How is Artificial Intelligence changing the landscape of cancer therapeutics?

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ABSTRACT

In 2020 alone, there were an estimated 9.7 million cancer-related deaths and 20 million new cancer diagnoses worldwide. (1). Routinely used cancer therapeutics and treatments have proven short of what is needed, and as a result new treatment methods are required to treat individual patient needs. Therefore, artificial intelligence (AI) has been a driving force behind the push for precision medicine. This review discusses how cancer is caused, current treatment methods, and how AI is implemented to improve current treatments. As cancer continues to be a significant global health issue, AI offers new methods for better understanding and diagnosing the disease to improve patient outcomes.

INTRODUCTION

Cancer continues to be a major global health crisis, profoundly affecting millions of lives each year. According to the National Cancer Institute, in 2020 alone, an estimated 1,806,590 new cases of cancer were diagnosed in the United States, with 606,520 fatalities attributed to the disease (2) . This stark statistic underscores the urgent need for advanced research and treatment strategies to combat this pervasive illness. Parallel to the traditional approaches in oncology, Artificial Intelligence (AI) is rapidly transforming the cancer treatment landscape. It is generally believed that AI tools will enhance, rather than replace, the work of healthcare professionals. AI can support administrative workflows, clinical documentation, patient outreach, and more specialized tasks such as image analysis and medical device automation (3). This paper delves into the dynamic interplay between AI and cancer therapies, exploring the innovations it has fostered and the profound impact it will continue to make in the field. Through a detailed analysis, the paper will highlight AI's revolutionary contributions to disease modeling, optimizing therapy selection, and reducing treatment-associated costs and adverse effects. Moreover, it will examine AI's instrumental role in the acceleration of drug discovery and the refinement of clinical trial methodologies, presenting a comprehensive overview of how AI is not just augmenting but in many ways, reshaping the landscape of cancer treatment.

DNA DAMAGE AND REPAIR

When discussing the genesis of cancer, it's crucial to understand the role of DNA mutations and their origins. Mutations can result from inaccuracies in the DNA replication process itself. If the replication machinery falters—due to inherent defects in enzymes like DNA polymerase or other components—errors can accumulate in the genetic code (4). These internal or endogenous sources of mutation stem from within the cell's biological processes. However, mutations also arise from external or exogenous sources. Environmental factors such as ultraviolet (UV) radiation from the sun, carcinogenic chemicals in tobacco smoke, and exposure to ionizing radiation can cause DNA damage. These factors introduce mutations by altering the structure of DNA, creating anomalies that, if not corrected, can lead to cancer (5).

Despite sophisticated DNA damage repair systems, not all DNA damage is caught and corrected. A deficiency in DNA repair proteins due to genetic mutations or transcription errors, can lead to a failure in these pathways, allowing damaged DNA to persist (6). This persistent damage can accumulate over time, leading to the genomic instability that characterizes many cancers. Key DNA repair pathways, such as mismatch repair and nucleotide excision repair, are often found mutated in various cancers, underscoring the critical role of these processes in maintaining cellular health and preventing oncogenesis.[1] Understanding the delicate balance between DNA replication, mutation introduction, and repair provides valuable insights into the cellular dysfunctions that lead to cancer. It highlights the importance of targeting these pathways in cancer therapy to enhance the precision and effectiveness of treatments in correcting or bypassing the cellular irregularities that drive tumor development (5).

HALLMARKS OF CANCER

The "hallmarks of cancer" are six essential traits that cancer cells acquire during their development, which help us understand the complex nature of cancer. These hallmarks include sustaining proliferative signaling (continuous growth signals), avoiding growth suppression, resisting cell death, enabling replicative immortality (limitless replication), inducing angiogenesis (creating new blood vessels), and activating invasion and metastasis (spreading to other tissues). Additionally, genetic instability and inflammation support these hallmarks (7). Recently, two more hallmarks were added: changing energy metabolism and avoiding the immune system (8). Understanding these hallmarks requires deep diving into the cell cycle and DNA replication.

