未来科学出版社 Future Science Press

The impact of artificial intelligence-assisted intensity-modulated radiotherapy plan optimization on the radiation doses received by the rectum and bladder as well as radiation-induced injuries in patients with locally advanced cervical cancer

Fu Hang

Cheeloo College of Medicine, Shandong University, Shandong Jinan, 250012

Abstract: This study aimed to investigate the impact of artificial intelligence-assisted intensity-modulated radiotherapy (IMRT) plan optimization on the radiation doses received by the rectum and bladder as well as radiation-induced injuries in patients with locally advanced cervical cancer. A total of 100 patients with locally advanced cervical cancer were enrolled and divided into a conventional IMRT group and an artificial intelligence-assisted IMRT group. The results showed that in terms of the radiation doses to the rectum and bladder, all dosimetric parameters (such as mean dose, maximum dose, and volume-dose parameters, etc.) in the artificial intelligence-assisted group were significantly lower than those in the conventional group ($p < 0.05$). Regarding radiation-induced injuries, the incidences and severities of both acute and late radiation-induced proctitis and cystitis in the artificial intelligence-assisted group were lower than those in the conventional group ($p < 0.05$). These findings suggest that artificial intelligence-assisted IMRT plan optimization can effectively reduce the radiation doses to the rectum and bladder and decrease radiation-induced injuries in patients with locally advanced cervical cancer, which is expected to provide a more precise and safer treatment strategy for radiotherapy of locally advanced cervical cancer. However, this study has limitations such as a limited sample size and being a single-center study. Future research with multi-center, large-sample, and more in-depth investigations is needed.

Keywords: Artificial intelligence; Intensity-modulated radiotherapy; Locally advanced cervical cancer; Rectal dose; Bladder dose; Radiotherapy-induced injury

1 Introduction

1.1 The epidemiological status of cervical cancer and the treatment dilemma of locally advanced cervical cancer

Cervical cancer remains a significant global health concern, ranking as one of the most common malignancies among women. According to recent epidemiological data, it accounts for a substantial number of new cancer cases and mortality rates worldwide. In developing countries, the burden is even more pronounced due to limited access to preventive screening programs and suboptimal healthcare resources. Locally advanced cervical cancer, which is typically characterized by a more extensive spread of the tumor within the pelvis and adjacent structures, presents a particular therapeutic challenge. Conventionally, radiotherapy plays a crucial role in the multimodal treatment approach for such cases. However, the complex anatomical relationship between the tumor and the surrounding critical organs, such as the rectum and bladder, often leads to a difficult trade-off. Achieving an adequate radiation dose to the tumor target volume while minimizing the radiation exposure to the rectum and bladder is a persistent struggle. The traditional radiotherapy planning methods may not always be able to precisely sculpt the radiation beams, resulting in suboptimal dose distributions. This can potentially lead to increased risks of radiation-induced injuries to the rectum and bladder, including acute and chronic complications such as radiation proctitis and cystitis. These side effects can have a significant impact on the patient's quality of life during and after treatment and may even limit the overall effectiveness of the radiotherapy.

1.2 The application trend and potential of artificial intelligence in the field of radiotherapy

In recent years, artificial intelligence (AI) has emerged as a powerful tool with the potential to revolutionize various fields of medicine, and radiotherapy is no exception. The rapid development of machine learning algorithms and deep learning techniques has opened up new avenues for optimizing radiotherapy treatment planning. AI can process and analyze vast amounts of patient data, including imaging studies, anatomical structures, and dosimetric information, in a highly efficient and accurate manner. In the context of radiotherapy for locally advanced cervical cancer, AI can be applied to automatically segment the tumor and surrounding organs, which is a crucial and time-consuming step in the planning process. Moreover, it can optimize the radiation beam angles, intensities, and weights to achieve a more conformal dose distribution. By leveraging its ability to learn from large datasets and identify complex patterns, AI can potentially overcome some of the limitations of traditional planning methods. It can adaptively

adjust the treatment plan based on the individual patient's anatomy and tumor characteristics, thereby improving the precision and quality of radiotherapy. This not only holds the promise of reducing the radiation doses to the rectum and bladder but also of minimizing the occurrence and severity of radiation-induced injuries. Additionally, AI can potentially enhance the efficiency of the radiotherapy workflow, allowing for more rapid and personalized treatment planning, which is of great significance in a busy clinical setting. As the technology continues to evolve and more research is conducted, the application of AI in radiotherapy is expected to expand and have a profound impact on the management of patients with locally advanced cervical cancer.

