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REVIEW ON ARTIFICIAL INTELLIGENCE THAT ARE USED IN A TREATMENT OF CANCER

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ABSTRACT

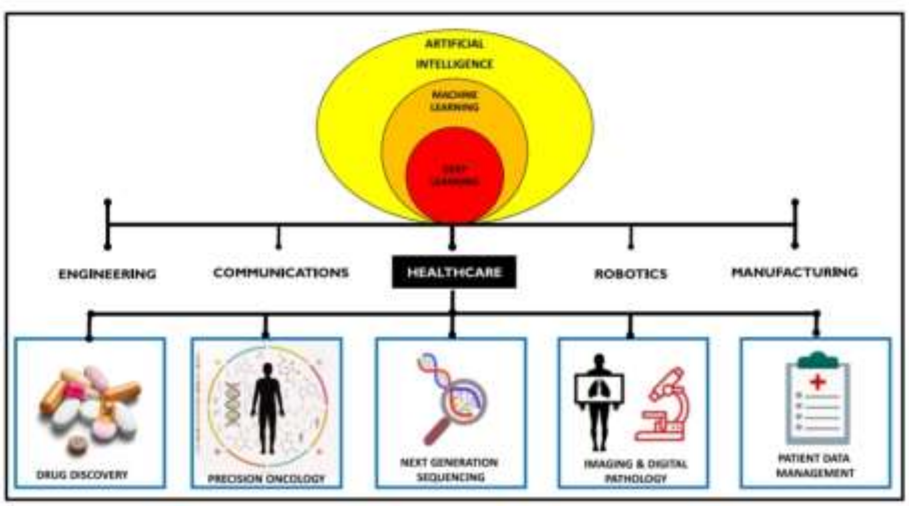
Artificial intelligence (AI) uses mathematical algorithms to replicate human thinking and tackle difficult healthcare problems, such as complex diseases like cancer. In the past decade, AI has rapidly advanced, showing great promise for enhancing decision-making, especially since humans struggle to process large amounts of data quickly. Cancer is a complicated disease with numerous genetic and epigenetic variations.AI-based algorithms have great potential to identify genetic mutations and abnormal protein interactions early on. Modern biomedical research is focused on integrating AI technology into clinics in a safe and ethical way.AI assistance for pathologists and physicians could greatly improve predictions of disease risk, diagnosis, prognosis, and treatment options. The use of AI and machine learning in cancer diagnosis and treatment represents the future of personalized medical care, allowing for quicker development of tailored therapies for each patient. With AI systems, researchers can collaborate in real-time and share knowledge digitally, potentially helping millions. This review focuses on how connecting biology with artificial intelligence can revolutionize clinics and help oncologists provide precise treatments.

KEYWORDS: *Artifcial intelligence, Machine learning, Cancer diagnosis, Treatment, Therapeutic interventions*

INTRODUCTION

The term "artificial intelligence" (AI) was first used at the Dartmouth Summer Workshop in 1956, where it was generally described as "thinking machines." In simple terms, AI refers to a machine's ability to learn, recognize patterns, and make decisions based on new data. AI is a broad term that often includes machine learning and deep learning.

Machine learning is a subset of AI, and deep learning is a type of machine learning that uses complex artificial neural networks with multiple layers. Recently, deep learning has become very popular, especially for tasks like face recognition and image classification. This capability has extended to cancer research and medicine, allowing for the automatic and accurate detection of cancer in images, which can help relieve pathologists and radiologists from repetitive tasks.



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Early Detection, Diagnosis, and Staging of Cancer

The timing of cancer detection, the accuracy of diagnosis, and staging are crucial factors that influence how aggressive a tumor is and affect clinical decisions and patient outcomes. In recent years, AI has significantly advanced this important area of oncology, achieving results that can match those of human experts while also providing benefits like scalability and automation.

Making Cancer Diagnoses More Accurate

Deep learning models are increasingly being used to diagnose cancer and identify cancer subtypes from histopathologic and other medical images. Deep neural networks (DNNs) are powerful algorithms that can analyze large images, such as H&E-stained whole slide images from biopsies or surgical samples.