The cell cycle is divided into four primary phases: G1, S, G2, and M. The G1 phase focuses on cell growth, where cells increase in size and synthesize new proteins and organelles. Transitioning into the S phase, the focus shifts to DNA replication, a critical process that must proceed flawlessly to prevent genetic abnormalities or repair any that may occur (9). During DNA replication, enzymes unwind the DNA double helix, and DNA polymerase creates new complementary strands, ensuring genetic integrity. If errors occur, mutations may arise, leading to cancer (6). Disruptions in the cell cycle or DNA replication can result in uncontrolled cell growth, a hallmark of cancer.

DNA replication involves complex mechanisms where enzymes first unwind the DNA double helix, allowing the strands to separate (figure 1). This unzipping process makes each strand accessible for replication. DNA polymerase, a key enzyme, then scans each strand, matching and attaching the appropriate nitrogenous bases to form new complementary strands. These actions result in two DNA molecules, each consisting of one original strand and one new

[1] Process by which normal cells are transformed into cancer cells.

strand, which coil back into the double helix structure. The precision of this process ensures the genetic integrity of the cells, forming the basis for healthy cell division. However, if DNA replication errs, mutations may occur (6).

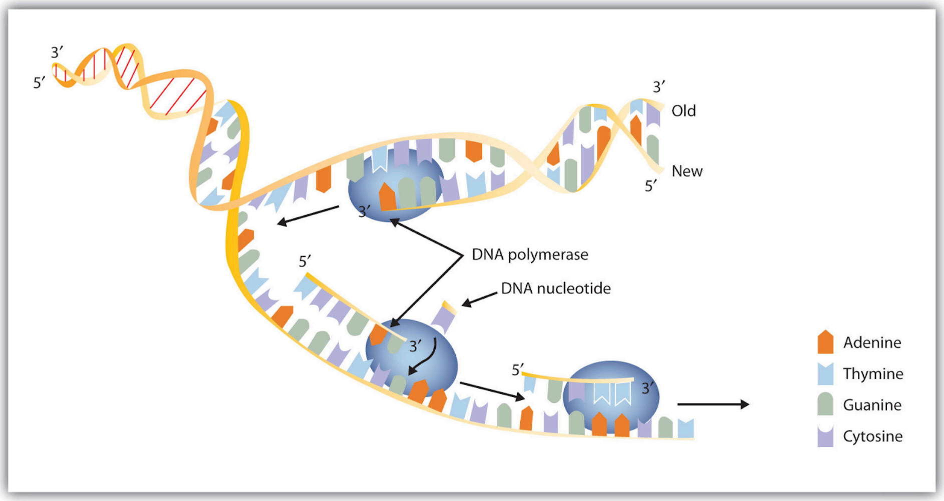

Figure 1. DNA REPLICATION PROCESS DURING THE CELL CYCLE. This diagram illustrates the DNA replication process, highlighting the role of DNA polymerase in synthesizing new DNA strands. DNA nucleotides, including adenine (orange), thymine (blue), guanine (green), and cytosine (purple), are added to the growing DNA chain, ensuring accurate replication of the genetic material. Understanding this process is crucial in cancer research, as errors in DNA replication can lead to mutations that drive cancer progression (10).

AI modules analyze data to assess the integrity of these hallmark pathways. By examining large amounts of biological data, such as genetic mutations and signaling disruptions, AI can identify patterns and anomalies linked to cancer. These insights help develop targeted therapies.

CANCER TREATMENTS

Although cancer treatment will vary based on individual patient diagnosis and progression of the disease, patients and physicians must understand all treatment options before choosing a course of action. Table one lists the six most common treatments used today.

Treatment	Explanation of	When treatment is used

	treatment	
Chemotherapy	Systemic administration of drugs to kill cancer cells	Chemotherapy is considered when there is a potential for future metastasis of cancer, regardless of the stage. The decision to use chemotherapy depends on the specific cancer stage and the effectiveness of available treatment interventions.
Radiation therapy	Use of high doses of radiation to kill cancer cells	Radiation therapy is employed to treat localized masses that are easily targetable. It may be utilized in the early stages of cancer or after the disease has spread.
Surgery	Surgically removing cancer from a patient's body	Surgery is typically recommended in the early stages of cancer, before metastasis, when the tumor can be excised and is still confined to its original location. This approach is most effective when the cancer has not yet spread.
Immunotherapy	Use of substances to suppress the immune system to help the body fight cancer	Immunotherapy is used to treat advanced cancer that has not responded to other forms of treatment. This approach harnesses the body's immune system to target and combat cancer cells.
Targeted therapy	Drugs or other substances are used to target specific cancer cells or proteins that control how cancer cells may grow and divide.	Targeted therapy may be employed before surgery to reduce the size of the cancer. This treatment focuses on specific genes, making it suitable for patients with mutations that can be addressed through targeted interventions.
Hormone therapy	A treatment that slows or stops the growth of cancer that uses hormones to	Hormone therapy is utilized when cancer relies on hormones to grow and spread. This treatment works by blocking or lowering the levels of hormones that fuel certain types of cancer.

