Application of titanium clip marking in localization of 37 cases of rectal cancer before radiotherapy

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Abstract

Objectives: At present, locating radiotherapy targets for rectal cancer is mostly assisted by computed tomography (CT) and/or magnetic resonance (MR) imaging. This article discusses the role of the upper and lower margins of rectal cancer lesions under colonoscopy in accurately delineating target areas of radiotherapy.

Methods: A total of 37 patients with rectal cancer diagnosed by histopathology at the Shandong Provincial Cancer Hospital, affiliated with Shandong University, from 1 July 2017 to 1 August 2018 were selected before treatment. The upper and lower margins of the lesion were marked by titanium clips under the assistance of ultrasound and a magnifying endoscope in each patient, as well as the lower edge of the titanium clip from the anal margin. In the same position and in a thermal plastic membrane body fixation device, patients underwent CT and MR examinations to outline the gross tumor target area (GTV). The radiation therapy planning system calculated the length of the GTV under CT and MR (GTV<sub>CT</sub>, GTV<sub>MR</sub>), and the distance from the lower edge of the GTV to the anal margin. The application value of titanium clip labeling by colonoscopy in radiotherapy localization for rectal cancer was evaluated according to differences of GTV lengths by three methods.

Results: GTVs measured by endoscopic titanium clip labeling, CT localization, and MR localization were 5.84 ± 2.035 cm, 6.97 ± 1.658 cm, and 5.45 ± 2.088 cm, respectively. The length of GTV<sub>titanium clip</sub> was not significantly different from the length of GTV<sub>MR</sub> (P = 0.162). The marked lesion lengths by the endoscopic titanium clips and MR localization were significantly smaller than that measured by CT (GTV<sub>titanium clip</sub> < GTV<sub>CT</sub>, GTV<sub>MR</sub> < GTV<sub>CT</sub>, P < 0.001). The distance between the lower margin of the titanium clip and the anal margin (4.19 ± 1.647 cm) was not significantly different from MR (4.41 ± 1.624 cm; P = 0.231). The distance from the inferior margin of the lesion to the anal margin was significantly greater in measurements from the endoscopic titanium clip and MR localization than CT localization (3.53 ± 1.394 cm; P < 0.001). None of the patients had adverse reactions, such as bleeding or perforation.
1 | INTRODUCTION

Rectal cancer is a common malignant tumor in the digestive tract, and its morbidity and mortality are still on the rise. The location of rectal cancer lesions are deep in the pelvic cavity, where the anatomy is complicated and operations are difficult. Patients with rectal cancer in China are mainly in the middle and late stages, from which it is easy to relapse. In recent years, the comprehensive treatment of surgery combined with radiotherapy and chemotherapy (neoadjuvant therapy) has been widely used in clinical practice, which has improved the outcome of locally advanced rectal cancer. Precise radiotherapy is a newly proposed treatment in recent years. With the continuous development of this technology, accurately positioning the gross tumor volume (GTV) is the premise and basis of radiotherapy. For rectal lesions, colonoscopy can enable surgeons to accurately see the size of the lesion, and the stratification of the lesion can be accurately determined by means of a magnifying endoscope and endoscopic ultrasound. In recent years, with the rapid development of minimally invasive endoscopic examinations and treatment technologies, endoscopic titanium clip-labeled upper and lower tumor boundaries, and GTVs mapped by computed tomography (CT) for esophageal cancer, bladder cancer, and pancreatic cancer have been studied more in China and abroad, and are popular in clinical application. At present, the determination of radiotherapy target areas for rectal cancer is mainly determined by abdominal pelvic CT and pelvic magnetic resonance (MR) imaging. According to the Chinese colorectal cancer diagnosis and treatment specifications (2017 edition), MR and CT are recommended as GTV-positioning applications before neoadjuvant radiotherapy for rectal cancer. The application of titanium clips during colonoscopy to locate the upper and lower margins of the tumor in the radiotherapy target area of rectal cancers is rarely studied in China and abroad. Therefore, applying this technique to assist in positioning and delineating the target area before radiotherapy for rectal cancer provides a new perspective.

