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CT-guided ^{125}I seeds interstitial brachytherapy for vaginal metastases of cervical cancer after radiotherapy

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Abstract: Objective:This retrospective research aims to evaluate the effectiveness and safety of computed tomography (CT)-guided I-125 seed interstitial brachytherapy for vaginal recurrent cervical cancer in patients with a history of pelvic radiotherapy. **Methods**:Six patients with vaginal recurrent cervical carcinoma were involved in this research between July 2012 and January 2017. They were all treated with CT-guided I-125 seed interstitial implantation in Hebei General Hospital. Follow-up was carried out after the surgery to evaluate the therapeutic efficacy, including symptoms of the patient and the local control rate of the tumor. Complications were also summarized to evaluate the safety. **Results**:In 6 patients, the efficacy evaluation was PR1 and SD5, the local control rate was 100% (6/6) at 1 month and 2 months after operation, and the efficacy evaluation was CR1、SD2 and PD2, the local control rate was 66.7% (4/6) at 4 months and 6 months after the operation. 6 patients had different degrees of vaginal discharge and bleeding decrease, and pain relief after the operation. 3 patients had 3, 4, and 8 seeds falling off within 10 days after surgery, and 1 patient developed hypothermia on the 2nd and 3rd day after surgery. No other serious adverse reactions were observed. **Conclusion**:Reirradiation with CT-guided I-125 seed interstitial brachytherapy is a safe, effective, and minimally invasive method to treat patients with vaginal recurrent cervical cancer after radiotherapy.
Keywords: Cervical cancer; Vaginal recurrent; I-125 seeds; Brachytherapy

Introduction

Cervical cancer often involves the vaginal wall downward. For patients with vaginal metastasis after external radiotherapy combined with brachytherapy, due to the dose limitation of bladder and rectum and other organs at risk, it is difficult to push the local dose of radiotherapy. As one of the methods of brachytherapy for malignant tumor, 125I seed interstitial implantation can effectively increase tumor tissue dose and reduce normal tissue dose. In our hospital, 6 cases of cervical cancer with vaginal metastasis after radiotherapy were treated with CT guided radioactive 125I seed implantation, and achieved certain curative effect.

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1. Materials and Methods

1.1 General information

From July 2012 to January 2017, 6 patients with cervical cancer vaginal metastases underwent CT guided ^{125}I seed implantation, with a median age of 51 years(43-70 years old). All of them were confirmed by pathology as vaginal metastasis of cervical squamous cell carcinoma, without operation opportunity. After radiotherapy and chemotherapy, they could not tolerate radiotherapy again. See Table 1.

1.2 Main instruments and equipment

(1) Treatment planning system (TPS): Prowess Panther Brachy V5.0 Brachytherapy planning system, USA prowess Co., Ltd. (2) The 18G implant needle, 1820-C type and Mick200-TPV Applicator gun are provided by Mick Radio-Nuclear company of the United States. (3) Radioactive ^{125}I particles: 6711-99 type, particle length 4.5 mm, diameter 0.8 mm, activity 0.3-0.6 mCi, energy 27-35 keV, half-life 59.4 d. (4) Activity meter: RM-905a well type ionization chamber, China Academy of metrology. (5) Vacuum pad: 120cm × 80cm × 4cm, Zibo Tianchen medical equipment factory.

Table 1. Clinical data of 6 patients with vaginal metastasis after radiotherapy and chemotherapy with ^{125}I seed implantation

No.	Stages of squamous cervical carcinoma	Age	Location of vaginal transfer	Previous radiotherapy history (external radiotherapy + afterloading treatment)	Particle activity(mCi)	Postoperative D90(Gy)
1	Ⅱb Cauliflower type	51	Posterior wall	52Gy/26f+(42Gy/7f+32Gy/5f+16Gy/3f)	0.4、0.6	60
2	IIIb Ulcerative type	57	Anterior wall	52Gy/26f+ 36Gy/6f	0.3	40
3	Ⅱb Nodular type	70	Left posterior wall	52Gy/26f+(36Gy/6f+49Gy/7f)	0.4	70
4	ⅣB Cauliflower type	43	All	50.4Gy/28f+(26Gy/4f+32Gy/5f)	0.3、0.5	60
5	ⅢBUlcerative type	47	Posterior wall	46Gy/23f+49Gy/7f	0.5	85
6	Ⅱb Cauliflower type	51	Left lateral wall	52Gy/26f+(42Gy/7f+16Gy/3f)	0.5、0.6	107

