91344_Auto_Edited -check.docx

Emerging molecules, tools, technology, and future of surgical knife in gastroenterology

Abstract

The 21st century has started with several innovations in the medical sciences, with its wide applications in health care management. This development has taken in the field of medicines (newer drugs/molecules), various tools and technology which has completely changed the patient management including the abdominal surgery. Surgery for abdominal diseases have moved from maximally invasive to minimally invasive (laparoscopic and robotic) surgery. Some of the newer medicines has its impact on need for surgical intervention. This article focuses on the development of these emerging molecules, tools and technology and its impact on present surgical form and its future effects on the surgical intervention in Gastroenterological diseases.

Key Words: Newer molecules; Tools and technology; Gastroenterology; Future of surgical knife

Kumar A, Goyal A. Emerging molecules, tools, technology, and future of surgical knife in gastroenterology. *World J Gastrointest Surg* 2024; In press

Core Tip: This editorial discusses the effect of newer medicines, emerging tools and technology, and its impact on surgery for gastrointestinal diseases and its future. Whether surgery is going to remain in its present form or will come up in a new makeover or vanish completely in the future?

INTRODUCTION

Surgical outcomes/results today are results of various refinements and innovations, which are ongoing and continuous in the field of surgical techniques, safer anaesthesia, post-operative management, and better diagnostic modalities for early and timely diagnosis. Various emerging molecules, *e.g.*, drugs, immunomodulators and targeted therapeutic agents, along with newer tools and techniques for early diagnosis, precise surgical planning, and intraoperative surgical decision-making have significantly reduced the postoperative complications and improved the survival of patients. Advancements in technology that have led to changes in surgery are computer-based tools, laparoscopes, robots, and artificial intelligence (AI). With this development, surgery has changed from maximally invasive (Open) to minimally invasive (MIS), from multi-port laparoscopic surgery to single port surgery (SILS) and now robotic surgery which is technically and oncological feasible even for malignant diseases with its added advantage over conventional surgery. In this editorial, we shall explore and discuss how the surgical knife has evolved and what shape it may take in the future in gastrointestinal (GI) surgery after all these developments.

HISTORICAL BACKGROUND

Historically the surgery can be traced back to the Before Christ (BC) era with the description of several procedures performed including amputation of leg[1]. In Egypt, nearly around 3000 BC, surgeons were immobilizing fractures, excising tumours and suturing was done with linen thread[2]. Sushruta close to 600 BC in India is known for pioneering surgical procedures and has written a book named Sushruta Samita which was the main source of surgical knowledge in ancient India[1]. Greek physician Hippocrates is considered the father of modern medicine as he was the one who described diseases and their treatment in a scientific manner[3]. Hanaoka in Japan was the first to perform Surgery using General anaesthesia[4]. The first known open appendicectomy was performed on an 11-year-old child with perforated appendicitis in St. George Hospital in 1735[5]. Othersen *et al*[6] removed a large ovarian tumour. Johnston *et al*[7] performed the first Belfast gastrectomy for cancer. Surgical results were poor because of sepsis[1].

In the latter half of the 19th century, Joseph Lister gave the concept of antisepsis and initially, carbolic acid was used to prevent postoperative infections[1]. It was in the late 1900s that the likelihood of surviving surgery was more than that of dying from surgery[8]. Surgery in the 20th century became relatively safer with the introduction of

Penicillin by Alexander Fleming in 1928. There were two notable developments in the latter half of the 20th century, which revolutionized surgery. First in transplant (first successful liver and pancreas transplant in 1967 and 1966 respectively) and second in MIS surgery/key role surgery in 1980 (laparoscopic/robotics)[1]. Today surgical armamentariums have more than 2500 different surgical techniques[1]. The focus of moving forward is placed more on refining these techniques to ensure better short and long-term results. Developments in the 21st century aim to make surgery less invasive through smaller incisions (robotics, SILS, MIS, and interventional techniques) and to make surgery more precise with the help of computronics and AI. Whether surgery is going to remain in its present form or a newer remake or vanish completely in the future is unknown.

NEWER DEVELOPMENTS/INNOVATIONS AFFECTING THE GI SURGERY

Newer medicines/molecules

Various new molecules have emerged in the past decades, which have been found useful in several GI diseases by avoiding/delaying surgical intervention. These molecules have been divided into mature, advancing, and emerging molecules based on their present role in the medical field.

Mature molecules: Mature molecules are ones which already established and proven their clinical efficacy and are in widespread use such as: (1) Small-molecule drugs; (2) recombinant proteins; and (3) monoclonal antibodies.

Small molecules peculiarly attracted researchers due to their ease of oral administration. JAK inhibitors (Tofacitinib & others) and sphingosine receptor modulators/agonists (Ozanimod & Etrasimod) are examples of small molecules which play an important in the treatment of ulcerative colitis. Sphingosine-1-phosphate receptor modulators/agonist induces the circulating lymphocytes to get collected in lymph nodes thereby decreasing effective circulating lymphocytes[9].

Recombinant proteins such as recombinant human IL-10 which by its anti-inflammatory action has helped in inducing remission in chronic active colitis[10]. Recombinant sjCystatin derived from Schistosoma japonicum, by upregulation of Th-

2 cells (helper T cells) and regulatory T cells, decreases/ameliorates colonic inflammation[11].

Monoclonal antibodies/Biological therapy act against the TNF-alpha and IL-12/23 which are proinflammatory mediators in the pathogenesis of inflammatory bowel disease. Anti-TNF-alpha molecules like Infliximab and Adalimumab have been shown in various randomized controlled studies where usage of these molecules has led to a decrease in the rate of colectomy in ulcerative colitis patients[9]. Similarly, anti IL12/23 therapy (Ustekinumab, Mirikizumab, and Risankizumab) and anti-integrin therapy (Vedolizumab and Etrolizumab) have shown promising results in moderate to severe ulcerative colitis patients. After the introduction of the biological agents for management of the inflammatory bowel disease, there is a decline in the rate of surgical intervention which is established in several trials[12].

Advancing molecules: Advancing molecules are those which have passed their proof of concept and are in the late stages of clinical trials such as: (1) RNAi therapeutics; (2) antibody-drug conjugates; (3) antibody-radio conjugates; (4) bispecific antibodies and derivatives; and (5) chimeric antigen receptor (CAR) T-cell therapy.

RNA modulation with small interfering RNA (siRNA) to target genes involved in pathogenesis of gastro-intestinal diseases such as inflammatory bowel disease, malignancy, gastroesophageal reflux disease (GERD), *etc*. siRNA can be designed to target messenger RNA coding faulty protein, proinflammatory cytokines. Therapeutic agents can be delivered by oral, rectal, and endoscopic delivery systems. Oral preparations have been modified to counter its degradation by acid and enzymes present in GIT[13].