2 | METHODS

2.1 Patient selection and general information

Patients with advanced rectal cancer admitted to Shandong Provincial Cancer Hospital affiliated with Shandong University, Jinan, China, from 1 July 2017 to 1 August 2018 were selected. The inclusion criteria were as follows: (i) pathological diagnosis of rectal adenocarcinoma (based on the American Joint Committee on Cancer 8th edition of the colorectal cancer staging system standard) clinical T stage of II–III; and (ii) pelvic radiotherapy history with no contraindications for radiotherapy. The exclusion criteria were as follows: (i) those with radiotherapy contraindications; (ii) those without metal in the body; (iii) inconsistencies between CT and MR scans; or (iv) scans with obvious artifacts. There were 37 patients with rectal adenocarcinoma who met the inclusion criteria, including 21 men (7 patients with pathological stage II, 14 patients with stage III) and 16 women (4 patients with pathological stage II, 12 patients with stage III). The age range was 33–82 years, with a median age of 57 years. The procedure followed in this study was approved by the ethics committee of Shandong Provincial Cancer Hospital affiliated with Shandong University (ethics number SDTHEC201808006), and all patients gave informed consent.

2.2 Study design

All patients emptied their intestinal tract and bladder in advance. Before radiotherapy localization, the same attending endoscopy physician or a more senior physician carried out colonoscopy with one titanium clip on each upper and lower edge of the rectal tumor, and recorded the length of the titanium clip mark on the upper and lower edge (GTV\textsubscript{titanium clip}) and the distance of the titanium clip on the lower edge from the anal edge. The patient was then given 1000 mL of water containing 20 mL 20% diatrizoate meglumine to drink 1 h before localization, and urine was suppressed before the CT scan. The patient was placed on the treatment bed according to the preferred position for intensity-modulated radiation therapy and fixed on the positioning bed plate with the abdominal pelvic fixator. A spiral CT scan (Brilliance16; Philips Healthcare, Amsterdam, the Netherlands) was carried out at a thickness of 5 mm from the upper margin of the second lumbar vertebra to the middle femur. After the CT localization scan, an MR localization scan was carried out immediately according to the same marker points and with the help of the abdominal pelvic fixator to ensure the same positioning. The MR scan was carried out by a GE Healthcare 750w (Chicago, IL, USA) MR imaging system from the upper edge of the third lumbar spine to the perineum at a thickness of 5 mm. After the scan, the target area was delineated by two professional physicians at or above the head of the radiotherapy department, and the length of GTVs (GTV\textsubscript{CT}, GTV\textsubscript{MR}) by CT and MR, and the distance between the lower margin of the GTV and the anal margin were calculated with the

Conclusions: Tumors labeled with titanium clips through colonoscopy contribute to the precise delineation of the target area before radiotherapy for rectal cancer. This technique is shown to have value in clinical application.

KEYWORDS
colonoscopy, radiotherapy, rectal cancer, titanium clip
FIGURE 1  Images of upper and lower margins of endoscopic titanium clip-labeled lesion in one patient with rectal adenocarcinoma. (a) Upper margin of lesion. (b) Lower margin of lesion

FIGURE 2  Computed tomography cross-sectional imaging of the upper and lower margins of lesions in a patient with rectal adenocarcinoma. (a) Upper margin of lesion. (b) Lower margin of lesion

help of a treatment planning system (Pinnacle 9.2; Philips Healthcare; window width 350, window level 40). The difference of the delineated target area length, and the distance between the lower and anal margins under the three methods were compared.

2.3   Statistical analysis

Statistical analysis was carried out using SPSS 17.0 (IBM, Armonk, NY, USA). Quantitative data are described. GTV lengths and distances between the lower and anal margins obtained by each method were normally distributed (Q-Q map test), and variance analysis of the block design was carried out. The test level was $\alpha = 0.05$ (bilateral), and $P < 0.05$ was considered statistically significant.

3   RESULTS

3.1   Comparison of GTV_{Titanium Clip}, GTV_{CT}, and GTV_{MR} lengths

The average lengths of endoscopic GTV_{Titanium Clip}, GTV_{CT}, and GTV_{MR} were 5.84 ± 2.035, 6.97 ± 1.658, and 5.45 ± 2.088 cm, respectively. The $F$ statistic for the three different methods was $F = 16.328$, $P = 0.000$. There was no significant difference between GTV_{Titanium Clip} and GTV_{MR} by the least significant difference and Student–Newman–Keuls methods ($P = 0.162$), but there was between GTV_{Titanium Clip} and GTV_{CT} ($P < 0.001$). There were significant differences between GTV_{MR} and GTV_{CT} ($P < 0.001$) Figures 1–3.
3.2 | Comparison of the distance between the titanium clip and CT and MR positioning

The average distances between the endoscopic titanium clip, the CT positioning margin, and the MR positioning margin from the anal margin were 4.19 ± 1.647, 3.53 ± 1.394, and 4.41 ± 1.624 cm, respectively. The F statistic for the three different methods was $F = 13.078$, $P = 0.000$. After least significant difference and Student–Newman–Keuls analysis, the distance between the lower margin of the titanium clip and the anal margin was similar to the distance from the anal margin to the MR-positioned margin ($P = 0.231$). The distance between the posterior margin of the titanium clip and the location of the MR-positioned margin was significantly higher than that from the location under CT ($P < 0.001$).