1.3 Planting method

One week before operation, all patients were fixed with negative pressure vacuum pad according to the operation position. The location line was marked along the CT positioning laser line at the skin level of the upper edge of the tumor surface projection, and two marking points were pasted on the horizontal line 3-4 cm. Enhanced CT scanning was performed with a slice thickness of 5 mm. The CT images were transmitted to TPS to outline the target area and organs at risk. According to the patient's previous treatment, the particles with 0.3-0.6 mCi activity were selected to determine the prescription dose of 40-100Gy. According to the location and size of vaginal metastases, their relationship with blood vessels, bones and organs at risk and other factors, the needle path was designed with a layer spacing of 5-10 mm. After reaching the prescription dose, the plan was submitted, and the CT sequence and the spatial position coordinates of all needle paths were output. Preoperative localization and reduction were referred to during operation. According to the data provided by TPS, the needle was punctured according to the anatomical structure under the guidance of CT. After the puncture was completed, CT was scanned again. After the position of the implantation needle was determined, the seeds were accurately implanted into the tumor according to the preoperative plan.

1.4 Postoperative verification

CT scan was performed immediately after implantation with 5 mm slice interval. TPS was introduced for postoperative planning verification. The target area and organs at risk were outlined, and particles were identified. The isodose curve distribution and dose volume histogram were obtained.

1.5 Follow-up survey and efficacy evaluation criteria

The tumor size was evaluated by CT at 1 month, 2 months, 4 months and 6 months after operation. Response Evaluation Criteria in Solid Tumors (RECIST 1.1) (Eisenhauer et al., 2009) was used to evaluate the efficacy: (1) Complete remission (CR) refers to the disappearance of all lesions for at least 4 weeks. (2) Partial remission (PR) refers to the target lesion length and diameter reduced by at least 30% compared with the baseline level and maintained for at least 4 weeks. (3) Stable disease (SD) refers to that the decrease of the target lesion does not reach PR, and the increase degree does not reach the PD level, which is between the two. (4) Progression disease (PD) refers to the increase of the length and

diameter of the target lesion by more than 20% than the baseline level or the appearance of new

lesions. Local control rate = (CR + PR + SD) / total cases × 100%.