	grow	

Table 1. Cancer treatments and when to use each.

Accurate diagnosis is essential for effective cancer treatment, and various diagnostic tools focus on different hallmarks of cancer. Biomarker screens identify specific molecules in blood, urine, or tissues that indicate the presence of cancer. These markers can show problems with cancer cell growth, endless cell replication, and evading immune destruction (11). For instance, elevated levels of PSA (prostate-specific antigen) can indicate prostate cancer (12.). Histology involves examining tissue samples under a microscope to look for abnormal cells, making it crucial for identifying changes in cell structure that indicate evading growth suppressors, resisting cell death, and sustaining proliferative signaling (13). CT and MRI scans provide detailed pictures of the inside of the body, essential for detecting tumors, determining their size, and checking for metastasis. These scans focus on things like new blood vessel growth to supply the tumor and cancer spreading to other tissues. By using these diagnostic methods and targeted treatments, doctors can better address the specific hallmarks of each cancer type. This integrated approach ensures that treatments are tailored to the individual patient's cancer profile, enhancing the precision and effectiveness of cancer therapy.

OVERVIEW OF AI

AI in medicine has revolutionized healthcare by simulating human intelligence and critical thinking through advanced technology. Initially described by Alan Turing in 1950 and later coined by John McCarthy in 1956, AI has evolved from simple "if-then" rules to complex, self-learning algorithms that mimic human cognition (15). Early AI systems faced significant limitations, but breakthroughs in the early 2000s allowed AI to analyze complex data and enhance clinical practices. Today, AI in medicine encompasses various technologies, including machine learning, deep learning, and computer vision, each contributing to different medical applications such as diagnostics, treatment planning, and workflow efficiency (16).

Even though AI began in the 1950s and 1960s, it has transformed from basic systems to advanced, multifaceted tools throughout history. In the 1950s and 1960s, AI was just beginning. Early innovations like the first industrial robot, Unimate, and the chatbot Eliza laid the groundwork for future advancements. The 1970s and 1980s, known as the "AI winter," saw reduced funding and interest, but significant developments like the MYCIN system and DXplain showed AI's potential in medical diagnostics and decision support. By the 2000s, renewed interest in machine learning and the emergence of deep learning marked a new era. Technologies like IBM's Watson and various convolutional neural networks (CNNs) significantly improved diagnostic accuracy and personalized patient care (16, figure 2). The progress of AI in medicine has been stimulated by the development of subfields such as Machine learning (ML) and deep learning (DL).