These models have proven very effective at classifying images, such as determining whether a digitized slide contains cancer cells. They achieve high accuracy in distinguishing tumor cells from healthy ones (with area under the curve scores above 0.99). DNNs are also used for more complex tasks, like differentiating closely related cancer subtypes (e.g., adenocarcinoma vs. adenoma in gastric and colon cancers or adenocarcinoma vs. squamous cell carcinoma in lung tumors) and detecting benign versus malignant tissues.

Cancer Staging and Grading

Cancer staging and grading, which determine how aggressive and advanced the cancer is, are crucial parts of the diagnostic process. Staging influences treatment decisions, such as whether to adopt a watchful waiting approach or pursue aggressive treatments like radiotherapy, surgery, or chemotherapyFor prostate cancer, staging is done using the Gleason score, which combines two scores based on the prevalence of tumor cells in two areas of a slide. Deep neural networks (DNNs) have shown promise in predicting Gleason scores from histopathology images of prostate tumors. For example, Nagpal and colleagues used whole slide images from prostatectomy specimens to train a DNN model (Inception-V3) and a k-nearest-neighbor classifier to predict Gleason scores. Their model achieved a prediction accuracy of 0.70, compared to 0.61 from a panel of 29 independent pathologists.Cancer staging can also be done using radiology images. Zhou and colleagues developed a deep learning method based on SENet and DenseNet to predict the grade (low vs. high) of liver cancer from MRI images, achieving an area under the curve (AUC) of 0.83. Overall, these studies suggest that AI has promising applications in cancer staging, performing comparably to trained experts despite some limitations in AUC scores.

On the Road to Early Cancer Detection

AI is making progress in the early detection of cancer through emerging minimally invasive techniques, such as liquid biopsies for circulating tumor DNA (ctDNA) or cell-free DNA (cfDNA). Liquid biopsies, which can be obtained through simple blood tests, offer the potential for early cancer detection, monitoring relapse risk over time, and guiding treatment options.For instance, the microsatellite instability (MSI) status can be predicted from ctDNA in patients with endometrial cancer to help inform immunotherapy treatments. Chabon and colleagues developed a machine learning method called Lung-CLiP, which predicts the likelihood of ctDNA in blood samples from lung cancer patients. This method first estimates the probability that a cfDNA mutation is linked to the tumor, using an elastic net model and features like cfDNA fragment size. It then combines this information with copy-number scores using an ensemble classifier with five different algorithms to predict the presence of ctDNA in the blood.The method showed modest predictive performance, with area under the curve (AUC) scores ranging from 0.69 to 0.98, depending on the cancer stage. There is also a trade-off between specificity and sensitivity in these predictions.

DETECTING CANCER MUTATIONS USING MACHINE LEARNING

The widespread use of next-generation sequencing (NGS) has enabled thousands of cancer laboratories to routinely sequence cancer genes, exomes, and genomes. While various computational tools can identify genetic variants and mutations in NGS data, they often struggle in situations like low coverage or complex, repeat-rich areas of the genome.Some researchers have approached mutation detection as a machine learning problem. For example, DeepVariant is a deep neural network (DNN) method based on the Inception-V2 architecture. It detects variants from aligned NGS reads by first creating read pileup images for potential variants, turning it into an image classification task. Then, it predicts the probabilities of different genotype states (homozygous reference, heterozygous variant, or homozygous variant). This method won an award for best performance in SNP detection at the second precision FDA Truth Challenge in 2016.

DISCOVERY OF THERAPEUTIC TARGETS AND DRUGS

Drug discovery and development typically involves high costs and significant time commitments. Making access to various treatments more affordable is essential.