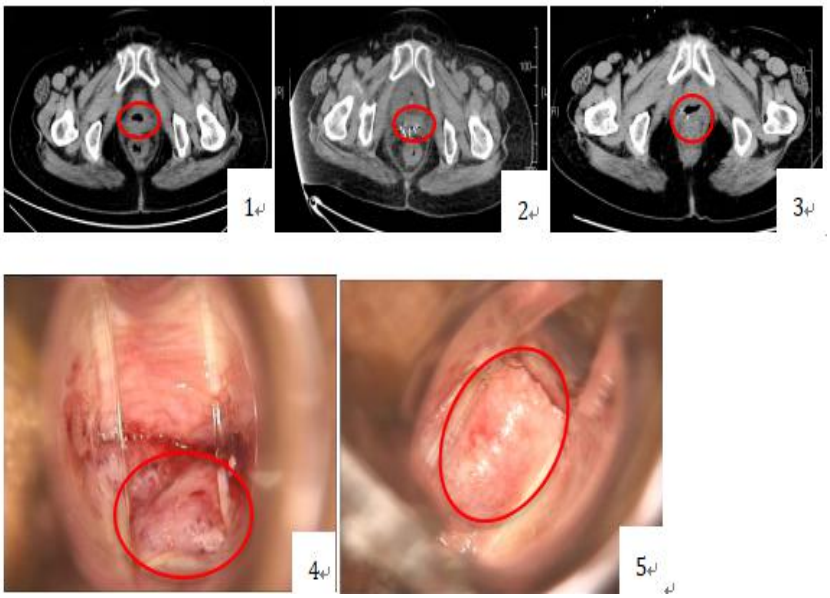
1.6 Evaluation of adverse reactions

The early and late adverse reactions, including hematology, digestive system, urinary system and reproductive system, were recorded according to the radiation oncology collaboration group (RTOG) acute and late radiation injury evaluation criteria in 1988. Early complications: from the beginning of treatment 1 ~ 90 days of radiotherapy reaction; late complications: 90 days after the occurrence of adverse reactions.

2. Results

2.1 curative effect

All the 6 patients were successfully operated. Postoperative CT scans of all the 6 patients showed reasonable distribution of particles within the tumor, and the 90% target dose (D90) was confirmed to be 40-107Gy immediately after surgery. CT review was conducted at 1 month, 2 months, 4 months and 6 months after surgery and compared with preoperative CT. According to the efficacy evaluation criteria, PR1 and SD5 cases were performed 1 month after surgery, and the local control rate was 100% (6/6). 2 months after operation: PR1 and SD5 cases, the local control rate was 100% (6/6). 4 months after surgery: CR1 (Figure 1), SD3, PD2, the local control rate was 66.7% (4/6). 6 months after operation: CR1,SD3, PD2 (Table 2), the local control rate was 66.7% (4/6). All the 6 patients had reduced vaginal discharge, bleeding and pain after operation.



①CT of Preoperative ; ②CT of Intraoperative ; ③CT of 6 months after operation ; ④Preoperative electronic colposcope; ⑤4 months after operation Electronic colposcopy

Figure 1 CT and electronic colposcopy images of patient 1

Table 2. 6 cases of postoperative efficacy evaluation and complications

No.	Efficacy and evaluation				Symptomatic relief	Untoward reaction
	1 month	2 months	4 months	6 months		
1	SD	PR	CR	CR	Vaginal discharge reduced, odor reduced	Three particles fell off
2	SD	SD	PD	PD	Pruritus vulvae reduced	None
3	SD	SD	SD	SD	Vaginal bleeding, drainage reduced, pain significantly relieved	Four particles fell off
4	SD	SD	SD	SD	Urination function recovered 10 days after operation	Fever occurred 2 and 3 days after operation
5	SD	SD	PD	PD	Urination pain relief	None
6	PR	SD	SD	SD	Vaginal discharge reduced, odor reduced	Eight particles fell off

2.2 Adverse reactions

The patient had fever on the 2nd and 3rd day after operation, and the highest temperature was 38.7 ℃. There was no shiver or night sweat. The patient's temperature dropped to normal after symptomatic cooling treatment, and no fever occurred. Three patients had particles falling off within 10 days after operation. Patient 1 found one particle falling off after urination on the 6th day after particle operation. On the 10th day after operation, the patient underwent pelvic double hip ortho position CR and showed 27 particles on X-ray. Two particles were lost unintentionally. At 8 hours after the operation, three particles were removed when the pressure hemostatic gauze was drawn out and the hemostatic Vaseline gauze was filled. On the first day after operation, three particles were lost during daytime urination, four particles were lost during night urination, and one particle was dropped on the third day after operation. No serious adverse reactions were observed.

3. Discussion

Cervical cancer is a common gynecologic malignancy. The incidence rate is the second highest in the world. The mortality rate is third (Torre et al., 2015), and about 1/3 of the patients will relapse. 75% of the recurrences occurred in (Goncalves et al., 2008) within 2 years, and pelvic recurrence is the main cause of death (Peiretti et al., 2012), the median survival time is only 12 months (Elit et al., 2014). In addition to lymph node metastasis, direct spread of cervical cancer is the most common, often involving the vaginal wall downward. Due to the special location of vaginal metastatic cancer, the space between the adjacent organs is small, and the operation is difficult. For patients who have received external radiotherapy combined with brachytherapy, the complications of re irradiation may increase as high as 30% - 56% (Elst et al., 2007). Therefore, cervical cancer with vaginal metastasis is a difficult problem for clinicians.