None of the patients had adverse reactions, such as bleeding or perforation.

4 | DISCUSSION

The key and foundation of radiotherapy for rectal cancer is accurate target delineation before radiotherapy. At present, targets for rectal cancer radiotherapy are mainly located by CT and MR imaging. Titanium clips inserted by endoscopy have the benefits of being small, light, resistant to corrosion, clip tightly, and are less likely to be rejected by the body, among many other advantages. These clips have been widely applied in the digestive tract in endoscopic minimally invasive treatments of bleeding and wound suturing, surgical positioning, and other fields, and they are frequently reported in early esophageal cancer before radiotherapy positioning with good results.11–12

As the lower section of the colorectal cancer had no obvious cavity within or near the density that could cause interference under CT localization, and MR has no radiation and high resolution of soft tissue, CT in combination with MR imaging is most commonly used to define targets for colorectal cancer radiotherapy. Domestic and foreign studies have shown that the lengths of GTVs mapped before radiotherapy for lower rectal cancer using MR localization are shorter than those under the original CT localization, and the lower margin of the tumor was further from the anal margin with higher accuracy.13–15

The results of the present study are similar to the domestic study. In that study, the MR positioning method measured the average GTV length to be significantly smaller than under CT localization, and the distance between the MR-positioned margin of the GTV from the anal margin was significantly greater than that of the CT-positioned GTV margin from the anal margin. Because of its precise positioning ability, MR has been widely used in colorectal cancer in clinical radiotherapy for target delineation in China and elsewhere, and the application of endoscopic titanium clip markers in middle-to-late colorectal cancer before radiotherapy positioning is not well studied.

The present study showed that for the vast majority of patients with locally advanced rectal cancer, tumor sizes measured by endoscopic titanium clips and MR localization are significantly smaller than those measured by CT localization, and there was no significant difference between GTVs measured by MR localization or titanium clips. To analyze the reasons, endoscopic ultrasonography can clearly show the lesion invasion depth and range and guide the titanium clip to mark the rectal tumor range in real time. Titanium clip markers are as accurate as MR. The mean distance between the lower margin marked by a titanium clip or MR-measured GTV and the anal margin was not significantly different. The distance between the lower margin of the titanium clip labeled under endoscopy and the anal margin was significantly greater than that of the lower margin of a CT-positioned GTV.

The results of the present study showed that for rectal cancer patients, the length and accuracy of a labeled tumor by endoscopy-placed titanium clips was shorter and more accurate than by CT localization, and its range was similar to that of MR, which could narrow the
target area so as to reduce the radiation damage to adjacent tissues and organs. In addition, the ranges of three of our patients with endoscopic titanium clips were greater than those measured by CT and MR. This is because for some patients with rectal cancer, their advanced lesions have not invaded very deep. The appearance of these lesions is two-toned as a result of their pathological changes, and their infringement on the surrounding mucosa is shallow. By CT and MR, these are hard to image. However, with endoscopic ultrasonography and magnifying endoscopes, surgeons can directly observe the microstructure and microvascular abnormalities of these lesions and their mucosal limits, more precisely guide titanium clips to mark pathological changes, and more intuitively and accurately sketch a target for radiotherapy positioning.

A small number of patients were enrolled in the present study, which might have some influence on the results. In future studies, we should continue to expand the sample size. In addition, the length of the titanium clip itself will still bring a slight error to the marker range, which has certain disadvantages for patients with large tumors with intestinal stenosis and difficult endoscopic access. This warrants further study and discussion in the future.

Overall, titanium clips applied through colonoscopy to stage II–III colorectal tumors before radiotherapy positioning are effective for shallow advanced infiltrating lesions, and those that cannot be properly seen by CT and MR imaging. Target mapping using endoscopic titanium clips is more intuitive than CT or MR imaging, and more accurate positioning can be carried out in conjunction with CT and MR radiotherapy as auxiliary means. At the same time, the endoscopic titanium clip marking operation is simple, involves no radiation, is cost-effective, is not affected by any metal already present in the patient, and the titanium clips carry little risk of falling off. In rectal cancer, especially stage II–III colorectal cancer, marking the tumor by titanium clips to delineate target areas for radiotherapy before CT guidance enables a more accurate sketch of a target area and has important clinical value.

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CONFLICT OF INTEREST
The authors declare that they have read the article and there are no competing interests.

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