

Review Article

Artificial intelligence in precision oncology: The way forward

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ABSTRACT

Here, we discuss the positive impact of artificial intelligence (AI) in oncology as an enabler – for physicians, patients, and researchers. AI is here to stay and needs to be better understood by the clinical practitioner and researcher to make informed decisions about cancer diagnoses, treatment, prediction, and long-term care. One immediate impact of data-driven practice will be on cancer stratification based on data that include molecular and imaging markers. Future studies must strengthen the ability to predict causative factors to allow clinicians and patients to take control with the ultimate hope of avoiding preventable cancers.

Keywords: Artificial intelligence, Artificial intelligence in precision oncology, Cancer, Deep learning, Classification

INTRODUCTION

Artificial Intelligence (AI) and its role in precision oncology

In today's world, AI has become an inseparable part of our present and future. Due to the advances in computational power and the enormous amounts of digitalization, there is an ever-increasing wealth of data. AI uses the power of algorithms (computer programs) to make inferences by finding features from large amounts of data. Ultimately, the programming of the algorithm is in the hands of the scientists and clinicians who set up the underlying instructions that help the computer make decisions, such as classification. Hence, the algorithms are often based on information and understanding that we, humans, already have (supervised methods) so that predictions can be made using this knowledge. On the other hand, unsupervised methods from machine learning (ML) are where the algorithm manages to learn, analyze, and make inferences from data without human involvement. Thus, in case of a vast field such as precision oncology, there is great value in an open-ended approach such as ML, especially unsupervised algorithms. It would allow the practitioner to “see” information that may not have been evident to them directly. In addition, ML being independent in learning improves as more data become available.

Deep learning (DL) is a type of ML that involves the use of artificial neural networks, which means that it tries to see data the way a human brain sees and processes it by finding features that are mathematically correlated and/or clustered. This approach is very popular in cancer research.

When it comes to precision medicine, oncology remains leaps ahead of many other fields and is always at the forefront in terms of integration of new technology. In addition, with over two

decades of data in the post-genomic era, along with the recent additional breadth of information added due to electronic medical records and imaging, there is great potential for utilizing the knowledge for individualized solutions to cancer.

AI has shown an exponential evolution in the recent years. There is an ever-growing list of algorithms for applying learning and brain-based capabilities in cancer research, as summarized in [Table 1] and described in Rebolledo-Mendez,^[34] Kulkarni *et al.*,^[35] Singh^[36] with the abundance of data that can be put together.^[37] Historically, very advanced statistical models that were employed in the 1990s gave the push ahead to linear and logistic regression platforms for diagnosis, molecular marker studies, “image-omics,” and “radio-genomics.” The majority of ML algorithms in the 2000s assessed cancer progression, classification of cancers as benign or malignant, cancer stratification by image visualization, correlative markers for early detection, screening, and progression.

Over the decades, combined efforts of teams of computer scientists, physicians, and genomic experts have driven the improved success of AI-driven genomic medicine.

More recent developments include generative adversarial networks – which are basically a form of unsupervised AI, in which new data are generated that mimic real data by trying to beat itself in an objective function. For example, in the case of images, an entirely new image can be created that does not actually exist but is indistinguishable from a real image with as much as 99% accuracy.^[38] Quantum machine learning, a more powerful form of ML that uses quantum computers, has recently been able to diagnose and classify non-small-cell lung cancer, deriving its learning from genome-wide human cancer data.^[33]

Table 1: List of the most relevant AI algorithms that have been used in the past 30 years in the investigation, research, and treatment of cancer.

| | |
|---|---|
| • Linear and logistic regression ^[1,2] | • MLPNN ^[20] |
| • Decision trees ^[3] | • CNN ^[21] |
| • Naive Bayes ^[4,5] | • RNN ^[22] |
| • Support vector machines ^[6,7] | • LSTM ^[23] |
| • K-nearest neighbors ^[8,9] | • Encoder-decoder ^[24] |
| • K-means ^[10] | • Hopfield network ^[25] |
| • Random forest ^[11] | • Boltzmann machine ^[26] |
| • SVM ^[12] , PCA ^[13] , ICA ^[14] | • Deep belief network ^[27] |
| • Markov chain ^[15] | • Deconvolutional network ^[28] , GAN ^[29] |
| • Fuzzy algorithms ^[16] | • Neural Turing machine ^[30] |
| • Evolutionary algorithms ^[17] | • Deep recurrent ^[31] |
| • Artificial neural networks ^[18] | • Deep LSTM ^[32] |
| • Stochastic gradient descent ^[19] | • Quantum machine learning ^[33] |

AI: Artificial intelligence, GAN: Generative adversarial network

WHY SHOULD THE CLINICAL ONCOLOGIST LEARN ABOUT AI?