^{125}I seed implantation is a widely used minimally invasive treatment. Radioactive ^{125}I seed implantation has been used as a standard treatment for early prostate cancer (Nag et al., 2002), and has unique advantages in the treatment of locally advanced tumors (Shi et al., 2012). At present, it has been extended to lung cancer(Huo et al., 2016), head and neck cancer and other malignant solid tumors, but there are few reports on the treatment of recurrent vaginal metastasis of cervical cancer. ^{125}I particles can directly deliver the accumulated dose to the target tumor, and have a very steep dose gradient outside the implanted volume, thus reducing the radiation dose of adjacent normal tissues (Yao et al., 2015), which is particularly important for the treatment of recurrent tumors after radiotherapy(Lin et al., 2015). Hu Feng (Feng et al., 2017) reported a case of cervical cancer with vaginal recurrence after radiotherapy, who received IMRT and ^{125}I seed implantation. The progression free survival time of the patient was 33 months, and the long-term adverse reactions were tolerable. It was considered that ^{125}I seed implantation could be used as a supplementary treatment for vaginal metastasis of cervical cancer. Han et al.(Han et al., 2016)performed CT guided seed implantation in 17 patients with recurrent cervical cancer, the prescription dose was 145Gy, and the clinical effective rate was 58%. The D90 values of 6 patients reported in this paper were 40-107 Gy, which were lower than those reported by the above-mentioned scholars, and 3 patients had particle shedding within 10 days after operation. 6 months after operation: 1 case of Cr, 3 cases of SD, 2 cases of PD. However, there is no reliable evidence of evidence-based medicine at home and abroad to confirm the choice of peripheral dose and particle activity of ^{125}I seed implantation for recurrent cervical cancer. In addition, there are only 6 cases in this report, the number of cases is too small, there may be deviation in case selection.

In ^{125}I seed implantation, the radiation dose coverage rate of the target area is high, while the radiation dose of surrounding normal tissues (including bladder and rectum) is low. Sharma (Sharma et al., 2007)and others believe that ^{125}I seed implantation is better than traditional afterloading radiotherapy. However, compared with the traditional brachytherapy, interstitial implantation is more invasive than brachytherapy. The implantation process needs to coordinate multiple implantation needles and repeated CT scans to determine and adjust the position and depth of needles, which increases the risk of bleeding, infection, radiation and the possibility of iatrogenic tumor seeding and metastasis. Tong L et al. (Tong et al., 2007) reported 35 cases of pelvic recurrent cervical cancer after radiotherapy treated with ^{125}I seed implantation. One case of rectovaginal fistula and one case of incomplete intestinal obstruction were found during postoperative follow-up. It was considered that the formation of fistula may be due to the local high-dose area caused by tumor contraction, which makes the radiation source closer to the organ. In addition, there were 2 cases of particles falling off, 1 case of particles falling into the abdominal cavity

and 1 case of particles falling off from vagina. Among the 6 cases reported in this paper, 3 cases had 3, 4 and 8 particles falling off within 10 days after operation, all of which were prolapsed through vagina. It is considered that it may be related to the movement of internal organs after implantation, local tumor necrosis and implantation technology. According to Beaulieu et al. (Beaulieu et al., 2004), the migration and migration of ^{125}I particles are more likely to affect the dose distribution of the target, rather than cause adverse reactions in normal tissues. To avoid ^{125}I particles falling off or shifting, we should have a good treatment plan, skilled surgical techniques and strict quality assurance and quality control. In addition, 1 patient had low fever on the 2nd and 3rd day after operation, which was considered as tumor absorption heat caused by tumor tissue ischemia and necrosis.