Antibody-drug conjugates are monoclonal antibodies which is covalently bound to cytotoxic drugs with the help of a linker. Monoclonal antibodies provide specificity to attach to the tumour cells followed by destruction of the tumour cells by cytotoxic moiety. Initially, these conjugates had a role in haematological malignancies but now its role has extended to GI malignancies including Oesophageal, Colonic and Pancreatic cancer. One such conjugate is Cetuximab sarotalocan in which a chimeric monoclonal antibody is conjugated with near-infrared dye. Photosensitizing dye can be activated with a laser to achieve targeted destruction of the cancerous cells[14].

Antibody-radio conjugates: Radiolabelled antibodies can target specific antigens present on the cancerous cells, with tumoricidal activity. Feasibility of the anti-CEA antigen-antibody labelled with I131 for pancreatic cancer has been demonstrated. Presently these studies are being done on unresectable cancer[15].

Bispecific antibodies and derivatives: Bispecific antibodies are the ones that have 2 antigen binding sites. One site will bind with T cells and the other site will bind with tumour cells expressing the antigen. When both sites are bound, it will lead to T cell activation with the release of cytokines and the destruction of tumour cells. Release of the cytokines will recruit further T cells[16].

In CAR-T cell therapy, the patient's native T cells are engineered to attack tumour cells. Initially, they were utilized for leukaemia but now they are also being utilized in solid tumours including Ovarian epithelial tumours, hepatocellular carcinoma, pancreatic, gastric, and biliary tract malignancy[17].

Biomarker-driven therapy for colorectal cancer: Some of the above-mentioned molecules are part of biomarker-driven therapy such as antibody-drug conjugates, antibody-radio conjugates, and bispecific antibodies. Biomarker-driven therapy for colorectal cancer is the one which targets cancer cells with particular mutations with drugs. Drugs such as tasins, statins and azithromycin act on APC (adenomatous polyposis coli) mutated cells which further leads to apoptosis of mutated cells. Similarly, drugs acting on other genetically mutated cells like KRAS/MEK/BRAF, SMAD 4/CDC4 and P53 are likely to have a strong future potential impact on the surgical treatment of similar abdominal diseases[18]. Biomarker-driven therapy may have the potential to treat abdominal cancer with surgery being reserved for complications such as bleeding, acute obstruction and perforation.

Emerging molecules: Emerging molecules are still in the proof-of-concept stage, *i.e.*, in the preclinical or early clinical stage and include oncolytic viruses, stem cells, *in vivo* gene editing (for example, CRISPR/Cas, ZEN, TALENs, or other mega nucleases)-

(discussed separately under heading genomics/stem cell therapy): (1) Microbiome treatments; (2) PROTACs, and several others; and (3) nanotechnology.

Microbiome treatments: Microbiome can modify the efficacy of cancer therapy by regulating metabolism to increase or decrease the immune response to the tumour by modulating the metabolism of antitumour agents. The interaction between the host immune response and the microbiome needs to be studied further to derive any conclusions[19].

PROTACs and several others: PROTAC stands for proteolysis targeting chimaera. PROTAC consists of three components namely protein of interest binding area (POI), E3 Ubiquitin binding area and a linker between these two areas. When POI binds with a cancer-causing protein or mutated protein, the ubiquitin site starts binding ubiquitin leading to mutated protein being recognized by proteasome and leads to its destruction. PROTAC has shown promising results. Presently trials are being conducted with PROTAC in breast and prostate cancer but in future many more cancers will be within reach of PROTAC therapy[20].

Nanotechnology: Gold nanoparticles (AuNPs) have a role in various medical applications such as spectroscopic cancer imaging, as imaging agents for cancer detection and prostate cancer treatment with fewer side effects. Nanosized particles are successful in evading the reticuloendothelial system. The development of nano theragnostic promises to improve the treatment of cancer through improved tumour targeting, controlled drug delivery, and therapeutic monitoring[21].

"Enhanced Permeability and Retention Effect" (EPR Effect), distinctly shown by gold nanoparticles have an enormous future impact on the treatment of cancer. Gold NPs of a particular size accumulate in higher concentrations in cancer cells than in healthy cells. Nanotechnology has led to advancement in the design of gold nanoparticles to allow for the generation of localized heat in the proximity of cancer tissues and additionally allow delivery of drugs in a controlled and targeted way. Colloidal Au can also be covalently linked onto adenoviral vectors for selective cancer targeting and induce hyperthermia by application of near-infrared laser light[21].

Newer treatment molecules for inflammatory bowel disease (IBD) include inhibitors of immune cell mobilization and inhibitory molecules against various cytokines involved in the inflammatory process of IBD. Surgical indications are limited and contained today. It seems surgical indications will be for complications of the disease, failure to respond to medical treatment, patient's choice due to drug-related issues and that too with MIS techniques.

Genetics/genomics of diseases/stem cell therapies

Gene therapy and stem cell therapy are part of the emerging molecules. Gene therapy acts *via* four mechanisms. Firstly, induction of apoptosis/increasing tumour sensitivity to conventional therapy. Secondly by insertion of the wild type of gene. Thirdly by arresting the expression of the oncogene and lastly by increasing the immunogenicity of the tumour cells so that a natural defence mechanism can take care of the tumour cells[22].

Oncolytic viruses: Oncolytic viruses are genetically modified viruses and play a role in cancer therapy by preferentially replicating in the tumour cells causing its lysis and further by stimulating the immunity of the host. Various oncolytic viruses such as vaccinia virus, Reo, herpes simplex virus, and adenovirus and oncolytic measles virus have shown promise in the treatment of colo-rectal cancer[23].

Stem cells: Pluripotent stem cells, adult stem cells and cancer stem cells have a role to play in cancer therapy. Various applications include post-cancer treatment, bone marrow suppression, as a therapeutic agent carrier, generation of immune effector cells and vaccine carrier[24].

***In vivo* gene editing and genomics:** This therapy involves non-viral delivery of RNA for silencing of oncogenes, DNA delivery of tumour suppressors, apoptosis inducers, suicide genes or immune-stimulatory molecules. Presently this therapy is being studied for colorectal, gastric, and liver cancer[25].

Advancements in genomics will improve surgical outcomes through prevention, prediction and early diagnosis by genomic sequencing and further manipulating the genes by genetic engineering. Many surgical diseases have genetic bases which will be detected swiftly and precisely by genome sequencing. The risk of developing disease will guide surgical intervention in the early stage leading to organ-sparing surgical intervention. Estimating/calculating the risk of having a disease will be of prime importance[26].

Genetic engineering will lead to the manipulation of genes involved in the disease process. For example, aiming genetic defects using CRSIPR-cas9 will lead to the introduction of a new subspeciality of surgery, genome surgery. Initiatives have already been underway to expand the CRISPR toolbox for making gene editing precise, effective, and safe[27].

Tools and technology

Surgery is undergoing evolution at a fast pace. On one hand, emerging technologies such as robotics, AI, and machine learning promise to improve standardization and effectiveness of diagnosis and treatment while on the other hand, there is always humanitarian concern such as disparities in equal access to the highest quality surgical care worldwide[28].

