

Role of Artificial Intelligence in High Throughput Diagnostics for Colorectal Cancer: Current Updates

Pankaj Kumar Tripathi and Chakresh Kumar Jain*

*Department of Biotechnology, Jaypee Institute of Information Technology,
A-10, Sector-62 Noida-201 309, Uttar Pradesh, India*

**Email: ckj522@yahoo.com*

ABSTRACT

The existence of cancer has been stated as a century's oldest challenge for the entire human race around the globe recording a large amount of mortality per year and as per the WHO data nearly 10 million deaths were reported in 2021 worldwide besides others. Colorectal cancer is considered a major threat as this is cancer-related to the colon and rectum with an incidence of 41/1,00,000 recorded annually to overcome this challenge our medical system requires more advanced, accurate and efficient high throughput techniques for the prognosis and effective treatment of this disease. Artificial intelligence's role in healthcare has been a matter of discussion among experts over the past few years, but more recently the spotlight has focused more specifically on the role that this technology can play in improving patient outcomes and improving the effectiveness of diagnosis and treatment processes. Artificial intelligence refers to a broad category of technologies, including machine learning, natural language processing and deep learning. Exploration of Molecular pathways with characteristics that helps in subtyping of Colorectal Cancer (CRC) leading to specific treatment response or prognosis, for the effective treatment, classification and early detection done using Artificial Intelligence based technologies have shown promising results so far, that it may be utilized to create prediction models in the current environment to distinguish between polyps, metastases, or normal cells in addition to early detection and effective cancer therapy. Nowadays many scientists are putting effort into designing such fabricating models by combining natural language processes and deep learning that can differentiate between non-adenomatous and adenomatous polyps to identify hyper-mutated tumours, genetic mutations and molecular pathways known as IDaRS strategy or iterative draw-and-rank sampling. The review study primarily focuses on the significance of emerging AI-based approaches for the diagnosis, detection, and prognosis of colorectal cancer in light of existing obstacles.

Keywords: Colorectal Cancer; Artificial Intelligence; High throughput; Natural Language Process

NOMENCLATURE

CRC	Colorectal cancer
AI	Artificial Intelligence
DL	Deep Learning
ML	Machine Learning
NLP	Natural Language Processing
HMMs	Hidden Markov Models
CNN	Convolutional Neural Network
ADR	Adenoma Detection Rate
CAD	Computer-Aided Diagnosis
N/A	Not Available/not mentioned by Author

1. INTRODUCTION

The uncontrolled growth of abnormal cells that destroys the human tissues causing hindrance in the body's normal functioning and control mechanism is termed cancer, resulting due to the inability of old cells

to die wherein they grow infinite in number without a regulating mechanism thus forming the mass of cells known as "Tumor". In the present scenario, one of the six deaths is due to cancer as per WHO 2021 thus, new treatments and controlled measures are need of the hour for early detection and prevention of this devastating disease. The emergence of Cancer has been linked to various factors like alcohol and tobacco consumption, low intake of fruit and vegetable, less physical activity and increased body mass index (BMI) along with high mental & physical stress. Hence, such factors induce hindrance in the normal cell division process by DNA mutations that inhibit the apoptosis phenomena in cells that can by no means be corrected by DNA damage and repair mechanisms resulting in cancer development and tumour formation.¹ The greatest challenge in the prevention of this disease is its late and non-accurate detection, as in most of the cases cancer is detected in an advanced stage where it nearly becomes impossible to cure, therefore to deal with this major problem there are certain early detection strategies used by many scientists such as Prostate and Cervical Cancer early detection might

be possible by routine tests as described by Loomans-Kropp², Skin Cancer tests by dermatologists if chances of risk of skin cancer, Lung Cancer people with the risk factors to be screened regularly, Colorectal Cancer can be detected by regular testing after the age of 45 with at-home kits or in the labs and Breast Cancer detection may be possible by mammograms for above the age of 45.³

Besides these strategies, there is a new breakthrough in modern technology known as Artificial Intelligence that is gaining popularity worldwide for its early detection mechanism for all forms of cancer^{4,5}. When people run a programme or code a computer, an algorithm or model is the code that instructs the machine on how to act, think, and learn. AI refers to a machine that performs activities often associated with human intelligence. The major topic of this article is the application of AI to cancer diagnosis.

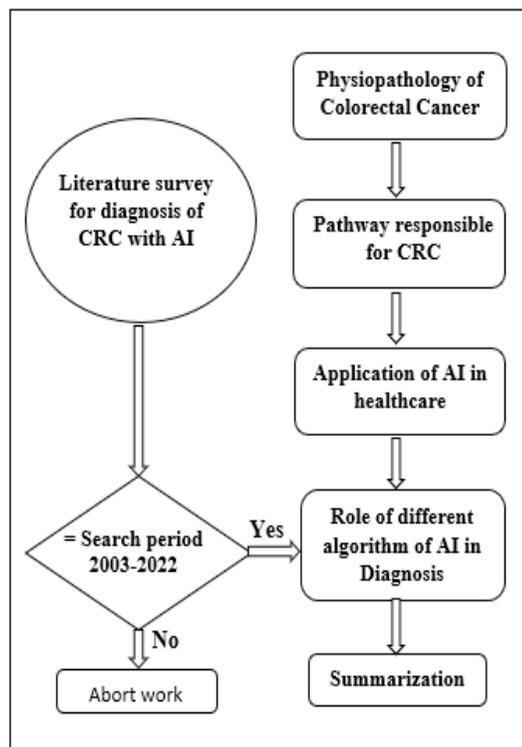


Figure 1. Schematic representation

2. COLORECTAL CANCER

The fourth most frequent type of cancer is colorectal cancer and the third is death around the world its initiation is recorded due to an unwanted growth in the lining of the rectum or colon resulting in a tumour and this growth is considered either genetic or environmental along with the presence of risk factors. If left untreated, polyps that grow in the lining of the colon or rectum as our body ages might eventually lead to colorectal cancer. The early stage of colorectal cancer begins as non-cancerous polyps that are usually critical for detection and the precancerous polyp surgery or removal identified by colonoscopy help in CRC prevention.⁶

2.1 Colorectal Cancer's molecular pathways

Worthley and Leggett⁷ portrayed three molecular pathways mainly the instability of the pure microsatellite pathway, the pathway of CpG island phenotype of methylator and the instability of chromosome instability pathway. CRC progression, growth and diversity are described based on molecular pathways, Pino and Chung⁸ *et al.*, explain the chromosomal instability (CIN) pathway as it is related to lower rates without progression in CRC2 while microsatellite instability (MSI) would classify the patients responding to immunotherapy was reported by Liu⁹ *et.al.*; and Singh¹⁰ *et al.*, Kather¹¹ *et.al.* (2019) delineated classification based on MSI7 and CpG island methylator subgroups phenotype (CIMP) as per the adjuvant therapy and survival responses. Moreno¹² *et al.*, reported molecular pathways and characteristics helps in the subtyping of CRC leading to specific treatments response or prognosis. FDA¹³ approved Pembrolizumab drug for the patients as treatment of the first line associated with mismatch repair deficient (dMMR) or MSI colorectal cancer.