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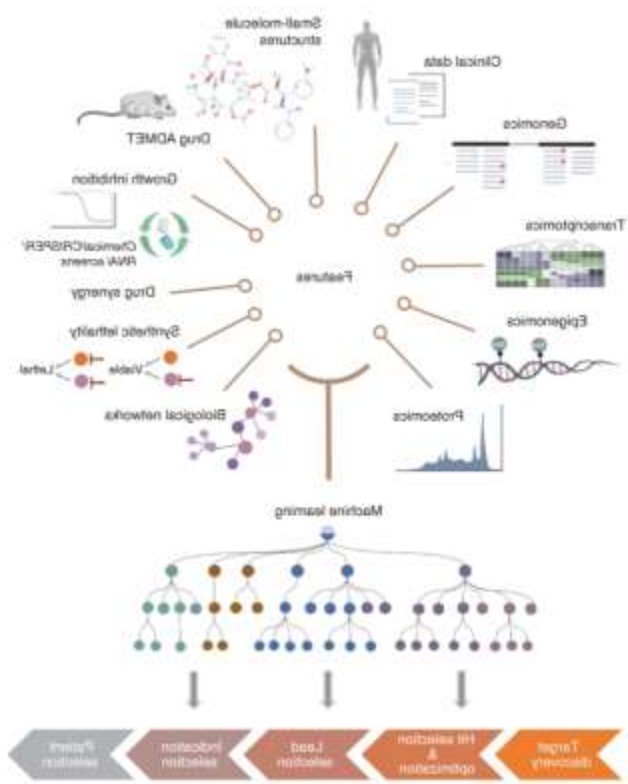

Artificial Intelligence (AI) in Cancer Medical Imaging

Artificial intelligence (AI) is transforming cancer medical imaging. Deep learning algorithms play a crucial role in healthcare by enhancing disease monitoring, diagnosis, surgical assistance, and overall disease management.In oncology, AI is particularly important in radiology across various imaging techniques like X-rays, ultrasounds, CT scans, MRIs, PET scans, and digital pathology. These advanced algorithms analyze images quickly and accurately, helping to differentiate between normal and abnormal findings. This distinction is vital for early cancer detection, which improves patient outcomes.AI enhances medical imaging by improving image quality, aiding in image interpretation, and advancing radiomics. Looking ahead, the focus will be on increasing efficiency and reducing costs in medical imaging.

1) Radiographic imaging

AI has made significant advancements in healthcare, especially in medical imaging. Extracting important data—like size, shape, and position—from medical images is vital for accurate diagnosis and treatment. However, this process can be slow and subject to human error, particularly with complex tumors. Therefore, there is a strong need for automated analysis in clinical care. To ensure accurate analysis of medical images, three key strategies are essential:

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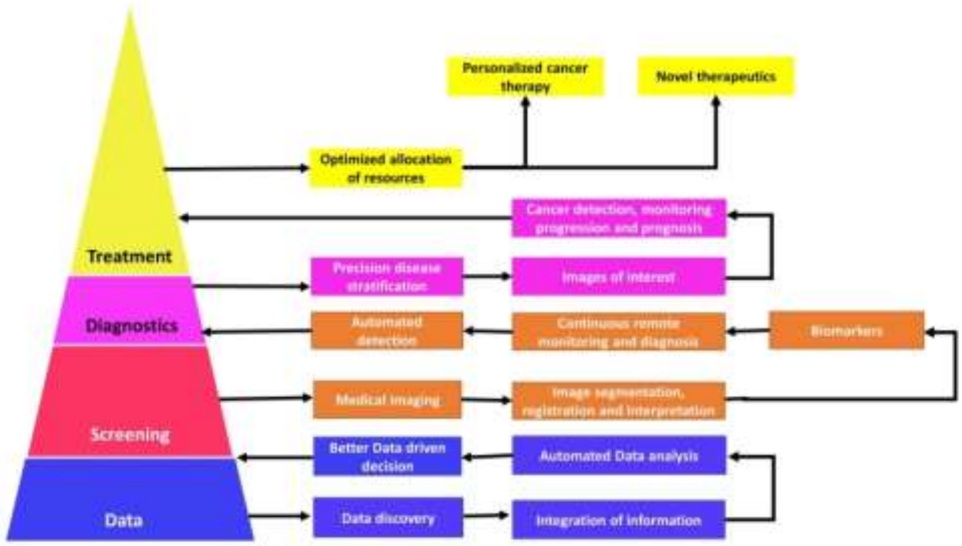
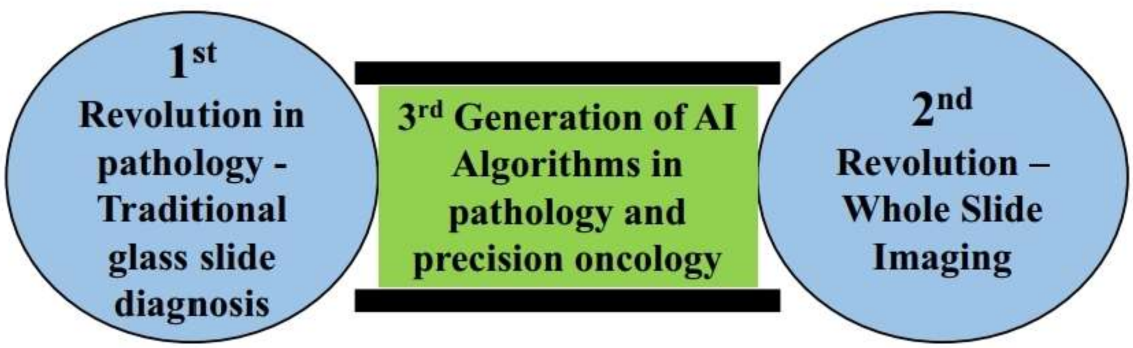


