

Understanding Artificial Intelligence and Applications in Oncology: Narrative Review

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ABSTRACT There is a rapid progression of information technologies in healthcare. One of the cornerstones of the process is AI, which uses a combination of multiple technologies in modern healthcare applications and has both administrative and clinical aspects. AI assists in the field of medicine by modifying the existing disease prevention procedures, diagnosis, treatment, drug development, clinical care, and other healthcare services; moreover, it is a promising modality in almost every field. In contrast, ethical issues such as accountability, personal data protection, patient safety, application bias, and trust issues are still debatable as they have not been fully addressed by AI. These discussions are based on the inadequacy of existing procedures, standards, and ethical rules for the ever-evolving AI technologies. Additionally, AI should be most intensively used for patients with oncology and oncological applications. Thus, this article aimed to provide deep insights for a simple understanding of AI for oncologists.

Keywords: Artificial intelligence; medicine; oncology; understanding; black-box

The significant changes in human life began through the use of tools and were continued with the agricultural and industrial revolution, followed by machines becoming a life component. In addition, business models have changed, especially using machines in jobs requiring muscle power and mass production. In recent years, this change has been remarkable, especially with its speed, and has progressed beyond the idea of machines used only as a tool assisting individuals toward becoming capable of thinking, deciding, and acting on their behalf.¹ Artificial intelligence (AI) technologies, defined as the application of human cognitive functions by computers, cause rapid transformations in life, such as in the fields of communication, transportation, health, education, and trade, and have created new opportunities.^{2,3} The design and development of AI are as

critical as the awareness of users or beneficiaries and achieving the targeted results. The physicians and AI applications have cooperated in facilitating, accelerating, and managing the prevention, screening, diagnosis, treatment, and follow-up processes of a catastrophic disease such as cancer.

HISTORY OF AI

McCulloch and Pitts in 1943 were the first to initiate the scientific steps toward AI development in 1943. They defined the mathematical models of neurons. In their study, McCulloch and Pitts demonstrated how neurons can learn and change their behavior over time.⁴

In 1943, electronic devices were developed through code analysis studies, and paved the way for

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the emergence of the concepts of “computer technologies” and “AI.” Alan Turing during World War II conducted studies on the cipher algorithm of the German “enigma” machine. The development of data processing logic is mediated by computer prototypes that emerged owing to these studies.⁵

Turing in 1950 published “Computing Machinery and Intelligence,” which raised the question “Can machines think?” and attempted to formulate this question using a test.⁶ Turing had assumed that AI could be successful in this test by the 2000s. Later, the term “AI” was first used by John McCarthy at the Dartmouth Conference in 1956.^{5,6}

Post-Dartmouth conference, more studies were conducted to determine the possibility of machines’ and computers’ thinking and understanding, and AI emerged as a scientific discipline. Research increased, especially in the 1960s, and scientific research funds were collected with the assumptions and efforts that AI could imitate human intelligence. However, the 1970s was a dark period for AI, with unfulfilled efforts and expectations and multiple disappointments. Since the desired results could not be achieved, there was a gradual decrease in the scientific research funds allocated to AI.^{5,7} Additionally, several challenges, such as errors in translating Russian to English language, combination errors in complex subjects, and the inability to present the most accurate options among alternatives, have led to a further decrease in belief and effort in AI. Thus, 1974-1980 was known as “the winter of AI” and referred to as a dark period.⁷

The revival of AI in the 1980s can be attributed to different factors. The expert systems were developed for specific actions in specific fields. These systems created a positive perspective on the re-development of AI, and research was focused on the ability to perceive, have a body, and move to prove that a computer can be intelligent.⁵ An application developed later could play chess similar to a human, bringing about a new era in the history of AI. Moreover, applications such as Watson, another AI application that IBM encountered with human intelligence, or AlphaGo of DeepMind by Google Inc. (US), which works with deep learning applications

and can learn on, have shown the superiority of AI to humans in certain areas.^{8,9}