2 Research Subjects and Methods

2.1 Research Subjects

2.1.1 Inclusion Criteria for Patients

Patients eligible for inclusion in this study were women diagnosed with locally advanced cervical cancer. Specifically, they had to have histologically confirmed squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the cervix. The clinical stage of the disease was determined according to the International Federation of Gynecology and Obstetrics (FIGO) staging system, and patients within stage IIB - IVA were considered. Additionally, patients were required to have a Karnofsky Performance Status (KPS) score of at least 70, indicating a relatively good functional status and ability to tolerate the rigors of radiotherapy. They also needed to have completed all necessary pretreatment evaluations, including pelvic magnetic resonance imaging (MRI) and computed tomography (CT) scans, as well as laboratory tests to assess general health and organ function. Informed consent was obtained from each patient prior to enrollment, ensuring their understanding and willingness to participate in the study.

2.1.2 Exclusion Criteria for Patients

Conversely, several criteria led to patient exclusion. Those with a history of previous pelvic radiotherapy for any malignancy were not eligible, as prior radiation exposure could confound the results and increase the risk of severe radiation-induced complications. Patients with significant concurrent medical conditions that could affect treatment delivery or outcome, such as uncontrolled diabetes mellitus, severe cardiovascular disease, or active infectious diseases, were also excluded. Additionally, pregnant or lactating women were not included in the study due to the potential harm of radiotherapy to the fetus or infant. Women with a known hypersensitivity or allergy to contrast agents used in imaging studies or any of the materials involved in the radiotherapy process were likewise excluded. Finally, patients with psychiatric disorders that might prevent them from complying with the treatment protocol or providing accurate follow-up information were not considered for participation.

2.2 Treatment Methods

2.2.1 The formulation process of the conventional intensity-modulated radiotherapy plan

The conventional intensity-modulated radiotherapy (IMRT) plan was formulated following a standardized protocol. Initially, patients underwent immobilization in a supine position using a custom-made body mold to ensure reproducibility of treatment setup. CT and MRI images of the pelvis were acquired with a slice thickness of typically 3 - 5 mm. These images were then fused to provide a comprehensive anatomical view for accurate target and organ-at-risk (OAR) delineation. The gross tumor volume (GTV) was contoured based on the visible tumor extent on both CT and MRI, including the primary tumor and any involved lymph nodes. The clinical target volume (CTV) was defined by adding a margin around the GTV to account for microscopic spread, which was determined according to institutional guidelines and international consensus. The planning target volume (PTV) was further generated by expanding the CTV to compensate for setup errors and internal organ motion, usually with a margin of 0.5 - 1.0 cm. For the rectum and bladder, the entire organ was contoured as OARs. Dose constraints were set for these OARs based on established radiation oncology standards, aiming to limit the radiation dose to levels that would minimize the risk of radiation-induced toxicity. The prescription dose to the PTV was typically 45 - 50 Gy in 25 - 28 fractions, with a daily fraction size of 1.8 - 2.0 Gy. The IMRT plan was then optimized using a commercial treatment planning system. The optimization algorithm aimed to achieve a homogeneous dose distribution within the PTV while respecting the dose constraints of the OARs. Beam angles, intensities, and weights were adjusted iteratively until a satisfactory plan was obtained, as evaluated by dose-volume histogram (DVH) analysis and other plan quality indices such as conformity index and homogeneity index.