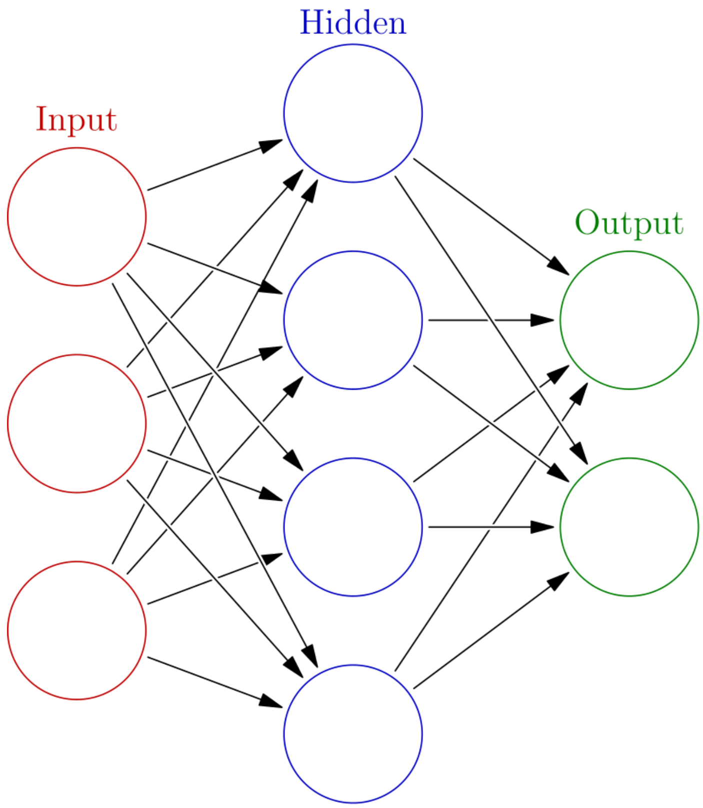

Figure 2. MACHINE LEARNING NEURAL NETWORK This diagram illustrates the structure of a simple neural network used in machine learning. It shows three layers: the input layer (red nodes), the hidden layer (blue nodes), and the output layer (green nodes). Each node within these layers represents an artificial neuron. Arrows between the nodes depict the connections that transmit signals from one neuron to another, starting from the input layer, moving through the hidden layer, and culminating in the output layer. This flow represents how a neural network processes information (17).

Machine Learning, defined as a computational system based on algorithms that analyze vast and diverse data, learns and improves from experience without explicit programming. Deep learning, a prominent technique within machine learning, has achieved groundbreaking results in tasks such as image classification and speech recognition (figure 3). Inspired by the human brain, deep learning uses multiple layers of artificial neural networks to process data in complex ways, finding patterns in large datasets. In the medical field, these technologies are revolutionizing diagnostics and treatment by analyzing medical images, predicting disease outcomes, and personalizing patient care. The rapid growth in computing power and data availability has sped up the use of machine learning and deep learning, making AI a crucial tool in modern healthcare (18). Projects like IBM Watson Health and AI-assisted care at Stanford

University exemplify the ongoing efforts to integrate AI into cancer care, enhancing diagnostic precision and optimizing therapeutic strategies (15).