Areas of technological advances which are having and going to impact surgical care are: (2) Computronics-advance computers or supercomputers; (2) MIS techniques such as laparoscopy or robotics; (3) MIS surgery with laparoscopy [standard, SILS, or natural orifice transluminal endoscopic surgery (NOTES)], interventional endoscopy and endoscopic ultrasound-guided procedures, endo-bariatrics along with its integration with AI; and (4) AI-based imaging, intraoperative surgical decision making and patient-specific implant/biomaterials[29].

MIS techniques: Refinement in surgical techniques has shown the world the era of MIS surgery and its benefits in terms of smaller incisions, better cosmesis, shorter hospital stays, less pain, less time for post-operative recovery, earlier resumption of daily activity with equivalent oncologic outcomes. Surgeons were initially sceptical about MIS surgery but trials have removed the doubts and concerns. The incorporation of charge-coupled devices (CCD) cameras added to the laparoscope, radically changed the perception of laparoscopic surgery[30].

Standard laparoscopic procedures: Laparoscopic cholecystectomy done by Philip Mouret, France in 1987 is considered the first laparoscopic surgery. Now in today's world laparoscopic cholecystectomy is the gold standard for cholelithiasis. The domain of laparoscopic surgery has been increasing since then with its definite advantages with equal long-term outcomes including oncological outcomes. Presently surgical procedures which are done laparoscopically and have improved patient outcomes include: Staging and diagnostic laparoscopy; cholecystectomy; CBD exploration; splenectomy; anti-reflux surgery; cardio-myotomy for achalasia cardia; laparoscopic anti-obesity procedures; laparoscopic colonic and rectal surgery; laparoscopic appendicectomy; laparoscopic hernia surgery/gastrectomy; pancreatic surgery; liver resection; and hepaticojejunostomy and many others. Today majority of abdominal surgeries are being performed or can be performed with laparoscopy.

NOTES: NOTES is the most difficult and complex technique among minimally accessible techniques. Access to the peritoneal cavity and intraabdominal organs can be oral (*via* oesophagus and stomach), trans-vaginal, trans-colonic and trans-vesical. Rendezvous NOTES is a term used when more than one portal for entry is used to access the target organ. The term "Hybrid NOTES" is used when along with laparoscopic access, NOTES access is used for completion of the surgical procedure[31].

The transvaginal route is associated with some amount of success in procedures like cholecystectomy and appendicectomy[32].

Presently there are hurdles associated with NOTES some of which are difficulty to achieve triangulation, delicate flexible endoscopic instruments to hold and retract the organs and excessive mobility associated with the technique[31].

NOTES technique has to undergo much refinement and improvement before its routine clinical use which seems difficult shortly.

SILS: Single incision laparoscopic surgery presently is in between standard laparoscopic technique and NOTES. In this technique single incision although somewhat larger than a standard laparoscopic incision because of the need to insert a camera and instruments *via* the same incision. Limitations of SILS include loss of triangulation, clashing of the telescope with instruments and limited mobility as compared with standard laparoscopy. Articulating instruments can circumvent the problem of triangulation but these articulating instruments cannot be placed through standard trocar and need special access devices like Triport and Quadport[31].

Another development is magnetic anchoring and guidance system technology in which a magnetic camera is delivered into the peritoneal cavity and the camera position is controlled with externally placed magnets on the abdominal wall. Limitations associated with this technology are the inability to clean the camera lens, insufficient lighting and the magnet can guide the camera in thin-built patients. SILS has not drastically changed the patient outcomes over standard laparoscopic procedures *vs* the results of standard laparoscopy over open surgical procedures. The benefits of SILS are more cosmetic[31].

Comparing SILS with standard laparoscopy, SILS may be potentially less invasive but it does not provide the same manoeuvrability as standard laparoscopy. Surgeons' experts in SILS technique have not shown a similar level of skills and manoeuvrability as they have with laparoscopy[33].

Robotic surgery: Robotic surgery has extended the capabilities of surgeons to be more precise in surgical intervention. Robotic-assisted surgeries have all the advantages of MIS and may have fewer complications and similar or better outcomes albeit at higher cost and need for specialized training. Robotic technology encompasses tremor-free filtration which steadies the instrument and also provides magnification improving the precision needed for complex surgery with a narrow margin of error[34].

As of today, surgical robots are remote control devices which help the surgeon to do complex manoeuvres intraoperatively with ease and precision. The surgical knife is still under the control of the surgeon. Technology or AI is a long way from delivering fully automated Surgical robots[35].

Some of robots like cyber knife are partially autonomous and robotic arm delivers radiation with a surgeon/physician monitoring it from another room[34]. The degree or level of autonomy depends upon the varying levels of AI. Vicarious, nextgeneration surgical robot has extraordinary reach and strength to mimic almost all surgical moves of the operating surgeon[36].

The fusion of AI programs with surgical robots can increase the efficacy of surgical procedures by decreasing technical errors, operating time and improving access to difficult body areas thereby reducing human errors[34].

Despite many advantages, robots have several issues and limitations which include expensive and bulky, lack of haptic feedback, single port access and NOTES, telesurgery, application with AI, lack of emotion and humanitarian touch, and automation in surgical tasks[37].

Endoscopy and endoscopic ultrasound-guided interventional procedures: Endoscopic procedures have advanced at the same pace as laparoscopic procedures. Initially from diagnostic endoscopy to simple endoscopic procedures such as polypectomy to complex endoscopic/endoscopic ultrasound-guided procedures. Currently, the scope of endoscopic procedures and guided interventions are possible for benign GI disease, malignant GI diseases, bariatric procedures, and hepatopancreatic biliary diseases.

Benign GI therapy: Includes procedures for achalasia cardia (per oral endoscopic myotomy), anti-reflux procedure (transoral incision-less fundoplication), and endoscopic ultrasound-guided gastrojejunostomy and stenting.

Malignant GI therapy: Includes endoscopic mucosal dissection, endoscopic submucosal dissection, endoscopic full-thickness resection, submucosal tunnelling mucosal resection, and stenting.

Endoscopic bariatric therapy: Various endoscopic therapies range from space-occupying devices to endoscopic procedures. Endoscopic procedure for the treatment of obesity includes primary obesity surgery endoluminal, endoscopic sleeve gastroplasty, transoral outlet reduction, duodenum-jejunal bypass sleeve (endo barrier), gastroduodenal-jejunal bypass (endo bypass system), and incisionless magnetic anastomotic system.

These procedures have been described, but compared with the standard surgical procedures such as laparoscopic sleeve gastrectomy or laparoscopic Roux-en-Y gastric bypass they are less efficacious in weight loss[38].

Hepatopancreatic biliary interventions: The scope of the endoscopic ultrasound ranges from diagnostic to therapeutic procedures and includes EUS-guided FNAC/FNAB, EUS-guided celiac plexus block, pancreatic collection drainage, EUS-guided biliary drainage procedures and EUS guided anti-tumoral therapy[39].