Grady¹⁴ *et al.*, had shown that near about 70-85 percent of CRCs develop via the CIN pathway due to chromosomal aberrations which can be identified by the lesion i.e. the dysplastic aberrant crypt focus (ACF) as reported by Freeman⁶⁹ *et al.* Boland¹⁵ *et al.*, characterized DNA repeat or microsatellite regions in germ line versus tumour as mismatch repair (MMR) results in dysfunction in MSI. Issa J.P.¹⁶, *et al.*, CIMP is important to detect the sporadic cases of CRC as it endows the epigenetic instability essential to methylate the promoter region in sporadic cancer therefore epigenetically inactivation is key to express the suppressor tumour gene e.g. MLH1.

2.2 CRC Precursor, Polyp Development and Artificial Intelligence

These pathways have characteristic features as pathological precursors that are clinically employed for diagnosis or prognosis where today with artificial intelligence systems scientists have developed models with precision and accuracy for the identification of the stage of cancer, effective treatment etc.

Grady¹⁴ and Whitehall¹⁷ *et al.*, studied adenomatous polyps as pathological symptom progression starting from very early-stage to advance the findings of adenocarcinoma precursors to CIN pathway and serrated polyps for the CIMP pathway and thus leading to a knowledge of the pathological sequence of developing serrated neoplasia. The sawtooth look on their crypt lumina or columns is due to a defect in apoptosis as shown by these polyps leading to increased signalling of RAS-RAF-MEK-ERK to build colonocytes as sawtooth and forms the basis for stage identification by AI methods.

Tiwari¹⁸ *et al.*, further explained that the adenomatous polyps or cells are identified with metastasis due to uncontrolled cell division and argued that pathways can be used for early detection or prognosis or treatment with good drug delivery systems. The researchers portrayed

that the target pathways for CRC therapy, diagnosis and prognosis have led to the developed algorithms for better accuracy. The genetic markers like transforming growth factor- β (TGF- β)/SMAD, Sonic Hedgehog (SHH), Wnt/ β -catenin, Notch pathways and EGFR have designed new models for detection and therapy^{19, 20}.

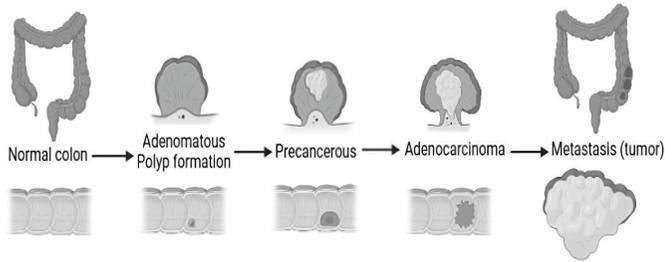


Figure 2. The graphical presentation of CRC's pathophysiology reveals its complexity, which entails several stages and processes of transforming a healthy colon into a tumor colon. Comprehending the process of transformation can be beneficial in the prompt detection and treatment of CRC. The illustration was produced utilizing the BioRender.com platform.

3. TARGET AND GENETIC THERAPY AND IMMUNOTHERAPY

Targeted gene therapies, which rely on uncommon cutting endonucleases to cleave at precise near to disease-causing genes, have emerged as promising treatments for several embryonic disorders. While immunotherapy has clinical potential in CRC and success depends on the AI model, targeted gene correction offers a template for homology-directed repair, enabling the cell's own repair pathways to delete the mutation and replace it with the right sequence to trigger the immune response. Similarly, Nanotechnology colon-specific drug delivery would improve pharmacotherapy with fewer side effects by using a deep learning algorithm, furthermore; unique and amazing nanomaterials with both diagnostic and therapeutic potential may be found in nanotechnology²¹. Materials like silica nanoparticles, gold nanoparticles, liposomes, dendrimers, carbon nanotubes, etc. are used very frequently in detecting CRC with precise accuracy²².

4. ARTIFICIAL INTELLIGENCE

With an in-depth understanding of molecular mechanisms and therapies, the researchers initiated artificial intelligence-based models to be used in the treatment and detection of CRC for prevention and better accuracy. Davenport²³ *et al.*, described the artificial intelligence potentiality in healthcare systems and its applications. Lee²⁴ *et al.* reported that traditional machine learning led to precision medicine to predict patient-based protocols of treatment and characteristics that need large datasets related to diseases like onset etc. is known as supervised learning. Sordo²⁵ reported neural network—complex machine learning is being used since 1960 to determine the probability of the patient suffering from a particular disease. The

neural network has been designed in the same way as the neuron signal process of the brain. Fakoor²¹ *et al.*, and Vial²⁶ *et al.*, delineated a recent deep learning model of machine learning with variable levels and fast processing based on cloud architecture that is being used to recognize cancerous lesions by radiological images along with the prediction of clinically relevant symptoms. Bohr²⁷ *et al.*, outlined the following transformational changes in healthcare by artificial intelligence such as the Brain-computer interface which unifies the machine and mind, employed in the machine and medical devices, development of Immunotherapy employed in cancer therapy, performs better the pathological images analysis, prediction of risk based on electronic health record, development of personal devices and wearable help to monitor health, designing for a powerful diagnostic tool through selfies from smartphone and used to reduce the usage of electronic health record burden usage.

AI is an operational model to upgrade the medical data information for epidemiological studies as the predictive value has practical value in the technology²⁸. AI applications are verified in safety and public health in order to manage malignant diseases e.g. cancer (Fig. 2).

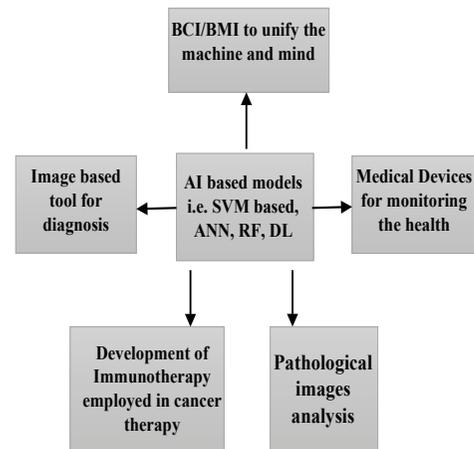


Figure 3. Application of artificial intelligence in healthcare

4.1 Artificial Intelligence as Diagnostic Tool

Restini²⁹ *et al.*, considered AI-supporting systems personalized and novel strategies AI to control colorectal cancer (CRC) management.

4.1.1 Diagnosis

Diagnosis is defined as the integration of different data with analysis, clinical symptoms, faster disease progression, reactions and drug susceptibility detection as per individual patient for the accurate diagnosis of the disease by AI qualitative methods. These methods have created a path for clinicians to the easier and more accurate diagnosis of cancer or CRC.³⁰ AI would lead to better in-sight comprehension of the diseases to facilitate the management for better detection of cancer thus treating the patients with precision and accuracy³¹ similarly, medical imaging has been improved with the techniques with more capability to visualize and interpret

images fast and good quality extraction by employing 3D technology.^{32, 33}

5. ARTIFICIAL INTELLIGENCE-BASED TECHNIQUES

5.1 Colonoscopy

Colorectal cancer (CRC) can be best detected at the early stage by the identification of polyps and the removal enhances the patient’s rate of survival. Colonoscopy is a method to study Artificial Intelligence (AI) applied in colonoscopy as the medical diagnostic tool to detect polyps and assess high-risk CRC patients’ CRC. Different studies have improved the adenoma detection rate (ADR).³⁴ The authors argued that AI and colonoscopy combination would improve the diagnostic accuracy and survival rate.