In analyzing the development of AI, a process of ups and downs, divided into periods with the names of seasons, is encountered that is as follows: “the beginning” in the 1950s, “the winter” between 1970 and 1980, “the spring” between 1990 and 2010, and “the summer” after 2010.^{7,8}

DEFINITIONS AND TERMS OF AI

In general, AI systems can solve advanced problems based on analytical models that generate predictions, rules, answers, recommendations, or similar results. Analytical models were earlier built based on programming known relationships, procedures, and decision logic into intelligent systems through handcrafted rules (Figure 1).^{5,7,8} Advanced learning algorithms are one of the most important elements in machine learning. Interconnected processing units [artificial neural networks (ANN)] form the basis of machine learning and then deep learning, each created for specific tasks and mimicking human neurons, which is the transformation of this network into a deepening architecture. Like the brain synapses, each connection between neurons transmits signals whose strength can be increased or decreased by a weight continuously adjusted throughout the learning process. If a certain threshold is exceeded, as determined by an activation function, the signals are only processed by subsequent neurons.^{10,11}

For better comprehension of the aforementioned concepts, the following concepts of the elements of AI and its operation must be understood.

ANNs are a computing technology inspired by the information processing technique of the human brain. It is the digital modeling of biological neuron cells and their synaptic connections.¹²⁻¹⁴ ANNs are mathematical systems comprising many processing units (neurons) connected in a weighted manner. A processing unit is an equation, also known as a transfer function. This processing unit receives signals from other neurons and combines and transforms them, producing a numerical result. In general, processing units roughly correspond to real neurons and are connected in a network; this structure forms neu-

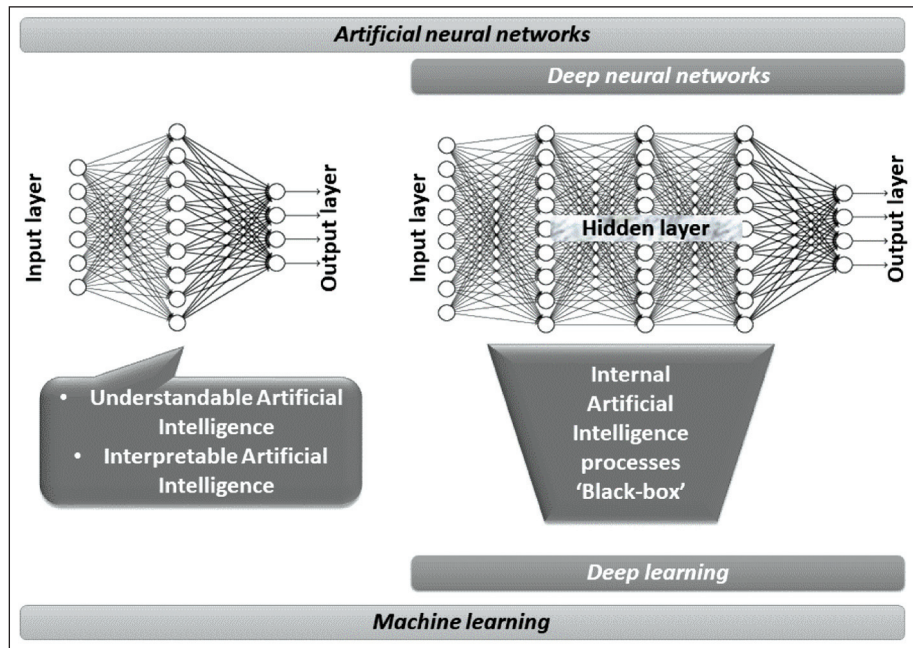


FIGURE 1: Simple and deep neural network modeling and black-box.

ral networks. Most ANNs are structured in layers of neurons with similar characteristics, and their transfer functions are run simultaneously. Almost all networks have neurons that receive data and neurons that produce output.⁴

Deep neural networks typically comprise multiple hidden layers organized in deeply nested network architectures.¹¹ They often contain advanced neurons, unlike simple ANNs. Instead of using a simple activation function, they can use advanced or multiple activations in a neuron.^{5,11,12,15} These features allow deep neural networks to use raw input data and automatically discover a representation that is needed for the learning task of interest. This is the core capability of networks commonly known as deep learning (Figure 1).