AI: Advancements in AI in the form of virtual reality (VR), mixed reality, and augmented reality (AR) are helping in the planning of surgical procedures and thus changing the outcomes of surgical procedures. VR helps to train surgeons for new procedures before they perform these procedures on patients in reality. VR can help surgeons practice various surgical procedures and invaluable lifesaving surgical manoeuvres. VR can also improve the efficiency of medical care by training medical professionals in rural and far-flung areas[36].

The most efficient treatment of cancer is surgery with sufficient surgical margins to avoid local recurrence. During the surgical procedure, a hitch for the surgeon during surgery is the identification of the correct plane of resection for tumour tissues. AI can guide the surgeon in intraoperative decision making which in true clinical practice comes by experience.

Three main ways in which AI guides surgeons regarding intraoperative decision-making are by retrieving the data of similar situations/scenarios and providing better insight into the intraoperative condition. Intraoperative pathological tissue discrimination from normal healthy tissue. Suggestion of the surgical step which can be appropriate for the situation.

AI by helping in the detection of the vital surrounding structures, helps in deciding the level of transection and anastomosis has led to a decrease in the complication rate and improved surgical outcomes. In colorectal surgery, AI can be used to detect the surrounding structures such as nerve plexus, presacral venous plexus, ureter, bladder, prostate, and seminal vesicles and lymph nodes so that vital structures are protected without compromising the radicality of the oncological procedure. Various techniques are used for *in vivo* detection of margin status, *i.e.*, optical biopsies using confocal laser endomicroscopy, hyperspectral imaging, optical coherence tomography, and contrast-enhanced ultrasonography[40].

AR inputs provide additional information intraoperatively in real-time which helps and guides the surgeon on table decision-making[35]. AR functions by providing the three-dimensional (3D) input of patient surgical anatomy based on preoperative imaging and provides surgeons with insight into the critical anatomical structures such as ureters, major vessels, CBD, *etc.* in the vicinity of the dissection field[41].

Virtual segmentation technique helps to view the deeper structures of the solid viscera thus guiding regarding the resection planes. Compared with mobile intraperitoneal organs such as small bowel, retroperitoneal structures are easily reconstructed. AR is much more beneficial in procedures involving the adrenal, kidney, pancreas and liver[41].

CAS-One system TM: CAS-One system TM (CAScination, Bern, Switzerland), which make use of preoperative images along with intraoperative ultrasonography, has been used successfully to accomplish complex liver resections[41].

Intraoperative molecular imaging and live diagnostic aim to detect small or residual tumours post neoadjuvant therapy, to differentiate between normal and tumour tissue and to detect metastasis in nodal tissues in real-time. Intraoperative molecular imaging makes use of fluorescence-tagged antibodies which bind to receptors expressed in malignant tissue and to optically active nanomaterial hybrid tracers[41].

Fluorescent tracers detect the tumour tissue and facilitate the resection while the hybrid tracers (both fluorescent and radioactive) help in the detection of deeper tumour tissue where fluorescent tracers fail to do that[42].

The advent of the I knife by Professor Zoltan Takats of Imperial College, London further facilitates to identify the cancerous tissue by analyzing the smoke of the tissue using a mass spectrometer (REIMS- rapid evaporative mass spectrometry) in real time[36].

AI-BASED IMAGING AND PATIENT-SPECIFIC IMPLANTS/BIOMATERIALS

Innovations in medical imaging on various fronts include: AI and machine learning; advanced functional imaging; 3D printing; photon counting computed tomography (CT) scanners; liquid biopsy imaging; and AI-based radio mimics.

AI and machine learning

Application of AI and machine learning with AI algorithm can help in segmentation of the solid viscera, differential diagnosis, histopathology prediction, early detection of recurrence, and evaluation of treatment response[43].

AI in the field of gastroenterology[44]: AI has vast applications in the field of gastroenterology which include Diagnosis, prognosis and analysis of images.

For diagnostic: Artificial neural networks (ANN) can help in diagnosis based on the study of various clinical parameters. Pace *et al*[45] showed with the ANN model in 2005 diagnosis of GERD can be made using only 45 clinical variables with an accuracy of 100%.

For prognosis: Various authors have compared ANN models against various scoring systems such as the RANSON score, APACHE score for pancreatitis, BLEED criteria for lower GI bleed, and Rockall criteria for upper GI bleed.

ANN models have greater accuracy in predicting prognosis, rebleed rate and operative intervention. Various SVM-based models predict lymph node metastasis by studying clinicopathological factors based on the endoscopically resected specimen. A prediction model using the SVM model decreased the rate of unnecessary additional surgery (77%) when misdiagnosing lymph node metastasis than those of a prediction model using American (85%), European (91%), and Japanese guidelines (91%).

Image analysis: AI models have been created to distinguish between early cancer and Barrett's oesophagus based on specific texture, colour filters, and machine learning.

Advanced functional imaging

Functional imaging using with fusion of positron emission tomography/magnetic resonance imaging (MRI) or with functional MRI gives us clues regarding the tumour activity and thus aids in treatment strategies.

3D printing

3D printing is the process in which virtual image of the patient organ of interest is taken digitally, processed, and later used to create 3D model. Primary usage of 3D printing is preoperative planning of resection procedures. It shows how intimate structures are related to the pathological tissues. Surgeons after reviewing the 3D printed models have changed surgical strategy in some cases. Other advantages of 3D printing in educating the surgical trainees and also informing/explaining the patient about the surgical procedure planned[41].

Photon counting CT scanners

Advantages of photon counting CT scanner over and above presently used state of art CT scanner is that they have greater resolution, high signal to noise ratio, superior non contrast imaging and spectral imaging data. First commercial photon counting got FDA approval in 2021[46].

Liquid biopsy

Over last 10 years, diagnosis and follow up of cancer patient has been shifting from invasive to less invasive procedure. Liquid biopsy is detection of cancers cells or its various products like circulating DNA, RNA, protein which are shed from tumour and is being detected. Liquid biopsy can also detect circulating tumour cells. EPISPOT assay based on liquid biopsy can even detect single circulating tumour cell and is used in the management of cancer such as breast cancer, colon, prostate and pancreas[47].

AI based radiomics

AI is a system which draws inferences from a large set of data. Typically, radiomics evaluates size, shape and textural features which are used to create models which help to arrive at the diagnosis and help in surgical decision making[48].

ETHICAL ISSUES ASSOCIATED WITH APPLICATION OF NEWER TOOLS AND TECHNOLOGY (AI) IN HEALTHCARE

Newer tools, technology, molecules, and procedures in medicines always come with enthusiasm and look attractive with many advantages described over conventional treatments and methods. However, many unanswered questions are always there be it long-term outcomes or side effects. Over and above are the ethical issues which are usually ignored. Some of the concerns are regarding ethical dilemmas, privacy and data protection, informed consent, social gaps, medical consultation, empathy, and sympathy. Before embarking on AI, we must not violate four principles of ethics which are Autonomy, Beneficence, Non-maleficence, and Justice[44].

General data protection regulation

Organisation such as Genetic Information Non-discrimination Acts in the United States prohibits employers from discrimination based on genetic health information. Clinical data collected by AI machines can be hacked and can be misused for discrimination.