5.2 Virtual Colonoscopy

Vining³⁵ *et al.* delineated a modified computed tomography (CT) examination known as computed tomographic colonography (CTC) or Virtual colonoscopy representing an alternative screening tool. Song⁶⁸ *et al.* presented computer and AI algorithms-based techniques i.e. Haralick texture analysis method for the pathological virtual screening to depict high-range differentiation along with curvature and gradient. AI-based methods are preferred as they are faster, accurate thus reduce human error as reported by Vidal³⁶ *et al.*, and Hosoe³⁷ *et al.*

5.3 Natural languages Process

Natural Language Processing (NLP) –data-driven concepts integrated with machine learning and Hidden Markov Models (HMMs) help to identify the patterns and numerical values.³⁸ The study conducted by Mehrotra³⁹ *et al.*, used NLP for the analysis of the reports of pathology and examinations of colonoscopy with an objective to predict ADR basis.

5.4 Convolutional Neural Network and Deep Learning

Urban⁴⁰ *et al.* implemented CNN architectures in order to increase the ADR and the result exhibited the models with polyp and random images of the polyps detection with 96.4 percent accuracy and 96.9 percent (5 percent FPR) sensitivity. Komeda⁴¹ *et al.* in the system of CNN for polyps in the colon to distinguish between adenomatous and non-adenomatous polyps accurately i.e. 70 percent. Byrne⁴² *et al.* also reported the CNN system to recognize polyps with 98 percent sensitivity, 83 percent specificity and 94 percent accuracy. Parikesit³⁴ *et al.*, proved deep learning types advantages in improved medical diagnosis to know AI algorithms principles applied in colonoscopy for CRC and Table 1 exhibits the studies conducted by using CNN or natural language (Table 1).

5.5 Machine Learning Algorithm: Colon Flag

Hilsden⁴³ *et al.* studied Colon Flags to predict the adenomatous polyps based on machine learning. The model pinpointed CRC-risk individuals depending on

Table 1. Review summary (Stefanus and Parikesit³⁴)

References	Algorithms	Sets of Data	Applications	Accurately	Sensitive	Description
Hilsden <i>et al.</i> , 2018	ML	Colonoscopy results and related pathology findings	Identify the likelihood of polyps at a colonoscopy	N/A	N/A	Individual model identification with CRC high-risk specificity 95%
Mehrotra <i>et al.</i> , 2018	NLP	Colonoscopies and associated pathology reports	Describe the medical practitioners associated with high ADR.	87–99%	N/A	NLP identified female doctors and well-trained doctors as having a greater ADR rate.
Urban <i>et al.</i> , 2018	CNN	8,641 manually tagged photos taken from 2,000 patients	Adenomas and polyps are identified	96.4%	96.9% (5%FPR) and 88.1% (1%FPR)	All polyps were recognized by pre-trained models, and further polyps were overlooked during the review
Komeda <i>et al.</i> , 2019	CNN	1,200 colonoscopy images	Identification of adenomas or polyps	70%	N/A	On seven out of ten occasions, the model’s conclusions are accurate.

Byrne <i>et al.</i> , 2017	CNN	Colonoscopy video	Identification of adenomas or polyps	94%	98%	The model's accuracy was 94%, while its sensitivity and specificity were both 98% and 83%.
Wang <i>et al.</i> , 2019	CNN	Colonoscopy video	Identification of adenomas or polyps	N/A	94.38%	Comparing a CAD system to a standard colonoscopy, the ADR increased to 29.1% and more polyps were found.
Krenzer, A.; <i>et al.</i> , 2021	ML	Colonic images	Classification of polyps based on features such as shape, color, texture, etc. Detection of polyps in medical imaging.	92.4%	90.1%	A type of artificial intelligence that uses statistical techniques to enable computer systems to learn and improve from experience without being explicitly programmed.
Wang S., <i>et al.</i> , 2021	CNN	Pathological images	Detection and classification of polyps in medical imaging. Feature extraction and selection for polyp recognition	97.5%	95.2%	A type of deep learning neural network that uses multiple layers to extract and learn features from images
Lee J.Y., <i>et al.</i> , 2020	NLP	screening colonoscopy report	Analysis of medical reports to identify polyps. Extraction of relevant features from clinical notes	95.9%	92.1%	A field of artificial intelligence that focuses on the interaction between computers and human language

age, gender, colonoscopy etc. and unscreened persons with a high risk of CRC with an objective for greater compliance with conventional screening.⁴

5.6 Limitations

Machine learning methodologies are useful but have many drawbacks too as stated in (Table 2).

6. AI PROSPECT

AI models have become an integral part of colonoscopy for the prevention of CRC and have promising prospects in near future, some of their important applications are an advanced approach that can help to classify the image and categorize polyps types thus improving the rate of survival and accuracy of diagnosis of the CRC patients, these polyps can be successfully detected by CNN and AI to ensures that all the polyps are removed completely from the lining and leaving no aspect for the reoccurrence of CRC. Machine learning can easily depicts high-risk patients and NLP for high ADR. According to Min⁴⁴ *et al.* AI assists in the diagnosis, examination or treatment of CRC but the systemic approach and research are still missing and further added in the future AI will be employed for therapy and diagnosis of CRC.

6.1 CRC Prediction in Tumours Grouped into Different Stages with AI

Bilal⁴⁵ *et al.* specified that CRC clinical stage is important to exactly know the spread of the disease and MSI status sideways helps to choose the adjuvant immunotherapy or chemotherapy treatment. Immunotherapy is the best option at the first stage of MSI and chemotherapy at stage IV MSI as identified by Sun⁴⁶. Further, he characterized the patients at the third stage who had more chances for survival with adjuvant chemotherapy. Bilal⁴⁵ *et al.* designed a model for fast prediction of slides in order to identify hyper-mutated tumours, genetic mutations and molecular pathways known as an IDaRS strategy i.e., iterative draw-and-rank sampling. The researchers claimed that the state-of-the-art methodology predicts automatically the pathway's sub-types (MSI, HM, CIMP and CIN) and mutations like TP53 and BRAF. Deep learning and molecular network model to distinguish between necrosis and inflammatory proportion in the mesenchyme and neoplastic cells as high percentage indicated high CIMP thus can respond better to immunotherapy, on the other hand, increased necrotic, mesenchyme and neoplastic cells lead to low patient outcome due to CIN phenotype i.e. linked with low progression and survival. IRS helps

Table 2. Limitation of Each Study (Bernard and Parikesit³⁴)

References	Algorithm	Application	Limitations
Hilsden <i>et al.</i> , 2018	ML	Identify the likelihood of polyps at a colonoscopy	A thorough description of sessile serrated polyps and specific details on the person’s history of CRC
Mehrotra <i>et al.</i> , 2018	NLP	Describe the medical practitioners with high ADR.	Medical professionals who participated in the study are not permitted to speak for all medical professionals.
Urban <i>et al.</i> ,2018	CNN	Identification of adenomas or polyps	The way CNN performs may differ depending on the indication (screening vs surveillance)
Komeda <i>et al.</i> , 2019	CNN	Identification of adenomas or polyps	The CNN- CAD’s system diagnostic accuracy is deemed unacceptable.
Byrne <i>et al.</i> ,2017	CNN	Identification of adenomas or polyps	Owing to the use of video footage, the determination has low confidence.
Wang <i>et al.</i> ,2019	CNN	Identification of adenomas or polyps	It is difficult to determine the system’s precise contribution.
Krenzer, A.; <i>et al.</i> , 2021	ML	Detection of polyps in medical imaging	May suffer from overfitting or under-fitting. May not be able to generalize well to new datasets.
Glissen Brown, J. R, 2022	CNN	Detection and classification of polyps in medical imaging.	Require large amounts of labeled data for training. Computationally intensive, requiring high-performance computing resources.
Wang S. <i>et al.</i> , 2021	CNN	Feature extraction and selection for polyp recognition	Sensitive to variations in image quality and resolution
Lee J.Y., <i>et al.</i> 2020	NLP	Analysis of medical reports to identify polyps. Extraction of relevant features from clinical notes	May be limited by the quality and completeness of medical records. Require significant pre-processing and cleaning of text data and understanding as well as interpreting medical jargon.

to identify histological characteristics and quantitative analyses also of CRC at pathways of the cellular level.