1. Image Segmentation: This identifies the area of interest in an image and marks its boundaries.
2. Image Registration: This establishes how different images relate spatially to each other.



3. Image Visualization: This extracts important data for clear interpretation.

Despite these developments, challenges persist due to the complexity of the data, the objects within the images, and validation issues. In many countries, especially developed ones, cancer diagnosis and treatment often involve a Multidisciplinary Team (MDT). These teams are specialized by cancer type and consist of various healthcare professionals who collaborate to decide on the best treatment plan.For example, an MDT for thoracic cancer might include a pulmonologist, radiologist, histopathologist, clinical nurse, radiotherapy oncologist, chemotherapy oncologist, palliative care physician, and thoracic surgeon, along with an administrator.The main advantage of this approach is that it allows for the selection of the most effective and current treatments, chosen by a team of experienced experts working together.

Digital Pathology

Pathology is the diagnosis of disease through the examination of body tissue, typically viewed under a microscope on glass slides. Certified pathologists usually make these diagnoses. However, traditional methods relying on glass slides can be time-consuming and prone to errors, leading to delays in second opinions and affecting patient care.To improve this process, diagnostic pathology is increasingly adopting digital imaging technologies. One of the latest innovations is Whole Slide Imaging (WSI), which allows for the viewing of entire slides as high-resolution scannedimages. This method not only improves image quality but also offers a more efficient way to store images compared to traditional glass slide storage.

AI for diagnosis of Colorectal Cancer

As technology advances, it's no surprise that AI is being used to improve how we diagnose cancer. AI helps make diagnoses more accurate and precise (Huang et al., 2019). One of its key advantages is handling large amounts of data and uncovering patterns that human experts might miss (Huang et al., 2019). Efforts to improve medical imaging now focus on using deep learning to detect cancer more effectively. These tools can scan and interpret images faster, improve workflows, enhance image quality, and even use 3D technologies to extract better images (Liu et al., 2018a; Topol, 2019; Thompson et al., 2018; Li et al., 2018).

While AI seems like a perfect fit for medical imaging, its potential in pathology and diagnosing genetic diseases is just as exciting and worth exploring. This could mean improving current medical tests or discovering new ways to identify diseases. Ultimately, enhancing imaging and testing methods with AI could bring transformative changes to healthcare.

Table 1 Potential implementation of Artifcial intelligence (AI) for epidemiology of colorectal cancer

	Definition	Function example	In colorectal cancer
GeoAI (Janowicz 2020)	Subfield of spatial data science to process geographic information using AI	Image classification, object detection, geo-enrichment	Etiological studies, such as food consumption, genetic predisposition, healthcare variance
Digital epidemiology—Global Public Health Intelligence Network (Tarkoma et al. 2020; Dion et al. 2015)	Increase situational (public health events) awareness and capability and global network links	Early detection of SARS	Increase global capacity to early-detect risks and tumor burdens
Digital epidemiology—HealthMap (Tarkoma et al. 2020; Dodson et al. 2016)	Utilizing online informal sources for disease surveillance	Real-time surveillance on COVID-19	Achieve a comprehensive view of global tumor burden
Digital epidemiology—Program for Monitoring Emerging Diseases (Tarkoma et al. 2020; Hii et al. 2018)	Exploiting the Internet and serving as a warning system	Early reports on COVID-19	Monitoring of emerging etiological factors associated with colorectal cancer

Understanding how AI is applied to visual imagery interpretation starts with exploring Convolutional Neural Networks (CNNs). These are specialized artificial neural networks designed to handle image data (Wu, 2017). By analyzing large datasets of images, CNNs learn patterns to recognize new objects and improve their performance over time. Since they are a branch of AI, they also allow for optimization and adaptability (O'Shea and Nash, 2015).Another key concept is computer vision, where AI processes and interprets real-time visual data from cameras or videos. This technology can be applied to tools like the endoscope, which is crucial for diagnosing colorectal cancer.