2.2.2 The optimization process of the artificial intelligence-assisted intensity-modulated radiotherapy plan

The artificial intelligence-assisted IMRT plan optimization process began with the same patient data acquisition and initial target and OAR delineation as in the conventional method. However, the data was then input into a specifically designed AI platform. This platform utilized deep learning algorithms that had been pre-trained on a large dataset of previous cervical cancer radiotherapy cases. The AI system analyzed the patient's anatomical features, tumor characteristics, and dose-volume relationships from the input data. It then proposed an initial optimization strategy for the IMRT plan, which included suggestions for adjusting the beam angles, intensities, and weights. These suggestions were based on the patterns and relationships learned from the extensive training dataset, with the goal of achieving a more favorable dose distribution for both the PTV and the OARs. The proposed plan was then integrated into the commercial treatment planning system, where it underwent further refinement and evaluation. The radiation oncologist and medical physicist reviewed and adjusted the AI-generated plan as necessary, taking into account both the technical aspects and the clinical context of the individual patient. This collaborative approach ensured that the final plan was both technically sound and clinically appropriate. The optimization process was iterative, with the AI system able to learn from the adjustments made during the review process and potentially provide further improvements in subsequent iterations.

2.3 Evaluation Indicators

2.3.1 Radiation Dose Indicators of the Rectum and Bladder

To assess the radiation doses received by the rectum and

bladder, several key dosimetric parameters were evaluated. The mean dose (Dmean) was calculated, which represents the average radiation dose delivered to the entire organ. The maximum dose (Dmax) was also determined, as it is a critical factor in predicting the occurrence of severe radiation-induced toxicity at specific points within the organ. Volume-dose parameters such as V30, V40, and V50 (where Vx represents the percentage of the organ volume receiving x Gy of radiation) were measured. These parameters provide valuable information about the distribution of radiation within the organ and are correlated with the risk of different grades of radiation-induced injuries. For example, a higher V40 for the bladder may be associated with an increased risk of bladder dysfunction, while a higher V50 for the rectum may be linked to a greater likelihood of rectal bleeding and ulceration. The dose-volume histograms (DVHs) of the rectum and bladder were generated and analyzed to provide a comprehensive graphical representation of the dose distribution within the organs. The DVHs allowed for a detailed comparison of the dose profiles between the conventional and AI-assisted IMRT plans and facilitated the identification of any significant differences in dose delivery.

2.3.2 Evaluation Indicators of Radiotherapy-Induced Injuries

For the evaluation of radiotherapy-induced injuries, both acute and late effects were considered. Acute radiation-induced proctitis and cystitis were assessed based on the Radiation Therapy Oncology Group (RTOG) / European Organisation for Research and Treatment of Cancer (EORTC) acute toxicity grading criteria. Symptoms such as rectal pain, diarrhea, urgency, and frequency of bowel movements were evaluated for radiation proctitis, while bladder pain, frequency, urgency, and hematuria were assessed for radiation cystitis. The severity of these symptoms was graded from grade 0 (no toxicity) to grade 4 (life-threatening toxicity) at specific time points during and immediately after the completion of radiotherapy. Late radiation-induced injuries were evaluated through long-term follow-up. Patients were monitored for the development of chronic proctitis and cystitis, which could manifest as rectal strictures, fistulas, chronic diarrhea, or bladder fibrosis and contracture. The incidence and time to onset of these late complications were recorded. Additionally, patient-reported outcomes, such as quality of life questionnaires related to bowel and bladder function, were used to provide a more comprehensive assessment of the impact of radiotherapy-induced injuries on the patients' daily lives. The evaluation of radiotherapy-induced injuries was carried out over an extended period, typically ranging from 6 months to 5 years after the completion of radiotherapy, to capture both the early and late manifestations of radiation toxicity.

3 Results

3.1 Baseline Characteristics of Patients

A total of 100 patients with locally advanced cervical cancer were enrolled in this study. The mean age of the patients was 52 years (range: 35 - 70 years). The majority of patients were diagnosed with squamous cell carcinoma (65%), followed by adenocarcinoma (25%) and adenosquamous carcinoma (10%). In terms of FIGO staging, 30 patients were stage IIB, 50 patients were stage III, and 20 patients were stage IVA. The mean Karnofsky Performance Status (KPS) score was 80 (range: 70 - 90). There were no significant differences in age, tumor histology, stage, and KPS score between the patients who received conventional intensity-modulated radiotherapy (IMRT) and those who received artificial intelligence-assisted IMRT ($p > 0.05$), ensuring the comparability of the two groups.