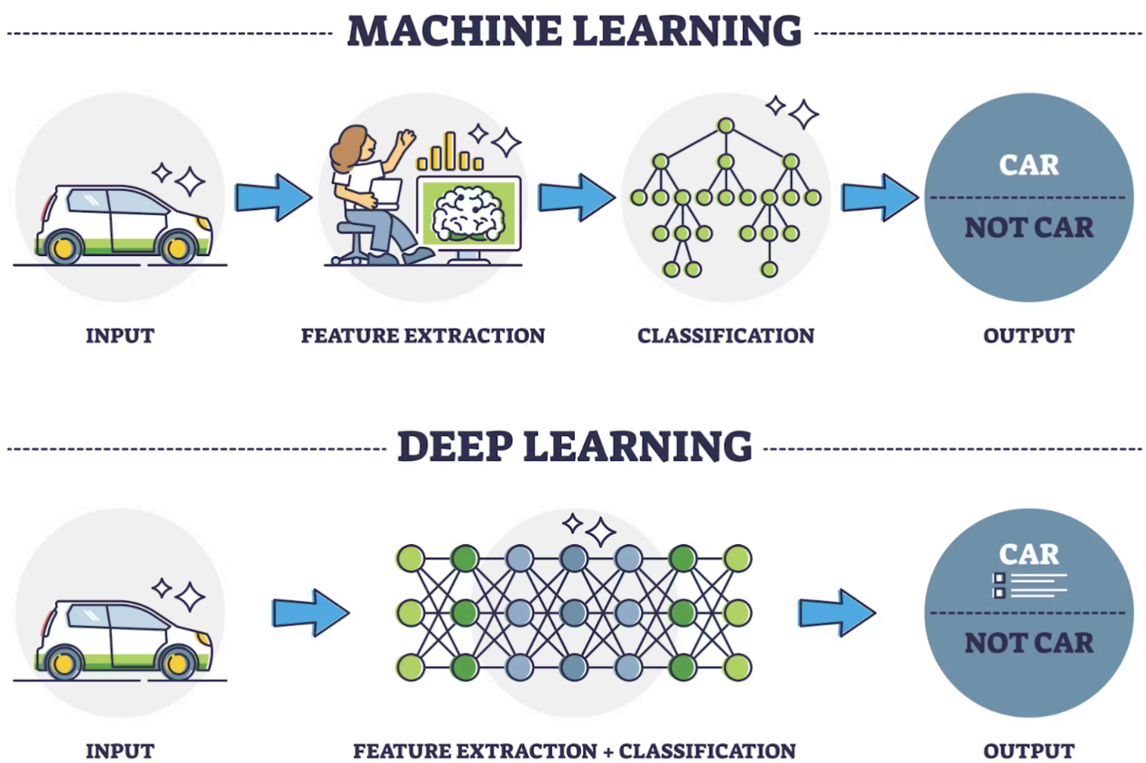

Figure 3. DIFFERENCE BETWEEN MACHINE LEARNING & DEEP LEARNING This image illustrates the difference between machine learning and deep learning. Machine learning involves manual feature extraction and classification through a simpler neural network. On the other hand, deep learning combines these steps into a single automated process using a complex neural network that learns directly from data, making it more efficient for tasks like image recognition (19).

AI IN CANCER TREATMENTS

AI is profoundly transforming the landscape of cancer therapeutics, transcending its initial foothold in diagnostics to revolutionize actual treatment methodologies. In areas such as radiology, surgery, and pharmacology, AI is not merely augmenting existing techniques but is also introducing advanced techniques that aim to improve the accuracy and effectiveness of cancer treatments (figure 4).