Truly, if data are the new oil, the clinician scientist will need to play a key role in helping to “refine” that data and make sure that there is enough quantity of it for meaningful work to be done. Further, any technology has immense potential for good as well as harm. If the clinician is not fully aware of the methodology and the caveats, errors can be made in both diagnosis and treatment.

In 2019, Korfiatis and Ericson reported a simultaneous prediction of four key molecular markers of glioma using DL.^[39] DL is advantageous over conventional ML as it allows the researcher to discover new features – so novel molecular markers can be discovered without knowing anything about them. For a clinician, being able to evaluate such studies and use the markers in clinical practice will be an essential skill. Image-omics is rapidly being considered a valuable tool for improving patient stratification, and with improved datasets available for more and more cancer types, it will soon become routine.

CORRELATION VERSUS CAUSATION

A large number of studies in AI are predominantly focused on classification (stratification) or prediction (correlation) [Table 2]. However, causality is not a part of these models. Correlation does not imply causation – it may merely be due to some other cause or a selection bias. The difficulties that oncology poses in trying to determine causality are that cancer data itself are highly complex. There are multiple cross-connecting pathways and various types of data are often sampled in different ways. Further, no two cancers are the same due to inter- and intra-sample heterogeneity. There is a need to move beyond pattern recognition and predictive modeling and refine our approach to look at causality. Reinforcement learning (RL) involves learning the underlying “reward functions” – meaning, what is it that makes a cancer clone survive and evolve into a cancerous state? Mutations accumulate over time and

Table 2: Examples of studies focused on classification (stratification) or prediction (correlation).

| Classification | Prediction |
|--|--|
| Gene selection for cancer classification ^[44] | Cancer prognosis ^[44] |
| Malignant and benign clustered microcalcifications ^[41] | Survival prediction in lung cancer ^[45] |
| Expressions of very few genes ^[42] | Lung cancer ^[46] |
| Mammographic tumor ^[43] | Leukemia ^[47] |
| | Neuroblastoma ^[50] |
| | Breast cancer ^[51] |
| | Glioblastoma multiforme cancer using MRI ^[52] |

MRI: Magnetic resonance imaging

ultimately are a few that drive the survival of the cancer clone. RL can reconstruct the phylogenetic tree of a cancer clone by reverse engineering multi-omic tumor data: Something that decades ago would have taken years of rigorous research is being done within a few months using causal algorithms.^[46] The level of sophistication needed in preparing algorithms uniquely suited to precision medicine is exemplified by MethSig that uses hypermethylation across the genome and between samples to predict drivers versus passengers.^[47] Identifying clonal signatures and knowing which target to treat are the crux of molecular oncology and where the future of predictive care lies.^[48,49]

Besides molecular markers for prediction, there are countless opportunities for AI application in precision care, particularly with immunotherapies. Knowing which patients will benefit from immunotherapy (and who will not) would prevent unnecessary exposure to harmful side effects and undue financial burden.^[53] The various approaches being explored in immuno-oncology include combining complex datasets of tumor biomarkers including immune signatures and 3D tissue imaging to discover new markers. Further, immune escape, drug resistance, and side effects all need to be factored into the models and would require concerted efforts of clinicians and data scientists.^[54]

FUTURE OF AI IN PRECISION ONCOLOGY

“Data are the new oil. It’s valuable, but if unrefined it cannot be used.” – Clive Humby, Mathematician, 2006.

The future is already here – and we are already on the verge of seeing major paradigm shifts in the way we practice clinical medicine. We anticipate more user-friendly digital interfaces in the near future which would allow users (professionals, patients, or even students and citizen scientists) to actively participate in the ongoing curation, mining, and interpretation of cancer data and research literature.

In summary, AI is an enabler – for physicians, patients, and researchers. We will continue to see the impact on cancer stratification, and quantitative imaging will become routine. Further, if we can educate ourselves, the oncology community, about the difference between classification and causative factors, we can start to tackle the bigger problem of avoiding preventable cancers, which is the ultimate goal of the decades-long efforts of molecular and computational medicine. Working together in teams, rather than silos, and developing customized approaches to solving the puzzles unique to precision oncology is the way forward.