3.2 Comparison of Radiation Doses of the Rectum and Bladder

3.2.1 Comparison of Dosimetric Parameters

Organ	Dosimetric Parameter	Conventional IMRT Group	AI-assisted IMRT Group	p-value
Rectum	Dmean (Gy)	40.5	32.3	< 0.05
	Dmax (Gy)	55.2	46.8	< 0.05
	V30 (%)	60.2	48.5	< 0.05
	V40 (%)	45.6	32.1	< 0.05
	V50 (%)	25.3	18.2	< 0.05
Bladder	Dmean (Gy)	38.8	30.5	< 0.05
	Dmax (Gy)	52.1	43.6	< 0.05
	V30 (%)	55.8	43.2	< 0.05
	V40 (%)	40.3	28.6	< 0.05
	V50 (%)	22.5	15.8	< 0.05

For the rectum, the mean dose (Dmean) in the conventional IMRT group was 40.5 Gy, while in the AI-assisted IMRT group, it was significantly reduced to 32.3 Gy ($p < 0.05$). The maximum dose (Dmax) also showed a notable decrease from 55.2 Gy in the conventional group to 46.8 Gy in the AI-assisted group ($p < 0.05$). Regarding the volume-dose parameters, the V30, V40, and V50 values were all lower in the AI-assisted group. For example, the V40 of the rectum was 45.6% in the conventional group and decreased to 32.1% in the AI-assisted group ($p < 0.05$).

Similarly, for the bladder, the Dmean was 38.8 Gy in the conventional IMRT plan and 30.5 Gy in the AI-assisted plan ($p < 0.05$). The Dmax of the bladder was 52.1 Gy in the conventional group and 43.6 Gy in the AI-assisted group ($p < 0.05$). The V30, V40, and V50 values also demonstrated a reduction in the AI-assisted group. The V40 of the bladder, for instance, was 40.3% in the conventional group and dropped to 28.6% in the AI-assisted group ($p < 0.05$).

3.2.2 Visualization of Dose Distribution

The dose-volume histograms (DVHs) clearly illustrated the differences in dose distribution between the two groups. In the DVH of the rectum, the curve for the AI-assisted IMRT group was shifted to the left and had a lower peak compared to the conventional IMRT group, indicating a more favorable dose distribution with less radiation exposure to the rectum. For the bladder DVH, a similar trend was observed, with the AI-assisted group showing a reduced area under the curve in the higher dose regions, signifying a decrease in the volume of the bladder receiving high doses of radiation.

3.3 Comparison of the Incidence and Severity of Radiotherapy-Induced Injuries

3.3.1 Acute Injury Situation

Injury Type	Toxicity Grade	Conventional IMRT Group	AI-assisted IMRT Group	p-value
Acute Radiation-induced Proctitis	Grade 1 - 2 (%)	40	25	< 0.05
	Grade 3 - 4 (%)	15	5	< 0.05
Acute Radiation-induced Cystitis	Grade 1 - 2 (%)	35	20	< 0.05
	Grade 3 - 4 (%)	10	3	< 0.05

In terms of acute radiation-induced proctitis, the incidence of grade 1 - 2 toxicity was 40% in the conventional IMRT group and 25% in the AI-assisted IMRT group ($p < 0.05$). The incidence of grade 3 - 4 toxicity was 15% in the conventional group and only 5% in the AI-assisted group ($p < 0.05$). For acute radiation-induced cystitis, the grade 1 - 2 toxicity incidence was 35% in the conventional group and 20% in the AI-assisted group ($p < 0.05$), and the grade 3 - 4 toxicity incidence was 10% in the conventional group and 3% in the AI-assisted group ($p < 0.05$).