The behavior of ANNs, and the relationship of input to output data, is primarily affected by the transfer functions of neurons, their connection, and the weights of these connections.^{5,10-12,15}

■ **Input Layer:** The attributes of the sample to be learned are given as input to a network in this layer. The number of input neurons should be similar to the number of attributes of the examples to be taught.^{5,15}

■ **Output Layer:** The group information or label value of the examples to be learned in the artificial network is calculated as output in this layer.^{5,15}

■ **Hidden Layers:** These lie between the input and output layers. The number of layers and neurons on them may vary depending on the problem. In these layers, forward calculations and error evaluations are performed. In general, the number of layers and neurons on the layers vary according to the complexity of the problem.^{5,15}

■ **Weights:** These are the parameters used to adjust the effect of inputs on outputs. Weights transmit the input values to various calculations. AI is to calculate the optimum weight values for the training set by evaluating the error margins of the weights in the learning and training process (Figure 2).^{5,15,16}

■ **Transfer Function:** Calculates the net input to a neuron. Different functions are used for this (Figure 2).^{5,15,16}

■ **Activation Function:** This processes the net value coming into the cell and produces the activation output of the neuron in response to this input (Figure 2).^{5,15,16}

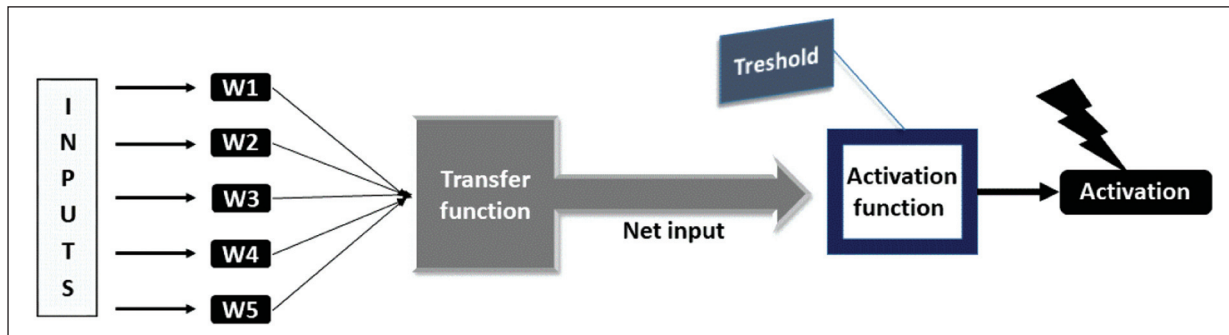


FIGURE 2: Demonstration of weights, transfer function, and activation function in artificial intelligence.

■ **Feature engineering** refers to using domain knowledge when building a model to select and transform the most relevant variables from raw data based on predictions using machine learning or statistical modeling.^{5,15}

■ **Feature learning** is a set of techniques using which the system automatically discovers representations needed for feature detection or classification from raw data.^{5,15}

■ **Black-box AI models** arrive at conclusions without providing any explanation of how they were reached. In these models, deep ANNs distribute data and decision-making processes across tens of thousands of neurons, leading to a complexity that can be as difficult to understand as that of the human brain. The internal mechanisms and contributing factors of black-box AI are unknown.^{5,15}

TRAINING OF THE ANN

■ This aims to learn the relationships between inputs and outputs using labeled samples and to determine the outputs of the model and new test samples.^{5,15}

■ The attributes of the training set are given as input to the ANN, and the outputs are provided to approach the actual label values, that is, updated to find the best values of the weights. The time spent is called **learning**.^{5,15}

■ If the number of samples given to the neural network is more than the optimum and is trained with excessive iteration, the neural network will not learn but memorize (**Overfitting**).¹⁷

■ If it is trained less than the optimum value, the samples will not be learned (**Underfitting**). If such situations are not avoided, the success rate of the network in the test set will be low.¹⁷

Thus, the definitions of AI, machine learning, and deep learning, which are often compared with each other, can be made as follows (Table 1, Figure 3).