Informed consent and autonomy

Patients have the right to information that if an AI algorithm goes wrong or equipment fails who is responsible?

Social gap and justice

With the introduction of AI, the standard level of care will increase which might not be available in poor resource countries leading to the widening of the social gap.

Medical consultation, empathy, sympathy

With AI machines working on behalf of doctors and nurses are not empathic and sympathetic towards patients which will lead to destruction of the doctor patient relationship (Tables 1 and 2)[45,49-61].

PRESENT STATUS OF KNIFE (SURGERY)

Based on current developments and innovations described in the literature, surgical knife (surgery) has a dominant and primary role in the management of abdominal diseases. However, it has moved from maximally invasive to MIS form, with better preoperative diagnosis, accurate surgical planning, precision surgery on the table and minimum complications. The newer molecules are delaying or replacing surgery in some of the benign abdominal pathology but have a limited role in malignant diseases. Open surgery still occupies a significant part of surgical procedures in developing and underdeveloped countries. Despite this change, it is important to train surgeons in open abdominal procedures and expose them to anatomical planes with haptic/tactile sensation and ergonomics. Open surgical exposure will be of great help for learning MIS and handling complications if laparotomy is required[62].

POSSIBLE FUTURE REALITY OF ABDOMINAL SURGERY

The abdominal surgeon of the future will need to adapt and learn a wider range of emerging technologies quicker than ever before. The amount of information that needs to be learnt will be enormous. The paradigm of training has changed from simple mentorship to proficiency-based, quantifiable assessment, and surgeons will be required to have higher standards than today. The extra amount of work will be required to achieve new standards with changing technology with greater responsibilities that the changes of the coming generation will bring. The future surgeon will not only hold the lives of their patients in their hands but may be responsible for the future of what it means to be human[63].

Future abdominal surgery would be miniature, MIS and hand-free. The knife will be replaced with an I knife or laser knife, and the Surgical trolly will be replaced simply by a computer, console, and robot with higher capability of AI but would be surgeon-centric. Surgical planning would be like a surgical strike on foreign soil with precision, in real-time execution of the task and return to the home ground safely with or without used arms and ammunition with success. Compliance would be like satellite launching and nuclear fission/fusion. The entire surgical team and instruments may be in the form of a surgical capsule, incorporated with 3D images, a nano computer with AI and an I knife/laser knife. The capsular theatre may be swallowed by patients for luminal lesions or it will be dropped into the peritoneal cavity (with a small incision or laparoscope) for extraluminal surgery. The incorporated information and the coded action will come out of the capsule at the precise site of the lesion, the knife will be released and an AI-based computer will execute the operation, albeit monitored and observed by an ungloved surgeon out of the surgical field. After the lesion is removed, or action is over, the lesion may be left in the abdominal cavity or removed subsequently either by an incision or by natural orifice. Once the designated task is over, the capsular operation theatre may come out by natural orifice or will disintegrate like a space shuttle based on its purpose and design.

The role of knife (surgery) in abdominal diseases may be contained or get limited with the developments of newer molecules and medicines. Some of the benign abdominal diseases may not require surgery or will have selective surgical intervention. Malignant luminal or solid organ pathology too will be treated with medicines but in a selective manner. However, surgery will always remain in the centre stage of treatment. The form of future surgery will be miniature, MIS, precise, and individualized but with no instrument. Still, without surgical gloves, the surgeon's role would be a meticulous planner for a successful, fruitful, and meaningful surgical strike. A world of caution and ethical issues will always be there for such futuristic operation theatre, of its design, use and application.

CONCLUSION

With the development of several newer molecules, targeted therapy, genomic manipulation (genetic surgery) and newer diagnostic tools for early and timely diagnosis some of the current surgical GI diseases may not require surgery or surgery may be delayed. Fast-emerging tools and technology have an impact on early and accurate diagnosis, pretreatment planning, intra-operative surgical decision-making and also on the mode of surgical intervention. MIS surgery, today has its fair amount of share in GI surgery and may likely to dominant in future over open surgery. However, open surgery is and will be at the centre stage, as it's the basis for the development of all the newer modes of surgical intervention and works as a pivot for teaching and training and will always going to remain there, albeit in its limited role. Miniature theatre, miniature robots and AI are the future possibilities of GI surgery. Judicious selection of technology, tools and molecules are warranted within ethical limit for patient's benefit.

REFERENCES

1 **Jennifer Whitlock RMF**. The Historical timeline of surgery. 2023. [cited 18 February 2024]. Available from: https://www.verywellhealth.com/the-history-of-surgery-timeline-3157332

2 **McKellar S**. A history of surgery: From superstition to science. *Can Med Assoc J* 2010; **182**: 809-809 [DOI: 10.1503/cmaj.100436]

3 **Grammaticos PC**, Diamantis A. Useful known and unknown views of the father of modern medicine, Hippocrates and his teacher Democritus. *Hell J Nucl Med* 2008; **11**: 2-4 [PMID: 18392218]

4 **Mestler GE**. A galaxy of old Japanese medical books with miscellaneous notes on early medicine in Japan. III. Urology, syphilology and dermatology; surgery and pathology. *Bull Med Libr Assoc* 1956; **44**: 125-159 [PMID: 13304528]

5 **Bellis S**. Surgery for an acute abdomen-an intriguing history of the laparotomy procedure. *Cambridge Med J* 2019 [DOI: 10.7244/cmj.2018.12.002]

6 **Othersen HB Jr**. Ephraim McDowell: the qualities of a good surgeon. *Ann Surg* 2004; **239**: 648-650 [PMID: 15082968 DOI: 10.1097/01.sla.0000124382.04128.5a]

7 **Johnston GW**. The rise and fall of the scalpel in peptic ulcer surgery. *Ulster Med J* 1998; **67** Suppl 1: 12-14 [PMID: 9807947]

8 **Brock C**. Risk, responsibility and surgery in the 1890s and early 1900s. *Med Hist* 2013; **57**: 317-337 [PMID: 24069882 DOI: 10.1017/mdh.2013.16]

9 **Cai Z**, Wang S, Li J. Treatment of Inflammatory Bowel Disease: A Comprehensive Review. *Front Med (Lausanne)* 2021; **8**: 765474 [PMID: 34988090 DOI: 10.3389/fmed.2021.765474]

10 **Schreiber S**, Fedorak RN, Nielsen OH, Wild G, Williams CN, Nikolaus S, Jacyna M, Lashner BA, Gangl A, Rutgeerts P, Isaacs K, van Deventer SJ, Koningsberger JC, Cohard M, LeBeaut A, Hanauer SB. Safety and efficacy of recombinant human interleukin 10 in chronic active Crohn's disease. Crohn's Disease IL-10 Cooperative Study Group. *Gastroenterology* 2000; **119**: 1461-1472 [PMID: 11113067 DOI: 10.1053/gast.2000.20196]