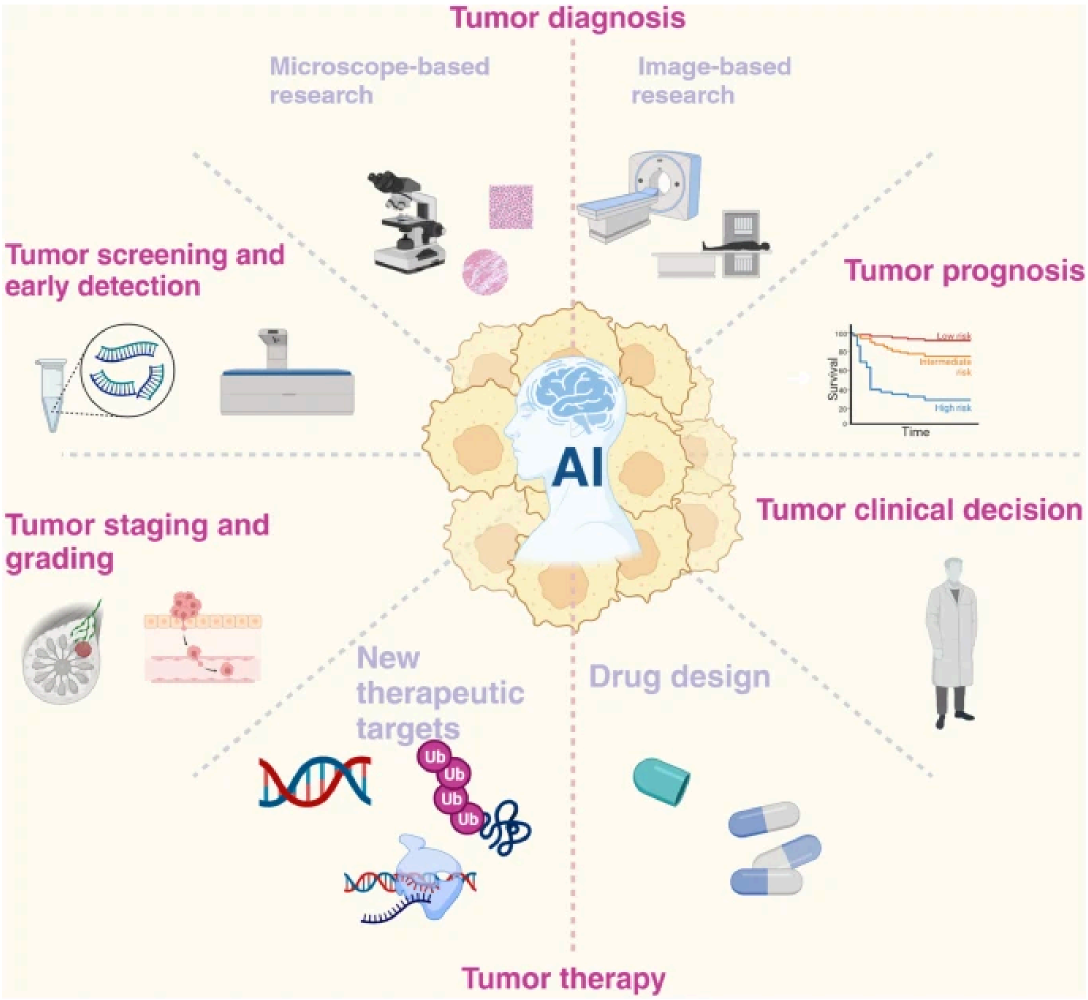

Figure 4. THE ROLE OF AI ACROSS THERAPEUTIC DOMAINS This diagram illustrates the multifaceted impact of artificial intelligence (AI) in advancing cancer treatment. Key areas include microscope-based research for tumor diagnosis, image-based analysis for more accurate tumor prognosis, and AI-driven tumor screening and early detection methods. AI also enhances tumor staging and grading, identifies new therapeutic targets, assists drug design, and informs clinical decision-making processes. Each segment highlights how AI integrates into different stages of cancer therapy, from initial detection to treatment planning, showcasing AI's potential to improve outcomes and personalize patient care in oncology (20).

DIAGNOSIS

Advanced technologies that capitalize on AI's ability to identify subtle and often overlooked patterns in medical data increasingly demonstrate AI's potential to enhance cancer diagnostics. In oncology, diagnostic screening plays a pivotal role in the early detection of cancer, significantly enhancing the potential for successful treatment. Traditional diagnostic methods, such as biopsies and various imaging tests, are the cornerstone for identifying malignancies. However, the integration of AI has revolutionized these practices.

AI's transformative role is exemplified by MIRAI, a mammography-based deep learning model developed by Dr. Constance Lehman, a Professor of Radiology at Harvard Medical School, and Dr. Regina Barzilay, who serves as a Professor at the Massachusetts Institute of Technology and the faculty lead for AI at the MIT Jameel Clinic. MIRAI utilizes a vast dataset of diverse patient information, including historical mammogram images and integrated risk factor data, to provide individualized, equitable, and cost-effective breast cancer risk assessments. This model has demonstrated its potential to surpass traditional risk models in accuracy, offering consistent results across mammography sites. Further, ongoing studies aim to validate MIRAI's ability to predict high-risk patients, potentially revolutionizing breast cancer screening guidelines and management protocols for those at elevated risk (21)

Moreover, AI is expanding into proteomics, where machine learning (ML) analysis of protein expression profiles can identify more specific and sensitive biomarkers. Analyzing proteomics data and other “-omics” datasets like genomics, transcriptomics, and metabolomics is incredibly complex and time-consuming for humans. Reliable AI models that can effectively parse this data are a massive time saver, making using such data much more practical. These models can help identify protein biomarkers indicative of specific cancer types, predict how cancer cells will respond to various treatments, and even uncover new therapeutic targets. This kind of analysis is crucial for diagnosing cancer, predicting patient prognosis, and even in the identification of therapeutic targets and evaluation of drug efficacy (22)

Another remarkable advancement comes from the Mayo Clinic, where researchers have developed an AI model that detects pancreatic cancer in CT scans with astonishing accuracy. This AI system can identify cancer approximately 475 days before clinical diagnosis, thus significantly enhancing the chances of successful treatment through early intervention (23). Furthermore, AI has demonstrated its efficacy in diagnosing gastrointestinal cancers, as exemplified by Horie et al.'s use of a deep learning CNN. This model was trained on thousands of images to diagnose esophageal small cell and adenocarcinoma, achieving a diagnostic sensitivity of 98% and identifying all cancers smaller than 10mm, showcasing AI's role in facilitating early and accurate cancer detection (23).