AI includes all technique that enables imitation and reproduction of human behavior by computers or overcoming human decision-making to solve complex tasks independently or with minimal human in-

TABLE 1: The definitions of AI, machine learning, and deep learning.	
AI	Any technique that enables computers to imitate and reproduce human behavior or overcome human decision-making to solve complex tasks independently or with minimal human intervention. ¹⁸
Machine learning	The performance of a computer program improves with experience with certain groups of tasks and performance metrics. ^{4,5,7,8,10-12,14,15}
Deep learning	A subfield of AI/machine learning that can use advanced operations or multiple activations in a neuron with advanced neurons, instead of using a simple activation function with simple ANNs. These features allow deep neural networks to be fed with raw input data and automatically discover a representation that is needed for the learning task. ^{4,5,7,8,10-12,14,15}

AI: Artificial intelligence.

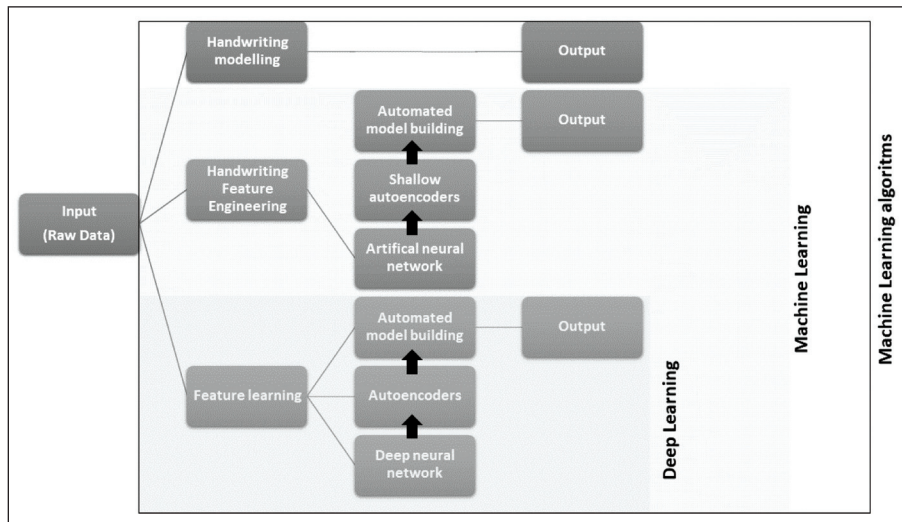


FIGURE 3: The demonstration of artificial intelligence, and machine and deep learning concepts.¹⁵

tervention.¹⁸ These techniques range from simple software to deep learning. Machine learning indicates improvement in the performance of a computer program with experience in certain groups of tasks and performance metrics.¹⁹ Machine learning can help produce reliable and repeatable decisions by learning from previous computations and extracting regularities from large databases. Machine learning includes deep learning. Deep learning differs from other machine learning methods, which are more open to human intervention and control, less layered, and address less complex questions. Deep learning is multilayered, containing autodidacts producing solutions to complex questions, is more closed to human intervention, and contains black boxes whose decision algorithms cannot be understood (Figure 1).