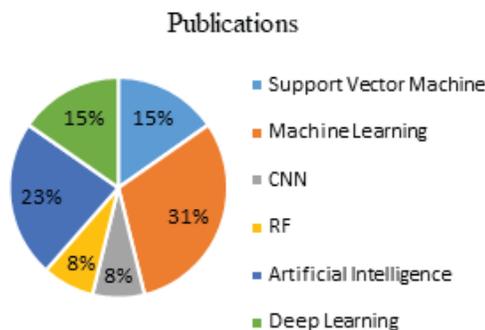


Figure 4. Frequency of different soft-computing methods used in colorectal cancer diagnosis.

Literature mining was performed from the year 2003-2022 which reveals the significant usage of ML-based methods toward the investigation of colorectal diagnosis, followed by AI, Deep Learning, SVM, Random Forest and CNN methods. This demonstrates the higher use of ML methods and their significance and opens new avenues for CNN/Deep learning-based approaches in future research (Fig. 2).

6.2 Diagnosis of CRC with AI

AI aids doctors in staging and qualitative diagnosis of colon cancer relying on pathological biopsy and colonoscopy and it can be identified by colonoscopy i.e. visualization of lesions images and biopsy for grading and diagnosis of CRC.⁴⁷ Acs⁴⁸ *et al.*, deduced novel colorectal cancer detection (CCD) model based on an SVM functional algorithm to classify malignant and biopsy images which would automatically perform grading. Deep learning and convolutional network system method were designed by Eycke⁴⁹ *et al.* for the annotation of histological epithelial glandular images.

6.3 Clinic Pathology Feature Analysis

Brenner⁵⁰ *et al.* applied AI to identify the cases from adenoma to carcinoma and stated that reduced incidence may result from early screening. Ito⁵¹ *et al.* depicted an endoscopic system built on a CNN using machine-learning pictures for the diagnosis of colon cancer. Song⁵² *et al.* combined machine learning with Fourier transform infrared technology to classify CRC patients into different periods with an accuracy of 90 percent or more. Kainz⁵³ *et al.* designed a gland segment

method established on neural network and deep learning for CRC grading diagnosis i.e. benign and malignant.

6.4 AI and Non-coding RNAs (ncRNAs) Diagnosis

ncRNAs are potential in diagnosis and treatment as it is being researched and advanced computational detection methodology is needed for ncRNA's role in tumour genesis but AI is acting as a bridge to associate tumour and ncRNAs.⁵⁴ Chang⁵⁵ *et al.* visualized the microRNA (miRNA) expression profile of the normal and stage II CRC cells and tissues. The authors fabricated an ANN algorithm and found three miRNAs (miR-31, miR-139-5p, and miR-17-92) to find the status or stage of tumour or CRC, Amirhah⁵⁶ *et al.* a miRNA-associated tumour prediction method to reveal interactions network between miRNA and target mRNA.

6.5 Deep Neural Network Platform for Rectal Cancer

Wu⁵⁷ *et al.* reported that the patient's treatment is done by preoperative staging accuracy and magnetic resonance imaging (MRI) plays an essential part in postoperative patients with rectal cancer. AI with recognition by MRI forms a static image platform analysis along with recognition and the authors in their study established a diagnostic automatic platform to predict rectal cancer before operation T-stage by using deep neural network technique. An objective and faster method i.e., Faster R-CNN AI has been constructed to identify T-staging of rectal cancer which is essential for the selection of treatment. In order to find the prognosis and treatment condition, the postoperative diagnosis is the gold standard. AI technology and deep learning have established a system of automated T-staging for the diagnosis of rectal cancer in large numbers. The automatic diagnosis system accuracy was assessed and confirmed by employing verification group data to find the practicability for clinical uses. The authors summarized the features of an automatic diagnostic platform in the combination of AI, engineering and medicine to develop an auxiliary tool for pathological identification with higher accuracy. Novel computational AI application /model to strengthen the computational technology in image analysis with accuracy and fast in order to serve as examination platforms for clinical treatment.

Wang⁵⁸ *et al.* formulated a procedure for the classification of histo-pathological images for the diagnosis of CRC with deep learning and AI algorithms. The method gave quick and accurate even for the large sample size from different clinics, healthy or CRC inflammatory patients. To date, this method of AI is thought to be a valid, robust and additional tool for initial CRC screening.

7. CRC SURGERY

Surgery is the best option for CRC but some complications can result in surgery like perforation or obstructions as reported by Boselli⁵⁹ *et al.* and Yang⁶⁰ *et al.* investigated the robot's security along with laparoscopic surgery to

protect the pelvic autonomic nerve and reported robot-assisted colorectal surgery provides protection for short and long term.

7.1 CRC Chemotherapy

Felfoul⁶¹ *et al.* researched the Nami robot for drug delivery and found that it targets cancer cells precisely by detecting the cells with reduced oxygen levels due to cell proliferation and the drug reaches hypoxic regions. Cruz⁶² *et al.* analyzed molecular and nuclear magnetic resonance to determine the IC50, or half-maximal inhibitory concentration, of a newly developed medication that targets the colon cancer cell line.

7.2 Personalization and Precision of CRC

Watson for Oncology (WFO) was developed by International Business Machines Corporation or AI system for the precision treatment of cancer as it automatically extracts the characters and then is translated them into practical language. Keshava⁶³ *et al.* fabricated an AI model to classify the patient population based on differential inhibitor reaction to visualize the resistance mechanism and pathway and even the genetic biomarkers can be analyzed. Metabolomics and AI also delineate drugs that are targeting cancer metabolism. Nowak⁶⁴ *et al.* carried out research intending to repurpose the drugs as per new indicators as they merged phenotypic study results with chemical genetics, mechanistic studies and Omics to design AI models for the prediction of disease-drug pairs. AI and CRC application visualizes that the big data would lead to diversified and personalized CRC treatment thus decipher more humanistic and accurate medical services.

7.3 Current Status of Precision Oncology in Colorectal Cancer

National Research Council (US) in 2011 stated that innate tumour differences have resulted in a new fast-developing domain of precision medicine which has transposed the present translational medicine prototype to personalize and target cures thus assisting medical professionals to manage decisions for better results. This strategy is based on individual patient genetic make-up, lifestyle or environment therefore more precise and accurate treatment can be ascribed for CRC. The genetically altered cancer gene-based treatment which plays a role in drug responses and precision oncology defines increased effective target therapies with a new hope for stratified therapeutic strategies.

