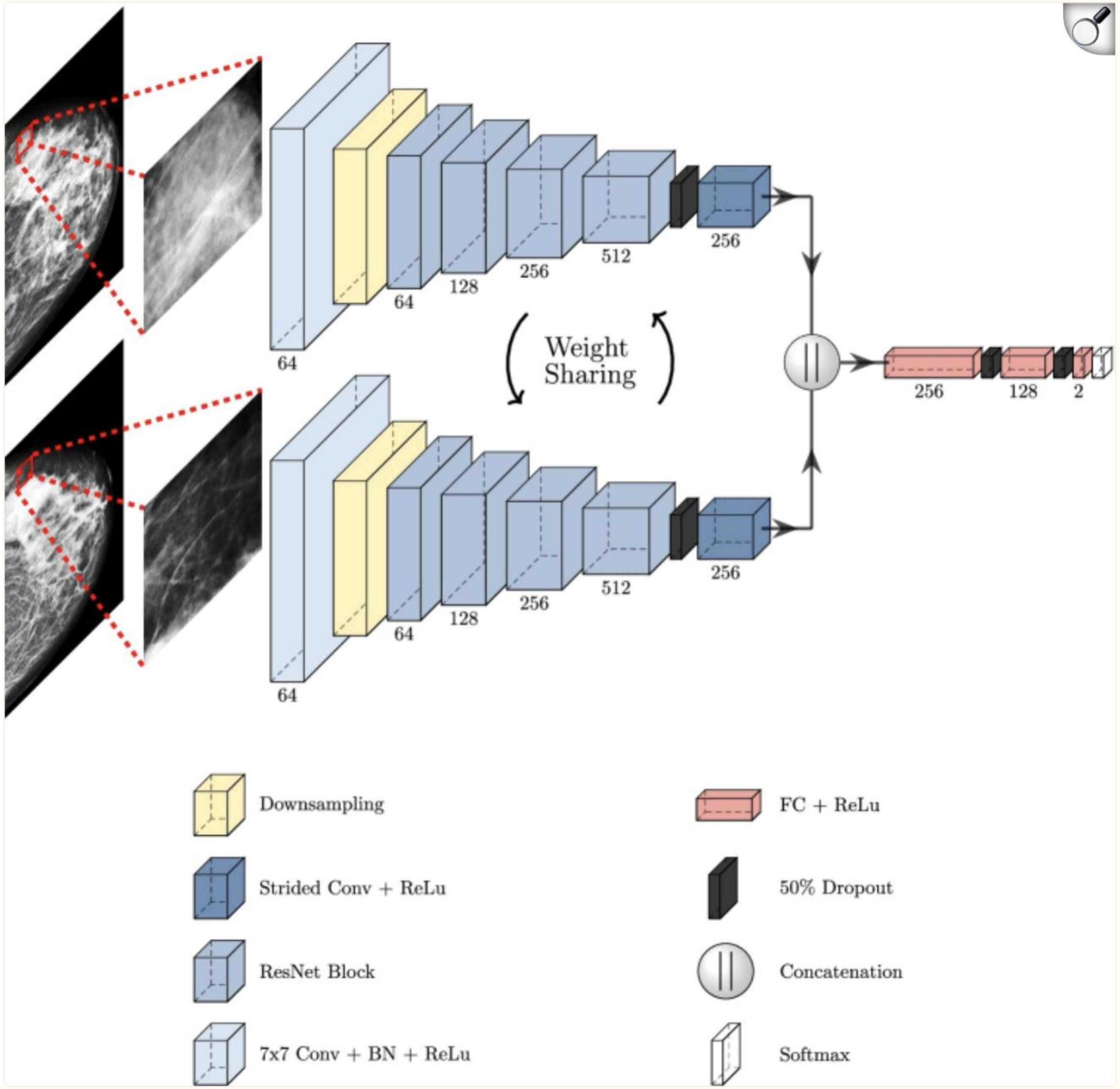
- The deep learning system used to predict pCR in DM consists of two main steps

  (1) A network for detection tumors is first applied to the DM

  (2) image patches are extracted around the detected tumor in addition to the same position in the reference image (contralateral cancer-free breast).

  The two image patches are fed into a classification network that predicted pCR.

  By extracting smaller image patches of interest, the classification network is forced to make predictions based on what was hypothesised to be relevant information instead of overfitting the information to irrelevant input.



https://pmc.ncbi.nlm.nih.gov/articles/PMC9038782/

Developing an AI Model: Step 1 – Training

- AI system needs to be fed data.
- You can do a **feasibility** study (test accuracy with x amount of data—then extrapolate what more data would do / how it would perform) to see if the data is enough and adequate.
  - **Features** are / is the data you want it to analyze.
  - **Labels**, aka the ‘answers’—what you want it to know / come to the conclusion of, from said features

  - *Tabular data, because it is already structured, make it less suited to maximize deep learning techniques. Deep learning leverages inherent structure in data—ie resonance in a pixel, and its relation to the pixels around it.*

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- Evaluating a model's performance during training is done using **proxy metrics.**
  - These are **context-dependent** without any universal definition of 'good', or 'health'. (ie, no defined confidence interval or p value)
- Classification accuracy
- Sensitivity & specificity
- Area under the receiver operating characteristic (ROC) curve (True positive over false positive)

  - One problem can be **overfitness**—the process was over-complicated and too 'fit' to knock the training data out of the park, but given its so contingent on that, its not as good with *additional* data that vary from that which it was trained on

Quantity *and* quality / quality labeling is crucial in training an AI model well

Developing an AI Model: Step 2 – Validation

- Tests model in a live environment, with pre-registered endpoints
  - Of note, learning / development of the model is ***paused*** during this process of demonstrating model's effectiveness in real-world scenarios.