11 **Wang S**, Xie Y, Yang X, Wang X, Yan K, Zhong Z, Wang X, Xu Y, Zhang Y, Liu F, Shen J. Therapeutic potential of recombinant cystatin from Schistosoma japonicum in TNBS-induced experimental colitis of mice. *Parasit Vectors* 2016; **9**: 6 [PMID: 26728323 DOI: 10.1186/s13071-015-1288-1]

12 **Loftus EV Jr**. The Impact of Biologic Therapy on Outcomes of Inflammatory Bowel Disease Surgery. *Gastroenterol Hepatol (N Y)* 2019; **15**: 274-276 [PMID: 31360141]

13 **Chevalier R**. siRNA Targeting and Treatment of Gastrointestinal Diseases. *Clin Transl Sci* 2019; **12**: 573-585 [PMID: 31309709 DOI: 10.1111/cts.12668]

14 **Fu Z**, Li S, Han S, Shi C, Zhang Y. Antibody drug conjugate: the "biological missile" for targeted cancer therapy. *Signal Transduct Target Ther* 2022; **7**: 93 [PMID: 35318309 DOI: 10.1038/s41392-022-00947-7]

15 **Shah M**, Da Silva R, Gravekamp C, Libutti SK, Abraham T, Dadachova E. Targeted radionuclide therapies for pancreatic cancer. *Cancer Gene Ther* 2015; **22**: 375-379 [PMID: 26227823 DOI: 10.1038/cgt.2015.32]

16 **Krishnamurthy A**, Jimeno A. Bispecific antibodies for cancer therapy: A review. *Pharmacol Ther* 2018; **185**: 122-134 [PMID: 29269044 DOI: 10.1016/j.pharmthera.2017.12.002]

17 **Siddiqui RS**, Sardar M. A Systematic Review of the Role of Chimeric Antigen Receptor T (CAR-T) Cell Therapy in the Treatment of Solid Tumors. *Cureus* 2021; **13** [DOI: 10.7759/cureus.14494]

18 **Kumar A**, Gautam V, Sandhu A, Rawat K, Sharma A, Saha L. Current and emerging therapeutic approaches for colorectal cancer: A comprehensive review. *World J Gastrointest Surg* 2023; **15**: 495-519 [PMID: 37206081 DOI: 10.4240/wjgs.v15.i4.495]

19 **Yu ZK**, Xie RL, You R, Liu YP, Chen XY, Chen MY, Huang PY. The role of the bacterial microbiome in the treatment of cancer. *BMC Cancer* 2021; **21**: 934 [PMID: 34412621 DOI: 10.1186/s12885-021-08664-0]

20 **Békés M**, Langley DR, Crews CM. PROTAC targeted protein degraders: the past is prologue. *Nat Rev Drug Discov* 2022; **21**: 181-200 [PMID: 35042991 DOI: 10.1038/s41573-021-00371-6]

21 **Jain S**, Hirst DG, O'Sullivan JM. Gold nanoparticles as novel agents for cancer therapy. *Br J Radiol* 2012; **85**: 101-113 [PMID: 22010024 DOI: 10.1259/bjr/59448833]

22 **Das SK**, Menezes ME, Bhatia S, Wang XY, Emdad L, Sarkar D, Fisher PB. Gene Therapies for Cancer: Strategies, Challenges and Successes. *J Cell Physiol* 2015; **230**: 259-271 [PMID: 25196387 DOI: 10.1002/jcp.24791]

23 **Ren Y**, Miao JM, Wang YY, Fan Z, Kong XB, Yang L, Cheng G. Oncolytic viruses combined with immune checkpoint therapy for colorectal cancer is a promising treatment option. *Front Immunol* 2022; **13**: 961796 [PMID: 35911673 DOI: 10.3389/fimmu.2022.961796]

24 **Chu DT**, Nguyen TT, Tien NLB, Tran DK, Jeong JH, Anh PG, Thanh VV, Truong DT, Dinh TC. Recent Progress of Stem Cell Therapy in Cancer Treatment: Molecular Mechanisms and Potential Applications. *Cells* 2020; **9** [PMID: 32121074 DOI: 10.3390/cells9030563]

25 **Mohammadinejad R**, Dehshahri A, Sagar Madamsetty V, Zahmatkeshan M, Tavakol S, Makvandi P, Khorsandi D, Pardakhty A, Ashrafizadeh M, Ghasemipour Afshar E, Zarrabi A. In vivo gene delivery mediated by non-viral vectors for cancer therapy. *J Control Release* 2020; **325**: 249-275 [PMID: 32634464 DOI: 10.1016/j.jconrel.2020.06.038]

26 **Kerr RS**. Surgery in the 2020s: Implications of advancing technology for patients and the workforce. *Future Healthc J* 2020; **7**: 46-49 [PMID: 32104765 DOI: 10.7861/fhj.2020-0001]

27 **Tarassoli SP**. Artificial intelligence, regenerative surgery, robotics? What is realistic for the future of surgery? *Ann Med Surg (Lond)* 2019; **41**: 53-55 [PMID: 31049197 DOI: 10.1016/j.amsu.2019.04.001]

28 **Pata F**, Rausei S, Scabini S, Pellino G. Editorial: Gastrointestinal Surgery: Emerging techniques, controversies and state of art. *Front Surg* 2022; **9**: 1033757 [PMID: 36386521 DOI: 10.3389/fsurg.2022.1033757]

29 **Tsui EY**. A new wave of technology is set to transform surgery for millions of patients. 2018. [cited 18 February 2024]. Available from: https://www.imperial.ac.uk/news/189492/wave-technology-transform-surgery-millions-patients/

30 **Morino M**. The Impact of Technology on Surgery: The Future Is Unwritten. *Ann Surg* 2018; **268**: 709-711 [PMID: 30048330 DOI: 10.1097/SLA.0000000000002936]

31 **Rao PP**, Rao PP, Bhagwat S. Single-incision laparoscopic surgery-current status and controversies. *J Minim Access Surg* 2011; **7**: 6-16 [PMID: 21197236 DOI: 10.4103/0972-9941.72360]

32 **Sotelo R**, de Andrade R, Fernández G, Ramirez D, Di Grazia E, Carmona O, Moreira O, Berger A, Aron M, Desai MM, Gill IS. NOTES hybrid transvaginal radical nephrectomy for tumor: stepwise progression toward a first successful clinical case. *Eur Urol* 2010; **57**: 138-144 [PMID: 19406563 DOI: 10.1016/j.eururo.2009.04.031]

33 **Santos BF**, Enter D, Soper NJ, Hungness ES. Single-incision laparoscopic surgery (SILS™) versus standard laparoscopic surgery: a comparison of performance using a surgical simulator. *Surg Endosc* 2011; **25**: 483-490 [PMID: 20585958 DOI: 10.1007/s00464-010-1197-5]

34 **Vanderbilt Engineering Graduate Admissions Team**. The Future of Surgery: Augmentation and Automation in Healthcare. August 24, 2023. [cited 18 February 2024]. Available from: https://blog.engineering.vanderbilt.edu/the-future-of-surgery-augmentation-and-automation-in-healthcare