In CNNs, one common method for object detection is the replicated feature approach, where copies of a feature detector are used to scan an image from different positions (Le, 2018). This approach has several advantages:

1. It reduces the number of free parameters.
2. It works across different scales and orientations.
3. It creates feature maps by replicating detectors, enabling consistent detection across the entire image (Le, 2018).

This Method Benefits Neural Networks by

1. Preserving translation invariance, ensuring features remain recognizable even when shifted.
2. Sharing useful features across all image areas, a concept known as invariant knowledge (Le, 2018).

These features make CNNs powerful tools for visual interpretation,particularly in medical imaging.

To understand how AI is used in visual imagery, it's important to start with Convolutional Neural Networks (CNNs). These are special types of artificial neural networks designed to work with image data (Wu, 2017). By analyzing large sets of images, CNNs learn to identify patterns and recognize new objects. Since they are part of AI, they can improve and adapt over time (O'Shea and Nash, 2015).AI also processes visual data in real time through a field called computer vision, which involves interpreting images or videos from cameras. This is especially useful in tools like the endoscope, which is important for diagnosing colorectal cancer.A common method CNNs use for object detection is called the replicated feature approach. This involves using multiple copies of the same feature detector to analyze an image from different positions (Le, 2018). This approach has key advantages:

1. It reduces complexity by lowering the number of parameters.
2. It works across different sizes and orientations.
3. It allows the same features to be recognized anywhere in the image, which is called invariant knowledge (Le, 2018).

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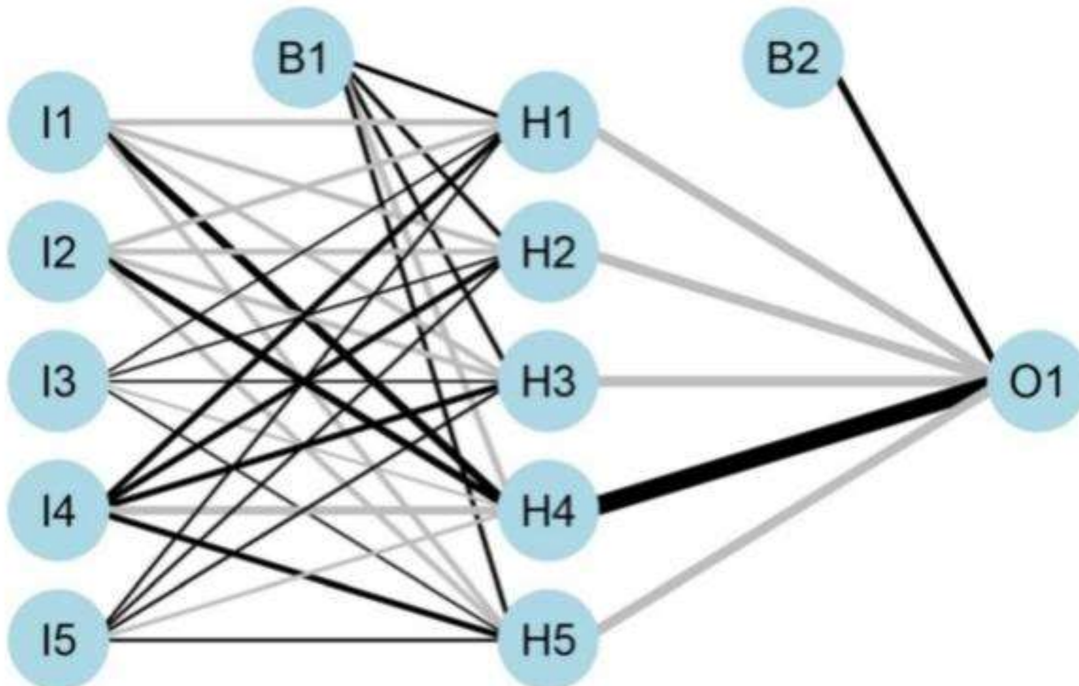
Overall, CNNs are powerful tools for analyzing images and are especially helpful in medical applications like detecting cancer.