AI APPLICATIONS AND CURRENT EXAMPLES IN ONCOLOGY

AI is the human cognitive function simulation by computers. When AI is defined as a set of applications with a superhuman performance inspired by biological neurons, it can be used at every stage where the human factor is involved (Figure 4). AI technologies have many application areas in healthcare, such as prediction and diagnosis of diseases, big data analysis, and providing efficiency and effectiveness in diseases. The specific application examples of AI in the field of oncology are as follows.²⁰

- Cancer screening
- Cancer diagnosis,
- Classification of cancer,
- Characterization of cancer genomics,
- Analysis of the tumor microenvironment,
- Evaluation of prognostic and predictive biomarkers
- Follow-up care
- New strategies for the drug administration
- New strategies for drug development
- Managing clinical trials

AI is used for early and accurate diagnosis of cancer diseases. A study demonstrated approximately a 99% accuracy rate in the interpretation of mammogram test results by AI, and thus faster detection of cancer than that by physicians. Thus, this situation will significantly reduce the necessity for biopsy and provide significant benefits to both patients and healthcare institutions.^{21,22}

The algorithm, developed in 2018 by the research unit of a China-based technology company developing AI solutions, achieved a higher accuracy rate than that of healthcare professionals in detecting breast cancer metastasis. According to the statement of the technology company, with laboratories in

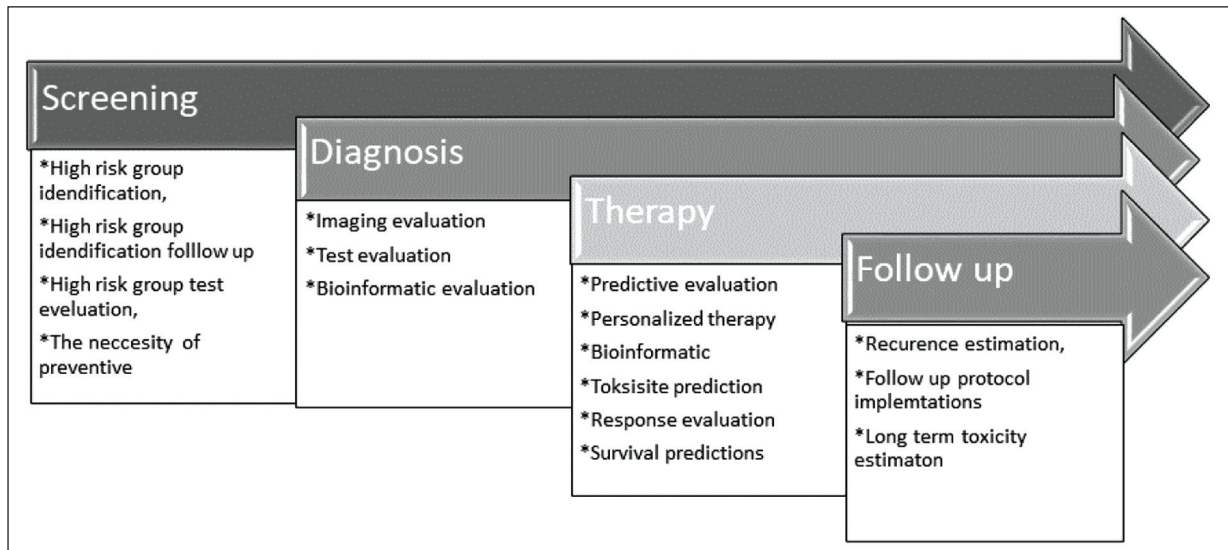


FIGURE 4: Application areas of artificial intelligence in oncology.