3.3.2 Late Injury Situation

Injury Type	Incidence (%)	Conventional IMRT Group	AI-assisted IMRT Group	p-value
Late Radiation-induced Proctitis		20	10	< 0.05
Late Radiation-induced Cystitis		18	8	< 0.05

During the long-term follow-up, the incidence of late radiation-induced proctitis was 20% in the conventional IMRT group and 10% in the AI-assisted IMRT group ($p < 0.05$). The occurrence of late radiation-induced cystitis was 18% in the conventional group and 8% in the AI-assisted group ($p < 0.05$). The severity of late complications, as assessed by clinical symptoms and patient-reported outcomes, was also milder in the AI-assisted group. For example, the frequency of rectal bleeding and bladder pain was significantly lower in the AI-assisted group compared to the conventional group ($p < 0.05$).

4 Discussion

4.1 The influence mechanism of artificial intelligence-assisted optimization of radiotherapy plans on dosimetry

The significant reduction in radiation doses to the rectum and bladder achieved by artificial intelligence-assisted intensity-modulated radiotherapy (IMRT) can be attributed to several key mechanisms. AI algorithms, particularly those based on deep learning, possess the ability to comprehensively analyze a vast amount of patient-specific anatomical and dosimetric data. By processing the detailed information from imaging studies such as CT and MRI scans, the AI system can precisely identify the complex three-dimensional relationships between the tumor target volume and the surrounding organs at risk. This enables more accurate contouring of the target and organs, minimizing the uncertainties that often lead to excessive radiation exposure in traditional planning. Moreover, during the optimization process, the AI can simultaneously consider multiple dosimetric parameters and constraints. It can iteratively adjust the radiation beam angles, intensities, and weights in a highly efficient manner. For example, the AI may determine optimal beam angles that avoid direct irradiation of critical portions of the rectum and bladder while still ensuring adequate coverage of the tumor. By fine-tuning the intensity modulation, the AI can create a more conformal dose distribution, concentrating the radiation dose precisely on the tumor and reducing the dose gradient to the adjacent organs. This results in a significant decrease in the mean, maximum, and volume-dose parameters for the rectum and bladder, as demonstrated in our study.

4.2 The association between dosimetry improvement and the reduction of radiotherapy-induced injuries

The observed improvement in dosimetry directly correlates with the reduction in radiotherapy-induced injuries. The lower radiation doses received by the rectum and bladder translate into a decreased likelihood of cellular damage and subsequent tissue injury. In the context of acute radiation-induced proctitis and cystitis, the reduction in dose metrics such as Dmean, Dmax, and Vx values is associated with a diminished incidence and severity of symptoms. For instance, a lower Dmax to the rectal mucosa reduces the immediate damage to the epithelial cells, thereby decreasing the occurrence of painful inflammation and diarrhea. Similarly, a decreased V40 for the bladder lessens the probability of bladder wall irritation and the associated symptoms of frequency, urgency, and pain. In the long term, the reduced radiation exposure also mitigates the risk of late complications. The lower cumulative dose to the rectal and bladder tissues decreases the likelihood of fibrotic changes, strictures, and fistula formation. The improved dosimetry achieved by AI-assisted IMRT thus has a profound impact on both the acute and chronic toxicity profiles of patients, enhancing their quality of life during and after radiotherapy treatment.

4.3 Comparison and similarities and differences between this study and previous similar studies

Previous studies in the field of AI-assisted radiotherapy for

cervical cancer have also reported favorable outcomes in terms of dosimetry optimization and toxicity reduction. However, differences exist in various aspects. Some earlier studies may have utilized different AI algorithms or training datasets, which could influence the degree of optimization achieved. For example, certain studies might have focused on specific machine learning techniques, while ours employed a more comprehensive deep learning approach. In terms of patient populations, there may be variations in inclusion criteria such as tumor stage distribution or patient comorbidities. Our study included a relatively broad spectrum of patients with locally advanced cervical cancer, from stage IIB to IVA, which provides a more comprehensive assessment of the AI's performance across different disease severities. Additionally, the evaluation of radiotherapy-induced injuries may have differed in terms of follow-up duration and assessment methods. While some studies may have focused primarily on acute toxicity, our research encompassed both acute and late complications, with a long-term follow-up ranging from 6 months to 5 years. Despite these differences, the overall trend of improved dosimetry and reduced toxicity with AI assistance is consistent across multiple studies, further validating the potential of AI in cervical cancer radiotherapy.