An artificial neural network (ANN) consists of four main components: an input layer (I), hidden layer (H), bias layer (B), and output layer (O). The connections between these layers are adjusted during training based on feedback.Positive correlations are shown with black lines, while negative correlations are shown with grey lines.The thickness of each line represents its importance or significance.This structure enables the ANN to process new inputs and generate specific outputs based on the learned patterns.In endoscopy, moving instruments can create unwanted artifacts that interfere with accurate diagnoses (Zhang and Xie, 2019). Researchers analyzed various datasets to develop methods for reducing the number of artifacts detected by segmentation tools.

Recently, Ali et al. conducted a large-scale study comparing 23 segmentation algorithms using common datasets (Ali et al., 2020). They found that while most algorithms performed similarly in detecting artifacts, many struggled with larger artifacts. This poses a significant challenge, as larger artifacts can lead to misinterpretations or false-positive findings (Ali et al., 2020).

Direct methods using CNNs in endoscopy have focused on diagnosing polyps. Misawa et al. developed their own algorithms to identify colorectal polyps from video datasets (Misawa et al., 2018). Their algorithm's results were compared to annotations made by two experts, considered the gold standard. The study found that the AI correctly diagnosed flat lesions, which are the hardest to identify, 64.5% of the time (100/155 cases) and correctly identified 94% of all test polyps (Misawa et al., 2018; Kudo et al., 2019; Liu et al., 2018b).
Building on this work, Mori et al. tested the same algorithm in a live experiment using an endocytoscope, which offers over 500x magnification while functioning like a regular endoscope (Mori et al., 2019). Six patients underwent the procedure, and the AI successfully identified all cases in real time as either adenoma or hyperplastic polyps. New features included:

1. A color change in the screen's corner to indicate abnormalities.
2. A warning sound.
3. The ability to distinguish between neoplastic and non-neoplastic polyps in real time using microscopic imaging (Mori et al., 2019).

Mori et al. suggest that incorporating deep learning into colonoscopies offers several benefits beyond improved diagnostic accuracy. These include:

1. Reducing variations in detection rates.
2. Providing better teaching tools for endoscopists and trainees.

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3. Minimizing unnecessary polypectomies (Mori et al., 2017).
AI-powered endoscopy research has grown significantly, as shown by multiple studies (Ichimasa et al., 2018; Nakajima et al., 2020; Lai et al., 2021; Yamada et al., 2019; Chen et al., 2018; Repici et al., 2020; Kudo et al., 2020; Mori et al., 2018; Nguyen et al., 2020; Deding et al., 2020). However, challenges remain, such as:
1.Technological limitations.
2.Lack of regulations and clinical trials.
Feasibility issues and risks of misdiagnosis (Kudo et al., 2019; Mori et al., 2017).A significant limitation is the scarcity of available datasets in this field. Since AI relies on data for training and improvement, this limits its capacity to learn and grow (Mori et al., 2017).In CT and MRI imaging, CNNs have also been impactful, particularly in detection, segmentation, and classification of images (Yamashita et al., 2018; Shan et al., 2019). For colorectal cancer, however, research on their use is limited. A notable example is a study by Shan et al., which demonstrated that AI can reconstruct low-dose CT scans effectively, indirectly improving patient health. Advancements in imaging technology have focused on reducing radiation exposure for patients during scans, minimizing unwanted side effects (Sharma and Aggarwal, 2010). One promising method is using deep learning for attenuation correction in PET/MR images, referred to as deep MRAC. This approach enhances image quality,leading to better diagnostic accuracy and improvements in segmentation techniques (Pesapane et al., 2018; Lundervold and Lundervold, 2019).