China and the USA, the algorithm mimics the pathologists' examination of the breast cancer tumor surrounding images; however, it can reach more accurate results because it can perform a more detailed examination. The algorithm's accuracy rate reached 80.74%, while the accuracy rate of pathologists remained at 72.4%.^{22,23}

Early diagnosis is also critical for the world's major technology companies. Microsoft Corporation (US) announced that with the detection of cancerous cells, a computer programmed to act against them at the molecular level will be developed. Microsoft Research experts believe that they can program cancerous cells to auto-destroy, similar to a computer program. Microsoft's studies on cancer will help physicians to better understand the dynamics of cancer formation and spread and to develop a personalized treatment. Additionally, Microsoft is working on an AI to diagnose cancer early based on the questions about early symptoms that individuals try to find in internet search engines before applying to doctors as of 2016.²⁴

OME Care (formerly Pathway Genomics), supported by IBM Watson, is working to detect some types of cancer early with an easy-to-apply blood test. The company can combine AI and deep learning with personal genetic data with the support of IBM. More-

over, the cancer test "Cancer Intercept Detect" can analyze more than 70 genes that may indicate cancer by taking blood samples of high-risk patients who have not been diagnosed with cancer before and providing results within 10 days. Additionally, they developed a mobile application called OME, which can provide personalized health information based on the user's health history.²⁵

The number of AI applications that help health-care professionals in diagnosis is increasing gradually. In particular, the recent increase in solutions helping in the interpretation of scanning and imaging results displays itself. With AI technologies, data on imaging can be obtained from cloud computing-supported online services. The acquired data can be scanned, recognized, analyzed, and stored using cloud computing and AI algorithms.^{22,26}

The physicians will be able to receive instant image interpretation through AI algorithms in the near future, for example, a surgeon performing a cancer operation can learn whether the tumor has been removed without interrupting the operation. The experts of Massachusetts Institute of Technology (MIT) University in the USA developed an algorithm that could analyze three-dimensional scan results 1000 times faster. The physicians require approximately 2 h to analyze three-dimensional scan results. Thus, the

results can be obtained almost instantaneously using the fast processor computers and advanced algorithms of MIT.^{22,23,27}

A three-legged system called “The Care Trio” has been developed by IBM Watson for oncologists to determine the most appropriate cancer treatment. The “CareEdit” tool provides clinical guidance for the most appropriate treatment for different types of cancer. “CareGuide” uses information from CareEdit to assist physicians in selecting the right treatment for the individual patient. After the clinical decision-making phase, the “CareView” tool evaluates the results and allows for the identification and comparison of patients who have received treatment other than that recommended. The Care Trio system is being trialed in a large oncology hospital in Italy. IBM Watson claims that the survival rate of cancer patients will increase and treatment costs will decrease using this system.²²⁻²⁷

The treatment of cancer, immune system diseases, and infectious diseases is becoming increasingly difficult using conventional methods owing to genetic, environmental, and lifestyle differences. Therefore, personalized medicine is a highly acceptable approach. However, AI is needed for the application of personalized medicine. Health institutions and technology companies have been working on AI. For example, AI used in the radiographic imaging evaluation of a tumor helps clinicians by distinguishing complex patterns in images, defining accurate volume and classification of tumor size in later stages, and parallel tracking of lesions.^{27,28}

One of the areas of use of AI technologies is in evidence presentation.²⁹ The replacement of AI with randomized clinical trials is one of the topics of discussion on the agenda. Randomized clinical trials are time-consuming, costly, and of long duration. AI represents a much larger segment of the population with its ability to collect and analyze big data and can provide faster, less costly, and more accurate results.²²⁻²⁷

Additionally, with AI technologies, the underprivileged society can be given the chance to benefit from medical expertise. As the results become more valid and accurate, the cost of healthcare services can be further reduced. Although AI technologies have been extensively tested, physicians should use their education and experience as the final decision-maker.²⁹

CONCLUSION

Inevitably, AI applications will be one of the most important elements of human life modifications today and in the future. Considering that ethical practices and legal regulations are lagging, understanding, correct implementation, and management are critical responsibilities for practitioners. Despite many fascinating developments that fascinate mankind, further research is needed. In this article, basic information is provided for healthcare professionals and oncologists for enhanced understanding and manageability of AI applications in their practice areas. Ethical, legal, and practical challenges will be discussed later in a separate article.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

This study is entirely author's own work and no other author contribution.

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