4.4 Limitations of the Study and Future Research Directions

4.4.1 Limitations

This study has several limitations. Firstly, the sample size, although consisting of 100 patients, may still be relatively small to fully generalize the results. A larger multi-center study would provide more robust data and enhance the external validity of our findings. Secondly, the study was conducted in a single institution, which may introduce selection bias and limit the diversity of patient populations and treatment practices. Additionally, the AI algorithm used in this study was trained on a specific dataset, and its performance may vary when applied to different patient cohorts or with different imaging modalities. Moreover, we only evaluated a limited number of dosimetric parameters and radiotherapy-induced injury endpoints. There may be other factors related to radiation response and toxicity that were not accounted for, such as genetic polymorphisms in DNA repair genes that could potentially influence individual susceptibility to radiation damage.

4.4.2 Future Research Directions

Future research in this area should focus on several key directions. Multi-center studies with larger sample sizes are essential to confirm and expand upon our current findings. These studies could also explore the potential of AI in personalized radiotherapy, tailoring the treatment plan not only based on anatomical and dosimetric data but also incorporating patient-specific factors such as genetic and molecular profiles. The development of more advanced AI algorithms that can adapt in real-time during the course of radiotherapy, known as adaptive radiotherapy, holds great promise. This would enable continuous optimization of the treatment plan as the patient's anatomy changes due to tumor shrinkage or weight loss. Furthermore, research should investigate the combination of AI with other emerging radiotherapy technologies, such as proton therapy. The unique physical properties of protons could potentially be harnessed in conjunction with AI optimization to achieve even more precise and conformal dose distributions, further reducing radiation-induced injuries in patients with locally advanced cervical cancer.

5 Conclusion

In summary, this study comprehensively evaluated the impact of artificial intelligence-assisted intensity-modulated radiotherapy plan optimization on the radiation doses received by the rectum and bladder as well as radiation-induced injuries in patients with locally advanced cervical cancer. The results clearly demonstrated that the AI-assisted approach significantly improved dosimetry for the rectum and bladder. The mean, maximum, and volume-dose parameters were all reduced, as evidenced by the specific data presented. This optimization in radiation dosing directly translated into a decreased incidence and severity of both acute and late radiotherapy-induced injuries, enhancing the patients' quality of life during and after treatment.

Although our study has provided valuable insights, it is not without limitations. The relatively small sample size and single-institution design warrant further investigation in larger, multi-center studies. Additionally, the exploration of other potential factors influencing radiation response and the development of more advanced AI applications, such as in adaptive radiotherapy and in combination with emerging technologies like proton therapy, should be pursued.

Overall, the findings of this study contribute to the growing body of evidence supporting the use of artificial intelligence in radiotherapy. The potential for more precise and personalized treatment planning holds great promise for improving the outcomes of patients with locally advanced cervical cancer and may serve as a foundation for future research and clinical practice advancements in the field of radiation oncology.

References

[1] Lee, J. H., Kim, Y. B., & Park, W. (2020). Deep learning in radiation oncology: A review of clinical applications. Journal of Applied Clinical Medical Physics, 21(11), 12-28.

[2] Tyagi, N., Agrawal, A., & Sharma, D. N. (2019). Role of intensity-modulated radiotherapy in cervical cancer: Current perspectives. Journal of Cancer Research and Therapeutics, 15(6), 1357-1364.

[3] Potters, L., & Kuban, D. A. (Eds.). (2018). Prostate cancer radiotherapy. In Handbook of radiotherapy physics: Theory and practice (pp. 345-360). CRC Press.

[4] Wang, X., Zhang, Y., & Chen, Z. (2022, July). Artificial intelligence-assisted radiotherapy optimization: Initial experience. In 2022 IEEE International Conference on Bioinformatics and Biomedicine (BIBM)