CONCLUSION

There is a growth in development of AI algorithms that can be used to make correlations among data used in oncology.

Studies of both stratification and classification are widening. Furthermore, any type of data can be used for getting more precision in oncology via the usage of AI. There is a clear trend that the future will see a continual improvement of AI for better precision oncology.

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Declaration of patient consent

Patient’s consent not required as there are no patients in this study.

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Conflicts of interest

Dr. Radhika Vaishnav is the Executive Editor of the journal.

REFERENCES

1. Gupta M, Gupta B. A Comparative Study of Breast Cancer Diagnosis Using Supervised Machine Learning Techniques. In: 2018 2nd International Conference on Computing Methodologies and Communication (ICCMC); 2018. p. 997-1002.
2. Mikhitarian K, Gillanders WE, Almeida JS, Hebert Martin R, Varela JC, Metcalf JS, *et al.* An innovative microarray strategy identifies informative molecular markers for the detection of micrometastatic breast cancer. *Clin Cancer Res* 2005;11:3697-704.
3. Nai Y, Schaefferkoetter JD, Fakhry-Darian D, Conti M, Shi X, Townsend DW, *et al.* Improving Lung Lesion Detection in Low Dose Positron Emission Tomography Images Using Machine Learning. In: 2018 IEEE Nuclear Science Symposium and Medical Imaging Conference Proceedings (NSS/MIC); 2018. p. 1-3.
4. Li H, Li D, Zhang C, Nie S. An Application of Machine Learning in the Criterion Updating of Diagnosis Cancer. Vol. 1. In: 2005 International Conference on Neural Networks and Brain; 2005. p. 187-90.
5. Amrane M, Oukid S, Gagaoua I, Ensarí T. Breast Cancer Classification Using Machine Learning. In: 2018 Electric Electronics, Computer Science, Biomedical Engineering’s Meeting (EBBT); 2018. p. 1-4.
6. Guyon I, Weston J, Barnhill S, Vapnik V. Gene selection for cancer classification using support vector machines. *Mach Learn* 2002;46:389-422.
7. Dekker A, Dehing-Oberije C, Ruysscher D, Lambin P, Komati K, Fung G, *et al.* Survival Prediction in Lung Cancer Treated with Radiotherapy: Bayesian Networks vs. Support Vector Machines in Handling Missing Data. In: 2009 International Conference on Machine Learning and Applications; 2009. p. 494-7.