35 **Sayburn A**. Will the machines take over surgery? *BULL RCA Surg England* 2017; **99**: 88-90 [DOI: 10.1308/rcsbull.2017.87]

36 Bertalan Meskó MP. The Technological Future Of Surgery. 2021.

37 **Kawashima K**, Kanno T, Tadano K. Robots in laparoscopic surgery: current and future status. *BMC Biomed Eng* 2019; **1**: 12 [PMID: 32903302 DOI: 10.1186/s42490-019-0012-1]

38 **Ibrahim Mohamed BK**, Barajas-Gamboa JS, Rodriguez J. Endoscopic Bariatric Therapies: Current Status and Future Perspectives. *JSLS* 2022; **26** [PMID: 35444403 DOI: 10.4293/JSLS.2021.00066]

39 **Tarantino I**, Barresi L. Interventional endoscopic ultrasound: Therapeutic capability and potential. *World J Gastrointest Endosc* 2009; **1**: 39-44 [PMID: 21160649 DOI: 10.4253/wjge.v1.i1.39]

40 **Ghosh NK**, Kumar A. Colorectal cancer: Artificial intelligence and its role in surgical decision making. *AI Gastroenterol* 2022; **3**: 36-45 [DOI: 10.35712/aig.v3.i2.36]

41 **O'Connell L**, Winter DC. Computer-assisted technology for enhanced abdominal surgery. *Br J Surg* 2021; **108**: 1014-1016 [PMID: 34041520 DOI: 10.1093/bjs/znab187]

42 **Azari F**, Zhang K, Kennedy GT, Chang A, Nadeem B, Delikatny EJ, Singhal S. Precision Surgery Guided by Intraoperative Molecular Imaging. *J Nucl Med* 2022; **63**: 1620-1627 [PMID: 35953303 DOI: 10.2967/jnumed.121.263409]

43 **Feng B**, Ma XH, Wang S, Cai W, Liu XB, Zhao XM. Application of artificial intelligence in preoperative imaging of hepatocellular carcinoma: Current status and future perspectives. *World J Gastroenterol* 2021; **27**: 5341-5350 [PMID: 34539136 DOI: 10.3748/wjg.v27.i32.5341]

44 **Farhud DD**, Zokaei S. Ethical Issues of Artificial Intelligence in Medicine and Healthcare. *Iran J Public Health* 2021; **50**: i-v [PMID: 35223619]

45 **Pace F**, Buscema M, Dominici P, Intraligi M, Baldi F, Cestari R, Passaretti S, Bianchi Porro G, Grossi E. Artificial neural networks are able to recognize gastro-oesophageal reflux disease patients solely on the basis of clinical data. *Eur J Gastroenterol Hepatol* 2005; **17**: 605-610 [PMID: 15879721 DOI: 10.1097/00042737-200506000-00003]

46 **Glick Y**, Botz B. Photon-counting computed tomography. [cited 18 February 2024]. Available from: https://radiopaedia.org/articles/photon-counting-computed-tomography

47 **Lone SN**, Nisar S, Masoodi T, Singh M, Rizwan A, Hashem S, El-Rifai W, Bedognetti D, Batra SK, Haris M, Bhat AA, Macha MA. Liquid biopsy: a step closer to

transform diagnosis, prognosis and future of cancer treatments. *Mol Cancer* 2022; **21**: 79 [PMID: 35303879 DOI: 10.1186/s12943-022-01543-7]

48 **Koçak B**, Durmaz EŞ, Ateş E, Kılıçkesmez Ö. Radiomics with artificial intelligence: a practical guide for beginners. *Diagn Interv Radiol* 2019; **25**: 485-495 [PMID: 31650960 DOI: 10.5152/dir.2019.19321]

49 **Penrice DD**, Rattan P, Simonetto DA. Artificial Intelligence and the Future of Gastroenterology and Hepatology. *Gastro Hep Advances* 2022; **1**: 581-595 [DOI: 10.1016/j.gastha.2022.02.025]

50 **Lahner E**, Grossi E, Intraligi M, Buscema M, Corleto VD, Delle Fave G, Annibale B. Possible contribution of artificial neural networks and linear discriminant analysis in recognition of patients with suspected atrophic body gastritis. *World J Gastroenterol* 2005; **11**: 5867-5873 [PMID: 16270400 DOI: 10.3748/wjg.v11.i37.5867]

51 **Yang YJ**, Bang CS. Application of artificial intelligence in gastroenterology. *World J Gastroenterol* 2019; **25**: 1666-1683 [PMID: 31011253 DOI: 10.3748/wjg.v25.i14.1666]

52 **Takayama T**, Okamoto S, Hisamatsu T, Naganuma M, Matsuoka K, Mizuno S, Bessho R, Hibi T, Kanai T. Computer-Aided Prediction of Long-Term Prognosis of Patients with Ulcerative Colitis after Cytoapheresis Therapy. *PLoS One* 2015; **10**: e0131197 [PMID: 26111148 DOI: 10.1371/journal.pone.0131197]

53 **Ichimasa K**, Kudo SE, Mori Y, Misawa M, Matsudaira S, Kouyama Y, Baba T, Hidaka E, Wakamura K, Hayashi T, Kudo T, Ishigaki T, Yagawa Y, Nakamura H, Takeda K, Haji A, Hamatani S, Mori K, Ishida F, Miyachi H. Artificial intelligence may help in predicting the need for additional surgery after endoscopic resection of T1 colorectal cancer. *Endoscopy* 2018; **50**: 230-240 [PMID: 29272905 DOI: 10.1055/s-0043-122385]

54 **Harangi B**, Hajdu A, Lampe R, Torok P. Recognizing Ureter and Uterine Artery in Endoscopic Images Using a Convolutional Neural Network. 2017 IEEE 30th International Symposium on Computer-Based Medical Systems (CBMS); 2017 June 22-24; Thessaloniki, Greece. IEEE, 2017: 726-727 [DOI: 10.1109/CBMS.2017.137]

55 **Ştefănescu D**, Streba C, Cârţână ET, Săftoiu A, Gruionu G, Gruionu LG. Computer Aided Diagnosis for Confocal Laser Endomicroscopy in Advanced Colorectal