Keshava⁶³, *et al.* formulated algorithms based on machine learning to uncover subpopulations i.e., patient-specific which respond differently to the target drugs etc. inhibitors thus endowing in-depth interpretation of resistance pathway and this new model for subpopulations of cancer would help to identify their drug combinations and biomarkers with more efficacy.

Recently researchers have utilized machine learning techniques along with specific phenotypic and mechanistic

studies, Omics and chemical genetics assays to envisage pairs of drug-disease with an aim of redefining present drugs for the treatment of CRC.⁶⁴ The preoperative data were collected by Horta⁶⁵ *et al.* to represent a predictive model for the clinical decisions of the post-operative patients and to manage among the surgeons and internists of some selected patients.

8. CONCLUSION AND FUTURE PROSPECTS OF AI

AI research and advancements have evolved CRC treatment and diagnosis methodology that is used at a molecular level for effective and precise identification in prognosis and diagnostics based on image analysis of pathological images of colorectal tumours consequently leading to better treatment. Further, this could also be recommended for personalized and precision medicine in CRA and with technological breakthrough, a lot of success has been recorded in CRC diagnostic although, the precise treatment and early detection is yet to be addressed.

Today AI is playing important in CRC therapy and has developed as a fertile ground for medical personnel. AI requires expert people as it raised limitations for its application like no proper gold standards and guidelines. Adamson and Welch⁶⁶ said that AI focus input data and other information about the patient is lacking thus reducing the reliability. Secondly, image signal strength stratification limits the accuracy of the diagnosis of CRC. Privacy issues arise due to internet-equipped methodology for detection etc. Lovis⁶⁷ suggested formulation to preserve the information for large data-driven models or genomic phenotypic data for analysis.

The combination of CRC screening, treatment and diagnosis by applying AI would enhance the prognosis and clinical results also of CRC patients. Deep learning models are being used for research in cancer and the main challenge is to develop the best therapy that would decipher novel or alternate options for therapeutic CRC. The review paper proposes to understand the opportunities of AI-based models for CRC screening, patient care and diagnosis. AI models are valuable tools to transform the future of precision oncology as the computer-aided systems would endow physicians to diagnose and detect precancer growth thus for the evaluation of the accuracy of diagnostic clinical trials at different clinics more AI algorithms are needed. From the review paper, it can be concluded that the amalgamation of AI models for diagnosis, screening or prognosis of CRC would increase better outcomes.

The precision of oncology and healthcare has been remodeled with AI usage and to endow computer-based systems to diagnose and detect CRC or lesions at an early stage. New algorithms based on machine learning or AI have given exceptional results for the characterization and detection of the lesions leading to cancer. The advancements in medical technologies or digital technologies have shifted the paradigm of treatments from chemotherapy to

immunotherapy and biological targets along with diagnosis to artificial intelligence tools. The use of biologics such as cytokines, vaccines or antibodies helps the patient to fight against the disease. The new screening techniques combined with innovative cure measures have resulted in better recovery and can reduce the incidence.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

REFERENCES

1. Cairns, J. Mutation and Cancer: The Antecedents to Our Studies of Adaptive Mutation. *Genetics* 1998, **148**(4), 1433–1440. doi:/10.1093/genetics/148.4.1433.
2. Loomans-Kropp, H. A. & Umar, A. Cancer Prevention and Screening: The next Step in the Era of Precision Medicine. *NPJ Precis. Oncol.* 2019, **3**(3). doi:/10.1038/s41698-018-0075-9.
3. Kelly, K. M.; Dean, J.; Lee, S.-J. & Comulada, W. S. Breast Cancer Detection: Radiologists' Performance Using Mammography with and without Automated Whole-Breast Ultrasound. *Eur. Radiol.* 2010, **20**(11), 2557–2564. doi:/10.1007/s00330-010-1844-1.
4. McCorduck, P. *Machines Who Think: A Personal Inquiry into the History and Prospects of Artificial Intelligence*, 2nd ed.; A K Peters: Natick, MA, 2004.
5. Majumder, A. & Sen, D. Artificial Intelligence in Cancer Diagnostics and Therapy: Current Perspectives. *Indian J. Cancer* 2021, **58**(4), 481–492. doi:/10.4103/ijc.IJC_399_20.
6. Parkin, D.M.; Bray, F.; Ferlay, J. & Pisani, P. Global Cancer Statistics, 2002. *CA Cancer J. Clin.* 2005, **55** (2), 74–108. doi:/10.3322/canjclin.55.2.74.
7. Worthley, D.L. & Leggett, B.A. Colorectal Cancer: Molecular Features and Clinical Opportunities. *Clin. Biochem. Rev.* 2010, **31**(2), 31–38.
8. Pino, M.S. & Chung, D.C. The Chromosomal Instability Pathway in Colon Cancer. *Gastroenterology* 2010, **138**(6), 2059–2072. doi:/10.1053/j.gastro.2009.12.065.
9. Liu, J.; Pan, Y.; Li, M.; Chen, Z.; Tang, L.; Lu, C. & Wang, J. Applications of Deep Learning to MRI Images: A Survey. *Big Data Min. Anal.* 2018, **1**(1), 1–18. doi:/10.26599/bdma.2018.9020001.
10. Singh, M. P.; Rai, S.; Pandey, A.; Singh, N.K. & Srivastava, S. Molecular Subtypes of Colorectal Cancer: An Emerging Therapeutic Opportunity for Personalized Medicine. *Genes Dis.* 2019. doi:/10.1016/j.gendis.2019.10.013.
11. Kather, J.N.; Pearson, A.T.; Halama, N.; Jäger, D.; Krause, J.; Loosen, S.H.; Marx, A.; Boor, P.; Tacke, F.; Neumann, U.P.; Grabsch, H.I.; Yoshikawa, T.; Brenner, H.; Chang-Claude, J.; Hoffmeister, M.;

