

Reply to the reviewer's comments:

To  
The Editor  
Artificial Intelligence in Cancer

September 18, 2023

Dear Sir,

Thank you for reviewing our manuscript entitled “*AI in rectal cancer: what is the future? - 86942*” and encouraging us. We have gone through the comments and made the necessary changes in the manuscript as asked by the reviewers and the editorial office. In the revised manuscript, the changes have been highlighted in yellow. The necessary grammatical corrections have been made. Tables and figures have been sent separately as requested.

Point by point, the reply to the reviewer's comments are as follows:

Reviewer's comments (Reviewer 1)	Reply
Thank you so much for the opportunity to review this paper: AI in rectal cancer: what is the future?" It is a good review, but with more suggestions that ideas.	Thank you very much for your encouraging comments. We fully agree with your opinion regarding more suggestions in our review. Data regarding the role of AI in rectal cancer is sparse, hence, most of our review consists of future propositions, on how AI can improve the diagnosis and management of patients with rectal cancer.
I think the authors should get deeper into the actual implementations of the Artificial Intelligence and what is going now, and the future of this tool. If you can modify this, and update the review, with the tools we are using today, it will be better.	Thanks for the valuable suggestion. We have added the following paragraph to our discussion section to make our points regarding the present and future roles of AI in rectal cancer.  <b>Current and future role of Artificial Intelligence (AI) in the management of rectal cancer:</b>  The role of AI in various diagnostic tools and management of rectal cancer is evolving.  Good research has been done in the field of

the detection of malignant polyps and AI algorithms have been added to CT, MRI, and PET for better staging and treatment decision-making. Radiomics is a new field of AI where computer algorithms analyze medical images, such as MRI scans, to identify features that may be unique to cancer. Currently, ESMO has come up with guidelines which are based on pre-operative MRI, for treatment planning. Hence, AI-based radiomics can then be used to help doctors plan treatment and predict the risk of recurrence. Precision medicine is another newer concept where a patient's genetic mutation is used to plan perioperative treatment. A sub-field of AI, machine learning can be used to identify genetic data and patient records to predict prognosis .

Intra-operative role of AI in assisting the surgeon in obtaining adequate resection margin, avoidance of injury to surrounding organs (Ureter, urethra, urinary bladder, pre-sacral venous plexus, prostate, iliac vessels, etc.), and autonomic nerve preservation is still in its infancy but seems promising.

Virtual reality is another domain of technology that creates a realistic simulation of surgery, which can be of help to train surgeons for difficult and challenging surgeries. The use of AI can help intra-operative identification of safe resection plane (conventional mesorectal plane vs. extended mesorectal plane), and surrounding organs. Virtual reality can also be used to deliver pain relief and relaxation therapy. As commonly discussed today in every sphere of life, a Chatbot (ChatGPT) can help a patient with rectal cancer to alleviate anxiety, regulate hospital visits, and check compliance with the treatment plans as it can simulate conversation with humans. Chatbots are being used to provide information and support to patients with rectal cancer, as well as to collect data that can be used to improve treatment. As oncologists have found a growing interest in the role of immunotherapy in rectal cancer, due to fewer side effects and better efficacy (Dostarlimab in mismatch repair deficient locally advanced rectal cancer),

	<p><b>theragnostic</b> which is a combined approach to diagnosis and treatment, AI can be used to develop personalized therapies (immunotherapy). Robotic surgery is a boon of AI in intra-operative assistance, with margin assessment, preventing injury to surrounding organs, such that rectal cancer surgeries are being done with greater precision and less risk of complications. AI is being used to develop robotic surgical systems that are even more precise and efficient. Further combination of clinical profile, and genetic mutation can help to prognostication and plan adjuvant treatment or a robust follow-up. Furthermore, AI-powered cytopathology in the detection of cancer cells, newer more effective drug discovery, personalized medicine, surgical decision-making, rehabilitation can improve patient outcome in rectal cancer.</p>
<p>Reviewer's comments (Reviewer 2)</p>	
<p>The authors provide an overview of the future application of AI technology in rectal cancer. The selected topic is closely related to clinical practice, and it describes the role of AI technology in the diagnosis/treatment</p>	<p>Thank you very much for acknowledging our manuscript which describes day-to-day issues in the management of rectal cancer and how AI can improve the diagnosis, management, and prognostication.</p>