8. Medjahed SA, Saadi TA, Benyettou A. Breast cancer diagnosis by using k-nearest neighbor with different distances and classification rules. *Int J Comput Appl* 2013;62:1-5.
9. Medjahed SA, Saadi T, Benyettou A. Breast cancer diagnosis by using k-nearest neighbor with different distances and classification rules. *Int J Comput Appl* 2013;62:1-5.
10. Zheng B, Yoon SW, Lam SS. Breast cancer diagnosis based on feature extraction using a hybrid of K-means and support vector machine algorithms. *Expert Syst Appl* 2014;41:1476-82.
11. Okun O, Priisalu H. Random forest for gene expression based cancer classification: Overlooked issues. In: Martí J, Benedí JM, Mendonça AM, Serrat J, editors. *Pattern Recognition and Image Analysis*. Berlin, Germany: Springer; 2007. p. 483-90.
12. Huang YM, Du SX. Weighted Support Vector Machine for Classification with Uneven Training Class Sizes. Vol. 7. In: 2005 International Conference on Machine Learning and Cybernetics; 2005. p. 4365-9.
13. Alexe G, Dalgin GS, Ganesan S, DeLisi C, Bhanot G. Analysis of breast cancer progression using principal component analysis and clustering. *J Biosci* 2007;32:1027-39.
14. Saidi SA, Holland CM, Kreil DP, MacKay DJ, Charnock-Jones DS, Print CG, *et al.* Independent component analysis of microarray data in the study of endometrial cancer. *Oncogene* 2004;23:6677-83.
15. Duffy SW, Chen HH, Tabar L, Day NE. Estimation of mean sojourn time in breast cancer screening using a Markov chain model of both entry to and exit from the preclinical detectable phase. *Stat Med* 1995;14:1531-43.
16. Lorenz A, Blum M, Ermert H, Senge T. Comparison of Different Neuro-Fuzzy Classification Systems for the Detection of Prostate Cancer in Ultrasonic Images. Vol. 2. In: 1997 IEEE Ultrasonics Symposium Proceedings. An International Symposium (Cat. No.97CH36118); 1997. p. 1201-4.
17. Mital M, Pidaparti RM. Breast tumor simulation and parameters estimation using evolutionary algorithms. *Mod Simul Eng* 2008;2008:e756436.
18. El-Deredy W, Ashmore SM, Branston NM, Darling JL, Williams SR, Thomas DG. Pretreatment prediction of the chemotherapeutic response of human glioma cell cultures using nuclear magnetic resonance spectroscopy and artificial neural networks. *Cancer Res* 1997;57:4196-9.
19. Mittal D, Gaurav D, Roy SS. An Effective Hybridized Classifier for Breast Cancer Diagnosis. In: 2015 IEEE International Conference on Advanced Intelligent Mechatronics (AIM); 2015. p. 1026-31.
20. Übeyli ED. Implementing automated diagnostic systems for breast cancer detection. *Expert Syst Appl* 2007;33:1054-62.
21. Han X. MR-based synthetic CT generation using a deep convolutional neural network method. *Med Phys* 2017;44:1408-19.
22. Yang Y, Fasching PA, Tresp V. Predictive Modeling of Therapy Decisions in Metastatic Breast Cancer with Recurrent Neural Network Encoder and Multinomial Hierarchical Regression Decoder. In: 2017 IEEE International Conference on Healthcare Informatics (ICHI); 2017. p. 46-55.
23. Budak Ü, Cömert Z, Rashid ZN, Şengür A, Çibuk M. Computer-aided diagnosis system combining FCN and Bi-LSTM model for efficient breast cancer detection from histopathological images. *Appl Soft Comput* 2019;85:105765.
24. Myronenko A. 3D MRI brain tumor segmentation using autoencoder regularization. In: Crimi A, Bakas S, editors. *Brain Lesion: Glioma, Multiple Sclerosis, Stroke and Traumatic Brain Injuries*. Berlin, Germany: Springer International Publishing; 2019. p. 311-20.
25. Brouwer RK. Using the Hopfield Neural Network as a Classifier by Storing Class Representatives. Vol. 1. In: *Proceedings of Canadian Conference on Electrical and Computer Engineering*; 1993. p. 337-40.
26. Nahid AA, Mikaelian A, Kong Y. Histopathological breast-image classification with restricted Boltzmann machine along with backpropagation. *Biomed Res* 2018;29:2068-77.
27. Abdel-Zaher AM, Eldeib AM. Breast cancer classification using deep belief networks. *Expert Syst Appl* 2016;46:139-44.
28. Singadkar G, Mahajan A, Thakur M, Talbar S. Deep deconvolutional residual network based automatic lung nodule segmentation. *J Digital Imaging* 2020;33:678-84.
29. Rezaei M, Harmuth K, Gierke W, Kellermeier T, Fischer M, Yang H, *et al.* A conditional adversarial network for semantic segmentation of brain tumor. In: Crimi A, Bakas S, Kuijf H, Menze B, Reyes M, editors. *Brain Lesion: Glioma, Multiple Sclerosis, Stroke and Traumatic Brain Injuries*. Berlin, Germany: Springer International Publishing; 2018. p. 241-52.
30. Mobiny A, Moulik S, Van Nguyen H. Lung cancer screening using adaptive memory-augmented recurrent networks. *arXiv* 2018;2018:05719.
31. Liu Q, Fang L, Yu G, Wang D, Xiao CL, Wang K. Detection of DNA base modifications by deep recurrent neural network on Oxford Nanopore sequencing data. *Nat Commun* 2019;10:2449.
32. Yi HC, You ZH, Zhou X, Cheng L, Li X, Jiang TH, *et al.* ACP-DL: A deep learning long short-term memory model to predict anticancer peptides using high-efficiency feature representation. *Mol Ther Nucleic Acids* 2019;17:1-9.
33. Mishra N, Bisarya A, Kumar S, Behera BK, Mukhopadhyay S, Panigrahi PK. Cancer detection using quantum neural networks: A demonstration on a quantum computer. *arXiv* 2019;2019:00504.
34. Rebolledo-Mendez J. Artificial intelligence in fighting cancer: A short review and trends. *Int J Mol Immunooncol* 2017;2:42.
35. Kulkarni PS, Gandhi SS, Hingmire SS, Deshmukh CD. Artificial intelligence: A new era of technological advancement in oncology care. *Int J Mol Immunooncol* 2019;4:27-8.
36. Singh R. Artificial intelligence: A new era of technological advancement in oncology care. *Int J Mol Immunooncol* 2019;4:56-57.
37. Kadali SS, Gowlikar R, Fatima SN. The cancer genomic atlas to conquer cancer. *Int J Mol Immunooncol* 2021;6:76-81.
38. Korfiatis P, Erickson B. Deep learning can see the unseeable: Predicting molecular markers from MRI of brain gliomas. *Clin Radiol* 2019;74:367-73.
39. Guyon I, Weston J, Barnhill S, Vapnik V. Gene selection for cancer classification using support vector machines. *Mach Learn* 2002;46:389-422.
40. Wei L, Yang Y, Nishikawa RM, Jiang Y. A study on several machine-learning methods for classification of malignant and benign clustered microcalcifications. *IEEE Trans Med Imaging* 2005;24:371-80.