Table 2 Endoscopic studies involving artifcial intelligence for diagnosis and prediction of colorectal cancer

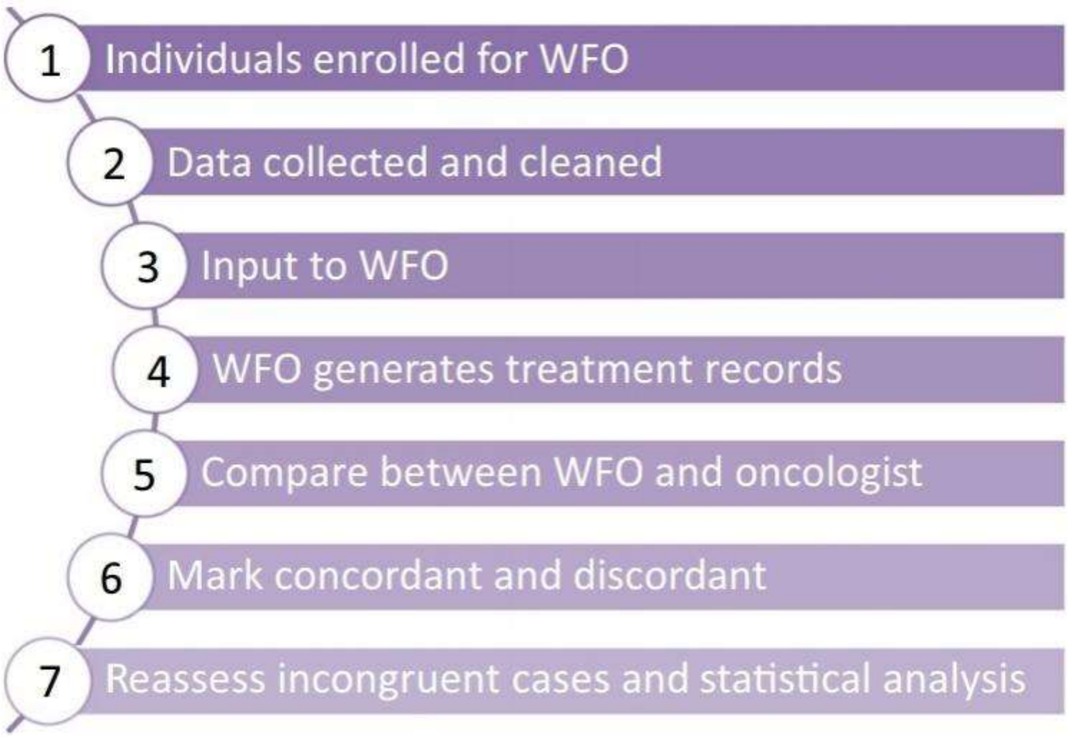
Ichimasa et al. (2018)	SVM	Prediction of lymph node metastasis post endoscopic resection of T1 colorectal cancer	100%	66%	–	69%
Nakajima et al. (2020)	CNN	Automatic diagnosis system by computer-aided diagnosis (CAD) based on plain endoscopic images	81%	87%	0.888	84%
Lai et al. (2021)	DNN	Improve polyp detection and discrimination by CAD	100%	100%	–	74–95%
Yamada et al. (2019)	CNN	Develop a real-time detection system for colorectal neoplasm	97.3%	99%	0.975	Good and excellent*
Chen et al. (2019)	DNN	Develop a CAD diagnosis system to analyze narrow-bind images	96.3%	78.1%	–	90.1
Repici et al. (2020)	CNN	To assess the safety and efficacy of a computer-aided detection (CADe) system	–	–	–	–
Kudo et al. (2020)	CNN	To determine diagnostic accuracy of EndoBRAIN	96.9%	100%	–	98%
Mori et al. (2018)	SVM	Evaluate the performance of real-time CADe with endocytoscope	91.3–95.2%	65.6–95.9%	–	–
Nguyen et al. (2020)	CNN	To pre-classify the in vivo endoscopic images	19.6–87.4%	42.5–90.6%	–	52.6–68.9%
Deding et al. (2020)	–	To investigate relative sensitivity of colon capsule endoscopies compared with computer tomography colongraphy	2.67[#]	–	–	–

SVM: support vector machines; CNN: convolutional neural network; DNN: deep neural network; AUC: area under the curve from the receiver operating characteristics; *shown using intersection over the union (IOU); [#]relative sensitivity