- Trautwein, C. & Luedde, T. Deep Learning Can Predict Microsatellite Instability Directly from Histology in Gastrointestinal Cancer. *Nat. Med.* 2019, **25**(7), 1054–1056. doi:/10.1038/s41591-019-0462-y.
12. Moreno, V. & Sanz-Pamplona, R. Altered Pathways and Colorectal Cancer Prognosis. *BMC Med.* 2015, **13**(1). doi:/10.1186/s12916-015-0307-6.
 13. Casak, S.J.; Marcus, L.; Fashoyin-Aje, L.; Mushti, S.L.; Cheng, J.; Shen, Y.L.; Pierce, W.F.; Her, L.; Goldberg, K.B.; Theoret, M.R.; Kluetz, P.G.; Pazdur, R. & Lemery, S.J. FDA Approval Summary: Pembrolizumab for the First-Line Treatment of Patients with MSI-H/DMMR Advanced Unresectable or Metastatic Colorectal Carcinoma. *Clin. Cancer Res.* 2021, **27** (17), 4680–4684. doi:/10.1158/1078-0432.ccr-21-0557.
 14. Grady, W.M. & Carethers, J.M. Genomic and Epigenetic Instability in Colorectal Cancer Pathogenesis. *Gastroenterology* 2008, **135**(4), 1079–1099. doi:/10.1053/j.gastro.2008.07.076.
 15. Boland, C.R.; Thibodeau, S.N.; Hamilton, S.R.; Sidransky, D.; Eshleman, J.R.; Burt, R.W.; Meltzer, S.J.; Rodriguez-Bigas, M.A.; Fodde, R.; Ranzani, G.N. & Srivastava, S. A National Cancer Institute Workshop on Microsatellite Instability for Cancer Detection and Familial Predisposition: Development of International Criteria for the Determination of Microsatellite Instability in Colorectal Cancer. *Cancer Res.* 1998, **58**(22), 5248–5257.
 16. Issa, J.P. Colon Cancer: It's CIN or CIMP. *Clin. Cancer Res.* 2008, **14** (19), 5939–5940. doi:/10.1158/1078-0432.CCR-08-1596.
 17. Whitehall, V.L.J. & Leggett, B.A. The Serrated Pathway of Colorectal Carcinogenesis. *Curr. Colorectal Cancer Rep.* 2009, **5** (2), 75–83. doi:/10.1007/s11888-009-0012-y.
 18. Tiwari, A.; Saraf, S.; Verma, A.; Panda, P.K. & Jain, S.K. Novel Targeting Approaches and Signaling Pathways of Colorectal Cancer: An Insight. *World J. Gastroenterol.* 2018, **24**(39), 4428–4435. doi:/10.3748/wjg.v24.i39.4428.
 19. Takebe, N.; Miele, L.; Harris, P. J.; Jeong, W.; Bando, H.; Kahn, M.; Yang, S.X. & Ivy, S.P. Targeting Notch, Hedgehog, and Wnt Pathways in Cancer Stem Cells: Clinical Update. *Nat. Rev. Clin. Oncol.* 2015, **12**(8), 445–464. doi:/10.1038/nrclinonc.2015.61.
 20. Gulbake, A.; Jain, A.; Jain, A.; Jain, A. & Jain, S. K. Insight to Drug Delivery Aspects for Colorectal Cancer. *World J. Gastroenterol.* 2016, **22** (2), 582–599. doi:/10.3748/wjg.v22.i2.582.
 21. Fakoor, R.; Ladhak, F.; Nazi, A. & Huber, M. Using Deep Learning to Enhance Cancer Diagnosis and Classification. A Conference Presentation. In *The 30th International Conference on Machine Learning*; 2013.
 22. Brar, B.; Ranjan, K.; Palria, A.; Kumar, R.; Ghosh, M.; Sihag, S. & Minakshi, P. Nanotechnology in Colorectal Cancer for Precision Diagnosis and Therapy. *Front. Nanotechnol.* 2021, **3**. doi:/10.3389/fnano.2021.699266.
 23. Davenport, T. & Kalakota, R. The Potential for Artificial Intelligence in Healthcare. *Future Healthc. J.* 2019, **6**(2), 94–98. doi:/10.7861/futurehosp.6-2-94.
 24. Lee, S.-I.; Celik, S.; Logsdon, B. A.; Lundberg, S. M.; Martins, T. J.; Oehler, V. G.; Estey, E. H.; Miller, C. P.; Chien, S.; Dai, J.; Saxena, A.; Blau, C. A. & Becker, P. S. A Machine Learning Approach to Integrate Big Data for Precision Medicine in Acute Myeloid Leukemia. *Nat. Commun.* 2018, **9**(1), 42. doi:/10.1038/s41467-017-02465-5.
 25. Sordo, M. *Introduction to Neural Networks in Healthcare Open Clinical*; 2002.
 26. Vial, A.; Stirling, D.; Field, M.; Ros, M.; Ritz, C.; Carolan, M.; Holloway, L. & Miller, A. A. The Role of Deep Learning and Radiomic Feature Extraction in Cancer-Specific Predictive Modelling: A Review. *Transl. Cancer Res.* 2018, **7** (3), 803–816. doi:/10.21037/tcr.2018.05.02.
 27. Bohr, A. & Memarzadeh, K. The Rise of Artificial Intelligence in Healthcare Applications. In *Artificial Intelligence in Healthcare*; Elsevier, 2020, 25–60.
 28. Chen, J. H. & Asch, S. M. Machine Learning and Prediction in Medicine - beyond the Peak of Inflated Expectations. *N. Engl. J. Med.* 2017, **376**(26), 2507–2509. doi:/10.1056/NEJMp1702071.
 29. Cianci, P. & Restini, E. Artificial Intelligence in Colorectal Cancer Management. *WArtificial Intelligence in Cancer* 2021, **2**(6), 79–89. doi:/10.35713/aic.v2.i6.79.
 30. Gupta, N.; Kupfer, S. S. & Davis, A. M. Colorectal Cancer Screening. *JAMA* 2019, **321**(20), 2022–2023. doi:/10.1001/jama.2019.4842.
 31. Huang, S.; Yang, J.; Fong, S. & Zhao, Q. Artificial Intelligence in Cancer Diagnosis and Prognosis: Opportunities and Challenges. *Cancer Lett.* 2020, **471**, 61–71. doi:/10.1016/j.canlet.2019.12.007.
 32. Liu, Y.; Sethi, N. S.; Hinoue, T.; Schneider, B. G.; Cherniack, A. D. & Mariamidze, A. Comparative Molecular Analysis of Gastrointestinal Adenocarcinomas. *Cancer Cell* 2018, **33**(4), 721–735.e8. doi:/10.1016/j.ccell.2018.03.010.
 33. Topol, E. J. High-Performance Medicine: The Convergence of Human and Artificial Intelligence. *Nat. Med.* 2019, **25** (1), 44–56. doi:/10.1038/s41591-018-0300-7.
 34. Bernard, S. & Parikesit, A. A. Artificial Intelligence in Colonoscopy: Improving Medical Diagnostic of Colorectal Cancer. *Front. Health Inform.* 2020, **9** (1), 27. doi:/10.30699/fhi.v9i1.209.
 35. Vining, D. J.; Gelfand, D. W.; Bechtold, R. E.; Scharling, E. S.; Grishaw, E. K. & Shifrin, R. Y. Technical Feasibility of Colon Imaging with Helical CT and Virtual Reality. *AJR Am. J. Roentgenol* 1994, **162**. doi:/10.11405/nisshoshi.107.718.
 36. Blanes-Vidal, V.; Baatrup, G. & Nadimi, E. S. Addressing Priority Challenges in the Detection and Assessment of Colorectal Polyps from Capsule Endoscopy and Colonoscopy in Colorectal Cancer