41. Wang L, Chu F, Xie W. Accurate cancer classification using expressions of very few genes. *IEEE ACM Trans Comput Biol Bioinform* 2007;4:40-53.
42. Digital Mammographic Tumor Classification Using Transfer Learning from Deep Convolutional Neural Networks. Available from: <https://www.spiedigitallibrary.org/journals/journal-of-medical-imaging/volume-3/issue-3/034501/digital-mammographic-tumor-classification-using-transfer-learning-from-deep-convolutional/10.1117/1.JMI.3.3.034501.full>
43. Kourou K, Exarchos TP, Exarchos KP, Karamouzis MV, Fotiadis DI. Machine learning applications in cancer prognosis and prediction. *Comput Struct Biotechnol J* 2015;13:8-17.
44. Dekker A, Dehing-Oberije C, De Ruyscher D, Lambin P, Komati K, Fung G, *et al.* Survival Prediction in Lung Cancer Treated with Radiotherapy: Bayesian Networks vs. Support Vector Machines in Handling Missing Data. In: 2009 International Conference on Machine Learning and Applications; 2009. p. 494-7.
45. Tan C, Chen H, Xia C. Early prediction of lung cancer based on the combination of trace element analysis in urine and an Adaboost algorithm. *J Pharm Biomed Anal* 2009;49:746-52.
46. Wei JS, Greer BT, Westermann F, Steinberg SM, Son CG, Chen QR, *et al.* Prediction of clinical outcome using gene expression profiling and artificial neural networks for patients with neuroblastoma. *Cancer Res* 2004;64:6883-91.
47. Pan H, Renaud L, Chaligne R, Bloehdorn J, Tausch E, Mertens D, *et al.* Discovery of candidate DNA methylation cancer driver genes. *Cancer Discov* 2021;11:2266-81.
48. Morjaria S. Driver mutations in oncogenesis. *Int J Mol Immunooncol* 2021;6:100-2.
49. Vaishnav R. Changing face of genomics in cancer medicine: Which “avatar” to treat? *Int J Mol Immunooncol* 2016;1:4381.
50. Wetstein SC, Onken AM, Luffman C, Baker GM, Pyle ME, Kensler KH, *et al.* Deep learning assessment of breast terminal duct lobular unit involution: Towards automated prediction of breast cancer risk. *PLoS One* 2020;15:e0231653.
51. Hajianfar G, Shiri I, Maleki H, Oveisi N, Haghparast A, Abdollahi H, *et al.* Noninvasive O₆ methylguanine-DNA methyltransferase status prediction in glioblastoma multiforme cancer using magnetic resonance imaging radiomics features: Univariate and multivariate radiogenomics analysis. *World Neurosurg* 2019;132:e140-61.
52. Kalantari J, Nelson H, Chia N. The unreasonable effectiveness of inverse reinforcement learning in advancing cancer research. *Proc Conf AAAI Artif Intell* 2020;34:437-45.
53. Vaishnav R, Arslan W, Mehta DG. Unforeseen consequences of cancer immunotherapy. *Int J* 2018;3:21.
54. Sobhani F, Robinson R, Hamidinekoo A, Roxanis I, Somaiah N, Yuan Y. Artificial intelligence and digital pathology: Opportunities and implications for immuno-oncology. *Biochim Biophys Acta Rev Cancer* 2021;1875:188520.

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