AI technology in medical imaging, such as endoscopy and CT/MRI, is not yet fully optimized for complete implementation. Human technicians remain essential for interpreting images accurately (Tajbakhsh et al., 2016). Pesapane et al. emphasize that machines are unlikely to replace radiologists entirely but highlight the importance of collaboration between radiologists and computer scientists to create better diagnostic tools, even if it reduces job opportunities in the field (Tajbakhsh et al., 2016). Lundervold et al. note that computational medicine is becoming a permanent part of healthcare, underscoring its integration into mainstream practices (Ribeiro et al., 2016).One area of focus is improving colonoscopy through AI, particularly in detecting polyps. This involves enhancing computer learning to better recognize shapes and boundaries, suggesting that refining existing technologies is more practical than developing new ones from scratch (Ali et al., 2020; Misawa et al., 2018; Borkowski et al., 2019; Marley and Nan, 2016).However, challenges remain in using convolutional neural networks (CNNs) for image and object recognition. These include:Image distortions caused by pixel abnormalities or poor-quality images.Variability in anatomy among individuals, which can lead to misinterpretations.Differences in patient positioning or anatomy affecting image accuracy.Difficulty in distinguishing relevant details from artifacts, such as bubbles or gases, that do not affect diagnosis (e.g., neoplasia)

Role of AI in surgery
AI is showing great promise in the field of surgery. Ichimasa et al. found that AI significantly reduced the need for unnecessary additional surgeries following endoscopic resection of T1 colorectal cancer (CRC) compared to clinical guidelines in the U.S. (NCCN), Europe (ESMO), and Japan (JSCCR). This was achieved using a support vector machine (SVM) for supervised machine learning, which helped identify patients who truly required further surgical intervention (Ichimasa et al., 2018 In another development, Meng et al. conducted a multicenter diagnostic study using AI to analyze early-stage CRC. This study involved 4,390 images of intraepithelial neoplasm, achieving an impressive diagnostic accuracy of 0.963 in the internal validation set (Kalis et al., 2018)
Typical fow diagram of WFO procedure

In terms of both sensitivity and specificity. Additionally, the authors stated that this approach is reliable for the early and effective prevention of colorectal cancer (CRC) (Kalis et al., 2018).



CURRENT CHALLENGES AND FUTURE PERSPECTIVES

AI great potential to improve cancer care and research, with high accuracy in laboratory settings that could transform traditional practices has in cancer diagnosis and treatment. However, the key question is when AI can be fully integrated into clinical settings for regular use by doctors and patients.

AI relies on data, and for it to work effectively in healthcare, the data must represent the entire population. It's clear that race, gender, and socioeconomic factors impact cancer risk and outcomes. For example, studies show that certain cancers, like prostate cancer, have race-specific differences in how they develop and progress. However, most datasets used to train AI models in cancer care are biased, often underrepresenting minority groups. The largest cancer dataset, TCGA, is mainly composed of white individuals, and many datasets lack diverse data, especially for metastatic cancers.Another challenge is that current cell lines used in cancer research do not perfectly match real-world patient profiles because they can change genetically over time. Newer, more stable models like patient-derived organoids could help fill this gap. Additionally, while data sharing is important for AI model development, access to data across platforms is still limited, especially for private or restricted datasets. As more inclusive and accessible datasets emerge, these challenges can be addressed.Another key issue is ensuring that AI models are transparent and reproducible. Sharing the code behind these models and explaining themethods used would help others validate and apply them. While code sharing is becoming more common, it’s not yet universally adopted. High-profile journals are starting to require code submissions, which is a step in the right direction.

AI models often focus on image and omics data, but another valuable resource is electronic health records (EHRs), which contain rich patient history. However, EHRs are often unstructured and messy, requiring cleaning and standardization. Efforts are underway to improve how EHRs are organized and analyzed, making them more useful for AI predictions.

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For AI to be widely accepted in the clinic, clinicians need to trust AI's decision-making. One way to build this trust is by measuring and communicating the uncertainty in AI predictions. Uncertainty can arise from issues like data quality, biases, or model errors. Ongoing research is working on ways to quantify and address these uncertainties, which will improve AI models and help integrate them into clinical practice.

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