<p>of rectal cancer more comprehensively, referring to many the latest advances in the field of AI, and the narrative is more comprehensive, three-dimensional, and relevant.</p>	
<p>However, there are some problems, is that the authors should fully consider the medical ethics involved in the clinical application of AI, as well as how to solve the deviation and the series of doctor-patient disputes and legal proceedings caused by the application of AI technology in clinical practice? In fact, the application of AI technology needs to be guaranteed by a standardized legal system, and it is crucial to further regulate the clinical application of AI technology from the legal level.</p>	<p>Yes, we think it is apt to mention a bit of ethics in our article, as AI is going to bring a lot of legal and ethical issues soon with its rampant use and even it is more when patient care and patient emotion is taken into consideration.</p> <p>Following paragraph has been added following the discussion section</p> <p><b>Rectal cancer, AI and Ethical implications:</b></p> <p>Today AI has infiltrated into everyone's day to day life in some or other form and its role in the medicine is immense. However, AI poses a risk to the basic tenets of patient care “right to health’ by compromising patients’ privacy, and autonomy and therefore is not beyond the ethical issues. Over the years, the potential risk of AI in terms of ethical, legal, and social implications include 1) neutral values reflected by AI algorithms (in carcinoma rectum, the neutral value i.e. not a bad or good risk doesn’t add to treatment planning, rather add to anxiety and concern), explain ability or interpretability of AI algorithms, data concerns (authenticity of a</p>

large volume of data provided for training of AI). In rectal cancer, data may be obtained from populations from different geographical locations, ethnicities, and genetic makeup, which prevents any algorithm unification. An AI algorithm can perform better in one population than another. Other drawbacks include professional responsibility, bias, and legal risk. Though AI can perform many tasks of the human brain, however, a patient-doctor relationship is essential for the psychological alleviation of anxiety and concern of any patient. The legal impact of AI may be categorized into- differential access to high-quality health care, transparency to doctors and patients, social bias, deviation from patient's well-being, risk of automation, de-skilling and change in liability, and risk to privacy. To regulate the patient-doctor relationship, the "Oviedo Convention-European Convention on Human Rights and Biomedicine- 1997" has been amended. In rectal cancer, the patient holds a key position, as its multimodality management needs

multiple doctors treating one patient and it cannot be made by a single algorithm.

As with any newer technology, AI also comes with some legal implications that need regulation. Currently, an international regulation system is lacking, however a few documents available are the Okinawa Charter on Global Information Society (G8 Kyushu-Okinawa Summit Meeting 2000, Kyushu-Okinawa Japan), OECD Council Recommendation on Artificial Intelligence (adopted by the Council at Ministerial Level on 22 May 2019), G20 Ministerial Statement on Trade and Digital Economy (2019, Japan), etc. The goals of legal regulation include the creation of a unified digital space in AI, harmonization of national and international legal regimens, non-discriminatory access to AI, and ensuring legal liability of AI developers, administrators, and operators. A good preoperative and perioperative deliberations between patient, relatives and treating team of doctors, about the benefits/ pros and cons/

	<p>technicality along with difference in the treatment outcomes which may arise out of AI based treatment versus pure classical clinical decision-based treatment. may resolve the patient-doctor conflict to great extent.</p> <p><b>(Minor changes also have been made in conclusions)</b></p>
Comments from the editorial office	
New language certificate along with the manuscript	Attached
I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the Artificial Intelligence in Cancer, and the manuscript is conditionally accepted.	Thank you.
Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned.	Table modification has been done.