CT guided radioactive ^{125}I seed implantation is safe and effective in the treatment of cervical cancer with vaginal metastasis after radiotherapy and chemotherapy. It provides a new treatment for patients with vaginal metastasis of advanced cervical cancer who lose the opportunity of surgery, fail to respond to chemotherapy, and can not tolerate radiotherapy again. The number of patients in this report is small and the observation time is short. The observation and evaluation of its long-term curative effect needs further study.

References

Beaulieu L, Archambault L, Aubin S. (2004). The robustness of dose distributions to displacement and migration of 125I permanent seed implants over a wide range of seed number, activity, and designs. Int J Radiat Oncol Biol Phys, 58(4): 1298-1308.

Eisenhauer EA, Therasse P, Bogaerts J. (2009). New response evaluation criteria in solid tumours：revised RECIST guideline(version 1.1). Eur J Cancer, 45(2):228-247.

Elit LM, Hirte H. (2014). Management of advanced or recurrent cervical cancer: Chemotherapy and beyond . Expert Rev Anticancer Ther, 14(3): 319-332.

Elst P, Ahankour F, Tjalma W. (2007). Management of recurrent cervical cancer. Review of the literature and case report . Eur J Gynaecol Oncol, 28(6): 435–441.

Feng H, Hu Y, Jin P. (2017). Intensity-modulated radiotherapy combined with iodine-125 seed implantation in non-central recurrence of cervical cancer: A case report and literature review. Oncol Lett, 14(4): 4085-4091.

Goncalves A, Fabbro M, Lhommé C. (2008). A phase II trial to evaluate getinib as second- or third-line treatment in patients with recurring loco regionally advanced or metastatic cervical cancer. Gynecol Oncol, 108(1): 42-46.

Han L, Li C, Wang J. (2016). Iodine-125 radioactive seed tissue implantation as a remedy treatment for recurrent cervical cancer. J Cancer Res Ther, 12(Supplement):C176-80.

Huo X, Wang H, Yang J. (2016). Effectiveness and safety of CT-guided 125I seed brachytherapy for postoperative loco regional recurrence in patients with none-small cell lung cancer. Brachytherapy, 15(3):370-380.

Lin L, Wang J, Jiang Y. (2015). Interstitial 125I seed implantation for cervical lymph node recurrence after multimodal treatment of thoracic esophageal squamous cell carcinoma . Technol Cancer Res Treat, 14(2): 201-207.

Nag S, Ellis RJ, Merrick GS. (2002). American Brachytherapy Society: American brachytherapy society recommendations for reporting morbidity after prostate brachytherapy . Int J Radiat Biol Phys, 54(2): 462-470.

Peiretti M, Zapardiel I, Zanagnolo V. (2012). Management of recurrent cervical cancer: a review of the literature . Surg Oncol, 21(2):59-66.

Sharma DN, Subramani V, Rath GK. (2007). Interstitial brachytherapy guided intensity modulated radiation therapy in cervical cancer: A dosimetric study . Int J Radiation Oncol Biol Phys, 69 (Supplement): S731-S732.

Shi L, Wu C, Wu J. (2012). Computed tomography-guided permanent brachytherapy
for loco regional recurrent gastric cancer. Radiat Oncol, 7(1): 114.

Tong L, Liu P, Huo B. (2017). CT-guided 125I interstitial brachytherapy for pelvic recurrent cervical carcinoma after radiotherapy. Oncotargets & Therapy, 10:4081-4088.

Torre LA, Bray F, Siegel RL. (2015). Global cancer statistics, 2012 . CA Cancer J Clin,65(2): 87-108.

Yao L, Wang J, Jiang Y. (2015). Permanent interstitial 125I seed implantation as a salvage therapy for pediatric recurrent or metastatic soft tissue sarcoma after multi-disciplinary treatment . World J Surg Oncol, 13(1): 1-9.

Zhu L, Jiang Y, Wang J. (2013). An investigation of 125 I seed permanent implantation for recurrent carcinoma in the head and neck after surgery and external beam radiotherapy. World J Surg Oncol, 11(1):60.