Adenocarcinoma. *PLoS One* 2016; **11**: e0154863 [PMID: 27144985 DOI: 10.1371/journal.pone.0154863]
56 **Jansen-Winkeln B**, Barberio M, Chalopin C, Schierle K, Diana M, Köhler H, Gockel I, Maktabi M. Feedforward Artificial Neural Network-Based Colorectal Cancer Detection Using Hyperspectral Imaging: A Step towards Automatic Optical Biopsy. *Cancers (Basel)* 2021; **13** [PMID: 33669082 DOI: 10.3390/cancers13050967]
57 **Kumazu Y**, Kobayashi N, Kitamura N, Rayan E, Neculoiu P, Misumi T, Hojo Y, Nakamura T, Kumamoto T, Kurahashi Y, Ishida Y, Masuda M, Shinohara H. Automated segmentation by deep learning of loose connective tissue fibers to define safe dissection planes in robot-assisted gastrectomy. *Sci Rep* 2021; **11**: 21198 [PMID: 34707141 DOI: 10.1038/s41598-021-00557-3]
58 **Das A**, Ben-Menachem T, Cooper GS, Chak A, Sivak MV Jr, Gonet JA, Wong RC. Prediction of outcome in acute lower-gastrointestinal haemorrhage based on an artificial neural network: internal and external validation of a predictive model. *Lancet* 2003; **362**: 1261-1266 [PMID: 14575969 DOI: 10.1016/S0140-6736(03)14568-0]
59 **Billah M**, Waheed S, Rahman MM. An Automatic Gastrointestinal Polyp Detection System in Video Endoscopy Using Fusion of Color Wavelet and Convolutional Neural Network Features. *Int J Biomed Imaging* 2017; **2017**: 9545920 [PMID: 28894460 DOI: 10.1155/2017/9545920]
60 **Wang K**, Lu X, Zhou H, Gao Y, Zheng J, Tong M, Wu C, Liu C, Huang L, Jiang T, Meng F, Lu Y, Ai H, Xie XY, Yin LP, Liang P, Tian J, Zheng R. Deep learning Radiomics of shear wave elastography significantly improved diagnostic performance for assessing liver fibrosis in chronic hepatitis B: a prospective multicentre study. *Gut* 2019; **68**: 729-741 [PMID: 29730602 DOI: 10.1136/gutjnl-2018-316204]
61 **Săftoiu A**, Vilmann P, Gorunescu F, Janssen J, Hocke M, Larsen M, Iglesias-Garcia J, Arcidiacono P, Will U, Giovannini M, Dietrich CF, Havre R, Gheorghe C, McKay C, Gheonea DI, Ciurea T; European EUS Elastography Multicentric Study Group. Efficacy of an artificial neural network-based approach to endoscopic ultrasound elastography in diagnosis of focal pancreatic masses. *Clin Gastroenterol Hepatol* 2012; **10**: 84-90.e1 [PMID: 21963957 DOI: 10.1016/j.cgh.2011.09.014]

62 **Zhao Z**, Gu J. Open surgery in the era of minimally invasive surgery. *Chin J Cancer Res* 2022; **34**: 63-65 [PMID: 35355929 DOI: 10.21147/j.issn.1000-9604.2022.01.06]

63 **Satava RM**. Advanced technologies and the future of medicine and surgery. *Yonsei Med J* 2008; **49**: 873-878 [PMID: 19108007 DOI: 10.3349/ymj.2008.49.6.873]

Table 1 Some of the application of machine learning in gastroenterology[49]

Modality	Clinical presentation/diagnosis	Application
Upper GI endoscopy	Barrett's oesophagus	Identification of early cancerous lesion; target site for biopsy; endoscopic assistance
	Oesophageal cancer	In the diagnosis of SCC
	H. pylori infection	Atrophy *vs* metaplasia
	Gastric cancer	Tumour *vs* non tumorous tissue; depth of invasion
Capsule endoscopy	GI bleed	Source of bleed; detecting pathologic lesions such as erosions and ulcers
	Celiac	Finding villous atrophy
Colonoscopy	Colorectal cancer	Bowel preparation assessment; adenoma detection; assistance
	Ulcerative colitis	Severity and relapses
Ultrasound-based test-fibro scan/elastography	Various liver diseases; benign & malignant	Fibrosis stage
	Pancreatic diseases	Tumour assessment, degree of intrapancreatic fat
	GI pathology	Survival prediction in colorectal cancer; identification of MSI; HCC *vs* cholangiocarcinoma; predict prognosis and survival in HCC

GI: Gastrointestinal; SCC: Squamous cell carcinoma; *H. Pylori*: *Helicobacter pylori*; HCC: Hepatocellular carcinoma.

Table 2 Current use and application of newer tools and technology in gastrointestinal surgery

Disease/pathology	Aim	Artificial intelligence used	Ref.
GERD, atrophic gastritis	Diagnosis	Artificial neural network	Pace *et al*[45], 2005; Lahner *et al*[50], 2005
Acute pancreatitis	Prediction of prognosis-comparing with RANSON, APACHE score	Artificial neural network	Yang *et al*[51], 2019
Ulcerative colitis	Prediction of prognosis after apheresis therapy	Artificial neural network	Takayama *et al*[52], 2015
Colorectal cancer	To predict lymph nodes metastasis	SVM	Ichimasa *et al*[53], 2018
	Recognition of ureter in endoscopic images	Convolutional neural network	Harangi *et al*[54], 2017
	To distinguish normal colonic mucosa from malignant lesion with confocal laser endomicroscopy	Fractal analysis and neural network modelling	Ştefănescu *et al*[55], 2016
	Differentiation of colonic carcinoma from adenoma and healthy mucosa using hyperspectral imaging	Artificial neural network	Jansen-Winkeln *et al*[56], 2021

Gastric cancer	To define safe dissection planes	Deep learning model based on u net	Kumazu *et al*[57], 2021
GI bleed	Predicting mortality, recurrent bleeding, need for therapeutic intervention	Artificial neural network	Das *et al*[58], 2003
GI polyp	On colonoscopy	SVM	Billah *et al*[59], 2017
HBV related fibrosis	Shear wave elastography	Convolutional neural network	Wang *et al*[60], 2019
Pancreatic adenocarcinoma	Image analysis of endoscopic ultrasound	Multilayer perception network	Săftoiu *et al*[61], 2012

GI: Gastrointestinal; GERD: Gastroesophageal reflux disease; APACHE: Accuracy of Acute Physiology and Chronic Health Evaluation; HBV: Hepatitis B virus; SVM: Support vector machine.

91344_Auto_Edited -check.docx

ORIGINALITY REPORT

9%

SIMILARITY INDEX

PRIMARY SOURCES

1	www.ncbi.nlm.nih.gov Internet	250 words — 4%
2	eurjmedres.biomedcentral.com Internet	53 words — 1%
3	L. O'Connell, D. C. Winter. "Computer-assisted technology for enhanced abdominal surgery", British Journal of Surgery, 2021 Crossref	35 words — 1%
4	Zi-Kun Yu, Rui-Ling Xie, Rui You, You-Ping Liu, Xu-Yin Chen, Ming-Yuan Chen, Pei-Yu Huang. "The role of the bacterial microbiome in the treatment of cancer", BMC Cancer, 2021 Crossref	33 words — 1%
5	www.wjgnet.com Internet	31 words — 1%
6	www.verywellhealth.com Internet	28 words — < 1%
7	www.bcg.com Internet	26 words — < 1%
8	Sam P. Tarassoli. "Artificial intelligence, regenerative surgery, robotics? What is realistic	19 words — < 1%

for the future of surgery?", Annals of Medicine and Surgery, 2019
Crossref

9 hdl.handle.net
Internet
17 words — < 1%