- Screening Using Machine Learning. *Acta Oncol.* 2019, **58** (sup1), S29–S36. doi:/10.1080/0284186X.2019.1584404.
37. Hosoe, N.; Limpas Kamiya, K. J. L.; Hayashi, Y.; Sujino, T.; Ogata, H. & Kanai, T. Current Status of Colon Capsule Endoscopy. *Dig. Endosc.* 2021, **33** (4), 529–537. doi:/10.1111/den.13769.
 38. Nadkarni, P. M.; Ohno-Machado, L. & Chapman, W. W. Natural Language Processing: An Introduction. *J. Am. Med. Inform. Assoc.* 2011, **18**(5), 544–551. doi:/10.1136/amiajnl-2011-000464.
 39. Mehrotra, A.; Morris, M.; Gourevitch, R.A.; Carrell, D. S.; Leffler, D. A.; Rose, S.; Greer, J.B.; Crockett, S. D.; Baer, A. & Schoen, R.E. Physician Characteristics Associated with Higher Adenoma Detection Rate. *Gastrointest. Endosc.* 2018, **87**(3), 778-786.e5. doi:/10.1016/j.gie.2017.08.023.
 40. Urban, G.; Tripathi, P.; Alkayali, T.; Mittal, M.; Jalali, F.; Karnes, W. & Baldi, P. Deep Learning Localizes and Identifies Polyps in Real Time with 96% Accuracy in Screening Colonoscopy. *Gastroenterology* 2018, **155**(4), 1069-1078.e8. doi:/10.1053/j.gastro.2018.06.037.
 41. Komeda, Y.; Handa, H.; Watanabe, T.; Nomura, T.; Kitahashi, M.; Sakurai, T.; Okamoto, A.; Minami, T.; Kono, M.; Arizumi, T.; Takenaka, M.; Hagiwara, S.; Matsui, S.; Nishida, N.; Kashida, H. & Kudo, M. Computer-Aided Diagnosis Based on Convolutional Neural Network System for Colorectal Polyp Classification: Preliminary Experience. *Oncology* 2017, **93**, Suppl 1 (Suppl. 1), 30–34. doi:/10.1159/000481227.
 42. Byrne, M. F.; Chapados, N.; Soudan, F.; Oertel, C.; Linares Pérez, M.; Kelly, R.; Iqbal, N.; Chandelier, F. & Rex, D. K. Real-Time Differentiation of Adenomatous and Hyperplastic Diminutive Colorectal Polyps during Analysis of Unaltered Videos of Standard Colonoscopy Using a Deep Learning Model. *Gut* 2019, **68**(1), 94–100. doi:/10.1136/gutjnl-2017-314547.
 43. Hilsden, R. J.; Heitman, S. J.; Mizrahi, B.; Narod, S. A. & Goshen, R. Prediction of Findings at Screening Colonoscopy Using a Machine Learning Algorithm Based on Complete Blood Counts (Colon Flag). *PLoS One* 2018, **13**, 1–9. doi:/10.1371/journal.pone.0207848.
 44. Min, J.K.; Kwak, M.S. & Cha, J.M. Overview of Deep Learning in Gastrointestinal Endoscopy. *Gut Liver* 2019, **13**(4), 388–393. doi:/10.5009/gnl18384.
 45. Bilal, M.; Raza, S. E. A.; Azam, A.; Graham, S.; Ilyas, M.; Cree, I. A.; Snead, D.; Minhas, F. & Rajpoot, N. M. Development and Validation of a Weakly Supervised Deep Learning Framework to Predict the Status of Molecular Pathways and Key Mutations in Colorectal Cancer from Routine Histology Images: A Retrospective Study. *Lancet Digit. Health* 2021, **3**(12), e763–e772. doi:/10.1016/S2589-7500(21)00180-1.
 46. Sun, C.-H.; Li, B.-B.; Wang, B.; Zhao, J.; Zhang, X.-Y.; Li, T.-T.; Li, W.-B.; Tang, D.; Qiu, M.-J.; Wang, X.-C.; Zhu, C.-M. & Qian, Z.-R. The Role of *Fusobacterium Nucleatum* in Colorectal Cancer: From Carcinogenesis to Clinical Management. *Chronic Dis. Transl. Med.* 2019, **5**(3), 178–187. doi:/10.1016/j.cdtm.2019.09.001.
 47. Rathore, S.; Hussain, M.; Aksam Iftikhar, M. & Jalil, A. Novel Structural Descriptors for Automated Colon Cancer Detection and Grading. *Comput. Methods Programs Biomed.* 2015, **121**(2), 92–108. doi:/10.1016/j.cmpb.2015.05.008.
 48. Acs, B.; Rantalainen, M. & Hartman, J. Artificial Intelligence as the next Step towards Precision Pathology. *J. Intern. Med.* 2020, **288**(1), 62–81. doi:/10.1111/joim.13030.
 49. Van Eycke, Y.-R.; Balsat, C.; Verset, L.; Debeir, O.; Salmon, I. & Decaestecker, C. Segmentation of Glandular Epithelium in Colorectal Tumours to Automatically Compartmentalise IHC Biomarker Quantification: A Deep Learning Approach. *Med. Image Anal.* 2018, **49**, 35–45. doi:/10.1016/j.media.2018.07.004.
 50. Brenner, H.; Kloor, M. & Pox, C. P. Colorectal Cancer. *Lancet* 2014, **383**(9927), 1490–1502. doi:/10.1016/S0140-6736(13)61649-9.
 51. Ito, N.; Kawahira, H.; Nakashima, H.; Uesato, M.; Miyauchi, H. & Matsubara, H. Endoscopic Diagnostic Support System for CT1b Colorectal Cancer Using Deep Learning. *Oncology* 2019, **96**(1), 44–50. doi:/10.1159/000491636.
 52. Song, C.L.; Vardaki, M. Z.; Goldin, R.D. & Kazarian, S. G. Fourier Transform Infrared Spectroscopic Imaging of Colon Tissues: Evaluating the Significance of Amide I and C–H Stretching Bands in Diagnostic Applications with Machine Learning. *Anal. Bioanal. Chem.* 2019, **411**(26), 6969–6981. doi:/10.1007/s00216-019-02069-6.
 53. Kainz, P.; Pfeiffer, M. & Urschler, M. Segmentation and Classification of Colon Glands with Deep Convolutional Neural Networks and Total Variation Regularization. *PeerJ* 2017, **5**(e3874), e3874. doi:/10.7717/peerj.3874.
 54. Tutar, Y. MiRNA and Cancer; Computational and Experimental Approaches. *Curr. Pharm. Biotechnol.* 2014, **15**(5), 429. doi:/10.2174/138920101505140828161335.
 55. Chang, K.H.; Miller, N.; Kheirleiseid, E.A.H.; Lemetre, C.; Ball, G.R.; Smith, M.J.; Regan, M.; McAnena, O.J. & Kerin, M.J. MicroRNA Signature Analysis in Colorectal Cancer: Identification of Expression Profiles in Stage II Tumors Associated with Aggressive Disease. *Int. J. Colorectal Dis.* 2011, **26**(11), 1415–1422. doi:/10.1007/s00384-011-1279-4.
 56. Amirkhah, R.; Farazmand, A.; Gupta, S. K.; Ahmadi, H.; Wolkenhauer, O. & Schmitz, U. Naïve Bayes Classifier Predicts Functional MicroRNA Target Interactions in Colorectal Cancer. *Mol. Biosyst.* 2015, **11**(8), 2126–2134. doi:/10.1039/c5mb00245a.
 57. Wu, Q.Y.; Liu, S.L.; Sun, P.; Li, Y.; Liu, G.W.; Liu, S.S.; Hu, J.L.; Niu, T.Y. & Lu, Y. Establishment and Clinical Application Value of an Automatic Diagnosis Platform for Rectal Cancer T-Staging Based on a