- Generalizability, of which can be an issue due to:
  - biases in training data, overfittness, and mismatch between the training environment vs the training one.

- **NOTE: most** AI studies have not undergone a prospective validation study. In other words, most are stage one only. This is a **huge gap** as it has not been tested for *real-world performance*.
  - This is the only way we go from theory, to a *practical* application.

Developing an AI Model: Step 3 – Deployment

- Integrate (on IT / tech level)
- Ensure regulations/compliance
- ….and be productive, or actually ‘work’

- AI fundamentally believes everything that happened yesterday, will happen tomorrow. That it is unchanging, and consistent.
  - Hence, not perpetuating inherent biases from:
    - Ordering behavior (geographically / regionally)
    - Previously biased studies / cohorts
    - Features unique to a locoregional patient population (ie smoking, obesity, etc)

are important.

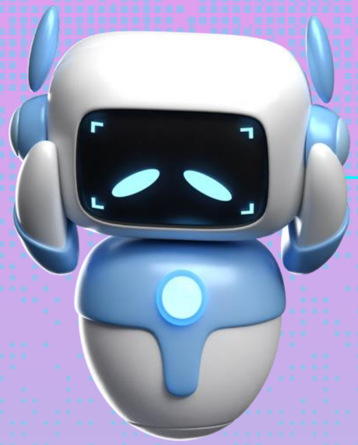
Article | Open access | Published: 23 May 2024

Early adverse physiological event detection using commercial wearables: challenges and opportunities

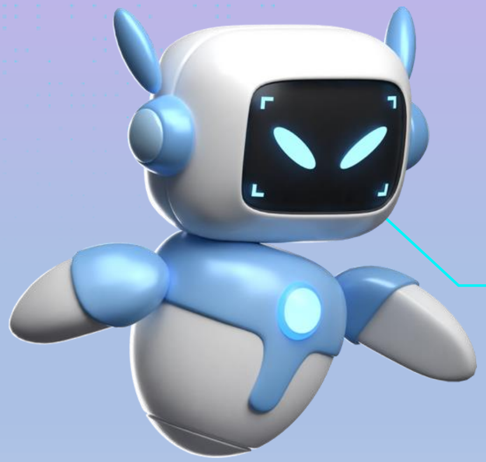
Jesse Phipps, Bryant Passage, Kaan Sel, Jonathan Martinez, Milad Saadat, Teddy Koker, Natalie Damaso, Shakti Davis, Jeffrey Palmer, Kajal Claypool, Christopher Kiley, Roderic I. Pettigrew & Roozbeh Jafari

npj Digital Medicine **7**, Article number: 136 (2024) | Cite this article

Potential problems



DEPENDENCE ON TECHNOLOGY



Trust Issues: Patient *and* Physician
Guideline vs AI assessment?

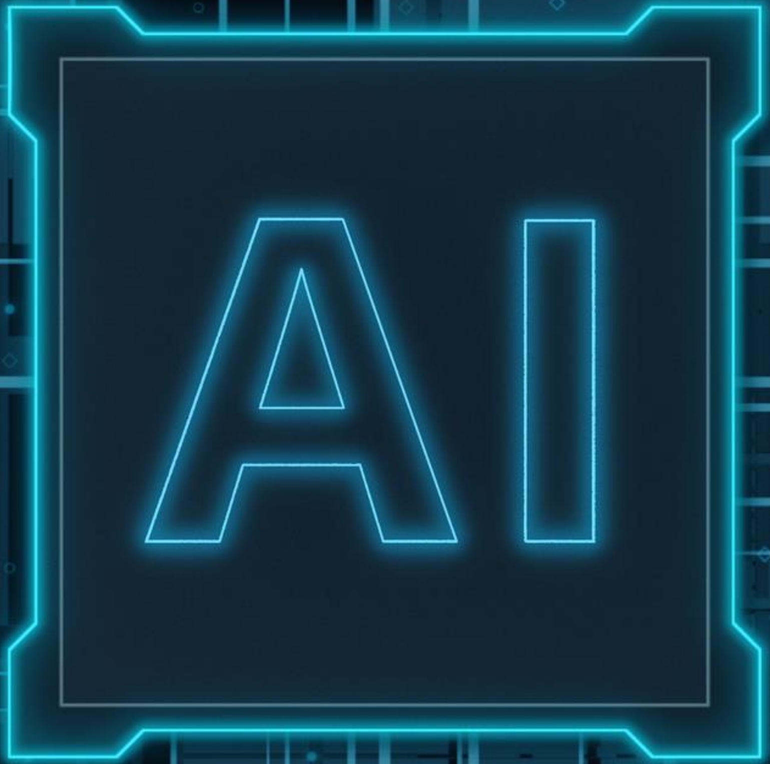
Is ‘Dependence’ Anything… New?

What would happen if Google maps & Waze disappeared?

Google Search. Kayak. Uber.

Social Media. Email.

Weather apps.
Amazon.
Costco & Wal-Mart online.



Chemotherapy dosing (kg, CrCl, mg/m2)

NCCN. NCBI. Package inserts. Uptodate. Toxicity grading. Holding parameters. Medication interactions.

Cancer analysis.
Pharmacogenomics/SNPS
Guideline querying.
Radiology reads.

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Thank You.

https://www.youtube.com/@ai-and-healthcare

Sanjay Juneja, MD
www.sjunejaMD.com
theoncdocteam@gmail.com