TREATMENT

In the realm of cancer treatment, there has been a big push toward precision medicine and the ability to use patient-target-specific treatments. Precision medicine has transformed AI in cancer treatment using algorithms to analyze genetic data, allowing for more personalized and effective therapies. However, AI is ushering in a transformative era across various domains, from radiology and surgery to drug treatments and tumor prevention.

AI in Radiology

AI's integration into radiology has significantly enhanced the accuracy of diagnostic imaging. With the advent of digital imaging, AI algorithms, particularly those using deep learning and CNNs, are now embedded seamlessly within radiology workflows. These algorithms can swiftly analyze vast datasets from multiple imaging modalities—such as X-rays, MRIs, and CT scans—pinpointing areas of interest with high precision (18). Innovations like "radiomics" further advance this field by extracting vast quantities of data from images down to the voxel level, enabling the detailed characterization of tumors and vastly improving detection and diagnostic capabilities for various cancers, including intricate CNS tumors (24).

AI in Surgery

AI's role in surgery is exemplified by a partnership at the UNC Department of Surgery, which developed an AI model to improve the accuracy of tumor removal during breast cancer surgeries. This model assists surgeons in real-time to ensure the complete removal of cancerous tissues, thus reducing the likelihood of multiple surgeries (25). Moreover, AI is anticipated to revolutionize surgical practice by enhancing training, augmenting the cognitive functions of surgeons, and advancing procedural automation (18). These developments promise a shift towards "digital surgery," where AI's role ranges from operational assistance to cognitive enhancement.

AI in Drug Treatments and Discovery

AI is profoundly influencing the field of pharmacology, from drug discovery to treatment personalization. Researchers at the National Institutes of Health (NIH) have developed an AI tool that uses single-cell RNA sequencing to predict cancer drug efficacy, potentially allowing for more precise therapy matching to individual patients' profiles (26).

Additionally, the integration of AI with protein structure prediction tools like AlphaFold is accelerating drug discovery processes. AlphaFold, developed by DeepMind (a subsidiary of Alphabet Inc.), is an instrumental tool in accelerating the identification of molecular targets for drug development, providing researchers with the ability to design new therapeutics based on detailed protein structure predictions rapidly. For instance, using AI, researchers created a novel drug candidate for hepatocellular carcinoma in just 30 days, showcasing AI's capability to identify and target novel therapeutic pathways rapidly (27).

These innovations signify a pivotal shift in cancer treatment paradigms, where AI enhances existing techniques and paves the way for novel approaches to prevention, diagnosis, and personalized treatment. As these technologies continue to evolve, they hold the promise of significantly improving cancer patients' outcomes by optimizing and personalizing the treatment process at every step.

LIMITATIONS AND CONTROVERSY

The integration of AI into cancer treatment, while offering groundbreaking advancements in diagnostics and personalized therapy, brings a series of substantial controversies and limitations. Ethical considerations, cost implications, and the societal impact of deploying AI in healthcare have become vital discussion points. AI’s implementation in cancer therapeutics is fraught with challenges such as data privacy issues, lack of diverse data sets leading to potential biases, and the 'black-box' nature of some AI systems, which obscure their decision-making processes (28). These factors can undermine trust in AI-driven systems.

There are also ethical dilemmas surrounding the use of AI in medicine. The automation of sensitive processes, such as patient diagnosis and prognosis, raises issues of accountability—mainly when errors occur (28). Who is responsible when an AI system fails—the healthcare provider or the algorithm's designer? Additionally, the potential for AI to replace jobs in healthcare adds to the unease about its widespread adoption (29).

In conclusion, while AI presents a transformative potential in cancer treatment, addressing its ethical, economic, and social implications is crucial. Ensuring that AI enhances rather than undermines patient care will require ongoing discussion among stakeholders, regulatory frameworks, and a commitment to addressing the ethical challenges posed by these advanced technologies.

CONCLUSION

With the current cancer diagnosis and treatment landscape, alongside society's adoption of technology in their daily lives, there is a push to harness this technology for improved therapeutics and precision medicine. An advancement in precision medicine and successful patient outcomes can lie in machine learning to enable more accurate and personalized care. However, integrating AI technologies into healthcare presents challenges that need further discussion and regulation. There is great potential for AI to improve therapeutics and the precision medicine landscape around cancer treatments to create a more patient-centered form of care.

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