- Deep Neural Network. *Chin. Med. J. (Engl.)* 2021, **134**(7), 821–828. doi:/10.1097/cm9.0000000000001401.
58. Wang, K.S.; Yu, G.; Xu, C.; Meng, X.H.; Zhou, J.; Zheng, C.; Xiao, H.M. & Deng, H.W. Accurate Diagnosis of Colorectal Cancer Based on Histopathology Images Using Artificial Intelligence. *BMC Med.* 2021, **19**(1). doi:/10.1186/s12916-021-01942-5.
 59. Boselli, C.; Cirocchi, R.; Gemini, A.; Grassi, V.; Avenia, S.; Polistena, A.; Sanguinetti, A.; Burattini, M.F.; Pironi, D.; Santoro, A.; Tabola, R. & Avenia, N. Surgery for Colorectal Cancer in Elderly: A Comparative Analysis of Risk Factor in Elective and Urgency Surgery. *Aging Clin. Exp. Res.* 2017, **29**(S1), 65–71. doi:/10.1007/s40520-016-0642-2.
 60. Yang, S.X.; Sun, Z.Q.; Zhou, Q.B.; Xu, J.Z.; Chang, Y.; Xia, K.K.; Wang, G.X.; Li, Z.; Song, J.M.; Zhang, Z.Y.; Yuan, W.T. & Liu, J.B. Security and Radical Assessment in Open, Laparoscopic, Robotic Colorectal Cancer Surgery: A Comparative Study. *Technol. Cancer Res. Treat.* 2018, **17**, 153303381879416. doi:/10.1177/1533033818794160.
 61. Felfoul, O.; Mohammadi, M.; Taherkhani, S.; de Lanauze, D.; Zhong Xu, Y.; Loghin, D.; Essa, S.; Jancik, S.; Houle, D.; Lafleur, M.; Gaboury, L.; Tabrizian, M.; Kaou, N.; Atkin, M.; Vuong, T.; Batist, G.; Beauchemin, N.; Radzioch, D. & Martel, S. Magneto-Aerotactic Bacteria Deliver Drug-Containing Nanoliposomes to Tumour Hypoxic Regions. *Nat. Nanotechnol.* 2016, **11**(11), 941–947. doi:/10.1038/nnano.2016.137.
 62. Cruz, S.; Gomes, S.E.; Borralho, P.M.; Rodrigues, C.M.P.; Gaudêncio, S.P. & Pereira, F. In Silico HCT116 Human Colon Cancer Cell-Based Models En Route to the Discovery of Lead-like Anticancer Drugs. *Biomolecules* 2018, **8**(3), 56. doi:/10.3390/biom8030056.
 63. Keshava, N.; Toh, T.S.; Yuan, H.; Yang, B.; Menden, M.P. & Wang, D. Defining Subpopulations of Differential Drug Response to Reveal Novel Target Populations. *NPJ Syst. Biol. Appl.* 2019, **5**(1), 36. doi:/10.1038/s41540-019-0113-4.
 64. Nowak-Sliwinska, P.; Scapozza, L. & Ruiz i Altaba, A. Drug Repurposing in Oncology: Compounds, Pathways, Phenotypes and Computational Approaches for Colorectal Cancer. *Biochim. Biophys. Acta Rev. Cancer* 2019, **1871**(2), 434–454. doi:/10.1016/j.bbcan.2019.04.005.
 65. Horta, A.B.; Salgado, C.; Fernandes, M.; Vieira, S.; Sousa, J.M.; Papoila, A.L. & Xavier, M. Clinical Decision Support Tool for Co-Management Signalling. *Int. J. Med. Inform.* 2018, **113**, 56–62. doi:/10.1016/j.ijmedinf.2018.02.014.
 66. Adamson, A.S. & Welch, H.G. Machine Learning and the Cancer-Diagnosis Problem — No Gold Standard. *N. Engl. J. Med.* 2019, **381**(24), 2285–2287. doi:/10.1056/nejmp1907407.
 67. Lovis, C. Unlocking the Power of Artificial Intelligence and Big Data in Medicine. *J. Med. Internet Res.* 2019, **21**(11), e16607. doi:/10.2196/16607.
 68. Song, B.; Zhang, G.; Lu, H.; Wang, H.; Zhu, W.; J. Pickhardt, P. & Liang, Z. Volumetric Texture Features from Higher-Order Images for Diagnosis of Colon Lesions via CT Colonography. *Int. J. Comput. Assist. Radiol. Surg.* 2014, **9**(6), 1021–1031. doi:/10.1007/s11548-014-0991-2.
 69. Freeman, D.J.; Norrie, J.; Sattar, N.; Neely, R.D. G.; Cobbe, S.M.; Ford, I.; Isles, C.; Lorimer, A. R.; Macfarlane, P.W.; McKillop, J.H.; Packard, C. J.; Shepherd, J. & Gaw, A. Pravastatin and the Development of Diabetes Mellitus: Evidence for a Protective Treatment Effect in the West of Scotland Coronary Prevention Study. *Circulation* 2001, **103**(3), 357–362. doi:/10.1161/01.cir.103.3.357.
 70. Laique, S.N.; Hayat, U.; Sarvepalli, S.; Vaughn, B.; Ibrahim, M.; McMichael, J.; Qaiser, K.N.; Burke, C.; Bhatt, A.; Rhodes, C. & Rizk, M.K. Application of Optical Character Recognition with Natural Language Processing for Large-Scale Quality Metric Data Extraction in Colonoscopy Reports. *Gastrointest. Endosc.* 2021, **93**(3), 750–757. doi:/10.1016/j.gie.2020.08.038.
 71. Krenzer, A.; Banck, M.; Makowski, K.; Hekalo, A.; Fitting, D.; Troya, J.; Sudarevic, B.; Zoller, W. G.; Hann, A. & Puppe, F. A Real-Time Polyp-Detection System with Clinical Application in Colonoscopy Using Deep Convolutional Neural Networks. *J. Imaging* 2023, **9**(2), 26. doi:/10.3390/jimaging9020026.
 72. Glissen Brown, J.R.; Mansour, N.M. & Wang, P. Deep Learning Computer-Aided Polyp Detection Reduces Adenoma Miss Rate: A U.S. Multi-Center Randomized Tandem Colonoscopy Study(CADeT-CS Trial). *Clin Gastroenterol Hepatol* 2022, **20**, 1499–1507.
 73. Wang, S.; Yin, Y.; Wang, D.; Lv, Z.; Wang, Y. & Jin, Y. An Interpretable Deep Neural Network for Colorectal Polyp Diagnosis under Colonoscopy. *Knowl. Based Syst.* 2021, **234**(107568), 107568. doi:/10.1016/j.knosys.2021.107568.
 74. Lee, J.Y.; Jeong, J.; Song, E.M.; Ha, C.; Lee, H.J.; Koo, J.E.; Yang, D.H.; Kim, N. & Byeon, J.S. Real-Time Detection of Colon Polyps during Colonoscopy Using Deep Learning: Systematic Validation with Four Independent Datasets. *Sci. Rep.* 2020, **10**(1), 8379. doi:/10.1038/s41598-020-65387-1.

CONTRIBUTORS

Mr Pankaj Kumar Tripathi is a research scholar in Jaypee Institute of Information Technology Noida. He is working on colorectal cancer in his PhD. He has contributed in the collection and analysis of literature and writing of the manuscript.

Dr Chakresh Kumar Jain is working as Associate Professor, Department of Biotechnology, Jaypee Institute of Information Technology, Noida. His interest areas are Bioinformatics, Artificial Intelligence, Pathogen Informatics, Cancer Genomics, Computer Aided Drug Designing, Machine learning/Deep learning etc. He has contributed in literature analysis and review of present manuscript.