125I implantation under computed tomography guidance to treat patients with recurrent pelvic tumors: Retrospective analysis of clinical results

ABSTRACT
Objective: The objective of the study was to evaluate computed tomography (CT)-guided 125I implantation for the treatment of recurrent and malignant pelvic tumors.

Materials and Methods: Fifteen cases of pelvic malignant tumors were studied. Tumor length/diameter was 4–10 cm (average: 6.8 ± 2.3 cm). In patients with pelvic recurrence or metastasis of malignant tumors, comprehensive treatment, including surgery, chemotherapy, or radiotherapy, was performed alongside CT-guided 125I implantation. The follow-up clinical benefit rate, rate of pain relief, quality of life score, and status of any complications were analyzed.

Results: The patients were followed up for 6 months after the operation, and evaluation of lesions revealed complete response (CR) in 3/15 cases, partial response (PR) in 8/15 cases, stable disease in 3/15 cases, and progressive disease in 1/15 cases. The total effective rate (CR + PR) was 73.3% (11/15), and the pain relief rate was 86.6% (13/15). No bleeding, pelvic abscesses, intestinal fistulas, intestinal perforations, or other complications were reported.

Conclusions: When using CT-guided 125I implantation, patients with malignant abdominal tumors undergo a convenient operation, sustain little trauma, and have an improved quality of life.

KEY WORDS: 125I seeds, clinical curative effect, malignant pelvic tumor

INTRODUCTION
Malignant tumors in the pelvic cavity have high rates of recurrence and metastasis, usually after surgery or chemoradiotherapy for gynecologic, colorectal, and urinary tract tumors. The efficacy of regional or systemic chemotherapy is relatively low, as it is difficult for drugs to enter the pelvis due to the tissue fibrosis that occurs after local operation or radiotherapy.[1] Patients are often symptomatic with intractable pain, discomfort when bearing down, bladder and/or rectal fistulas, and other complications, which drastically reduce their quality of life. External irradiation is affected by the hypoxia of tumor cells and carries side effects such as radiation enteritis, intestinal stenosis, and cystitis. It is also difficult to increase the radiation dose when the patient has a history of radiotherapy, so its application is limited in controlling tumors effectively. For recurrent and refractory pelvic tumors, radioactive seed implantation is a relatively good treatment method.[2] From July 2016 to June 2018, our hospital used computed tomography (CT)-guided 125I radioactive seed implantation brachytherapy as the rescue treatment for 15 patients with malignant pelvic tumors and achieved good short-term clinical outcomes. The summary of the report is as follows.

MATERIALS AND METHODS
Case data
We retrospectively analyzed the clinical data of patients with malignant pelvic tumors, who were admitted to our hospital between June 2016 and June 2018. The patients were 11 male and 4 female,
aged 53–80 years. The diagnoses for these patients had been pathologically confirmed. Following surgical evaluation, those patients who underwent unbearable radical surgery still had at least one measurable target lesion. Based on the tumor, node, metastasis staging system, 4 cases were at Stage III and 11 cases were at Stage IV [Table 1].

**Instruments and equipment**

Toshiba CT-simulated positioner, Beijing Astro Technology seed implantation planning system, radiotherapy planning workstation of medical image management system, Mick seed implantation gun, seed implantation positioning navigation system, and the Siemens (Germany) X-ray digital subtraction angiography system were used.

**Treatment methods**

**Preoperative preparation**

Before the operation, tests including a complete blood count, coagulation function, hepatic and renal functions, and cardiopulmonary function were carried out, and contrast-enhanced CT examination was performed to determine the location and size of the tumor, adjacent blood vessels, nerves, and other structures.

**Formulation of the seed implantation plan**

The treatment planning system (TPS) was used to determine the dose, the number of radioactive seeds to be implanted, and the placement location. The clinical target volume (CTV) was defined as the gross tumor volume (GTV) expanded by 1.0 cm. The edge of the CTV was covered by the 90% isodose curve. Simultaneously, those organs surrounding the tumor that was at risk were delineated.

**Intraoperative operation**

Under routine electrocardiography monitoring and CT scan positioning, a puncture was advanced step-by-step until the needle was in place. After confirming the absence of blood reflux upon needle withdrawal, $^{125}$I seeds were placed as per the preoperative plan. CT scan reexamination was performed following treatment for radiation quality evaluation, after which seeds could be added to the radiation cold area to ensure sufficient radiation dose for the whole target area.

**Postoperative treatment**

Symptomatic treatments such as routine hemostasis and nutritional support were given for 3 days after seed implantation, and anti-inflammatory treatment was provided as appropriate. CT reexamination was performed after implantation [Figure 1a-f].

**Outcome evaluation**

**Evaluation of clinical benefit status**

CT or positron emission tomography-CT examination was performed 2 months after the operation to evaluate local tumor control. Changes in the lesion were evaluated using the RECIST 1.1 criteria.[3] The clinical benefit rate was defined as complete response (CR) + partial response (PR) + stable disease (SD). CR refers to the disappearance of enhanced imaging in the arterial phase of all target lesions. PR indicates that the total diameter of the surviving target lesions (arterial phase-contrast enhancement) is reduced by 30% or more.

![CT scan images](image_url)

**Table 1: General conditions of patients**

| Indicator                        | n (%) |
|----------------------------------|-------|
| Age (years)                      | 63 (53-80) years |
| Sex                              |       |
| Male                             | 11 (74) |
| Female                           | 4 (26)  |
| Primary lesion                   |       |
| Cervical cancer                  | 3 (20)  |
| Colon cancer                     | 8 (53)  |
| Rectal cancer                    | 4 (27)  |
| Pathological type                |       |
| Poorly differentiated adenocarcinoma | 5 (33) |
| Moderately differentiated adenocarcinoma | 9 (60) |
| Moderately differentiated squamous cell carcinoma | 1 (7) |
| Number of pelvic lesions         |       |
| 1                                | 12 (80) |
| 2                                | 3 (20)  |
| TNM staging                      |       |
| Stage III                        | 4 (26)  |
| Stage IV                         | 11 (74) |

1TNM=Tumor, node-, metastasis

**Figure 1:** (a) Enhanced computed tomography before seed implantation. (b) Preoperative plan for seed implantation. (c) Simulated needle path before seed implantation. (d) Needle placement during seed implantation. (e) Computed tomography dose verification after seed implantation. (f) Seed distribution at the lesion 2 months after operation.

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Progressive disease (PD) refers to an increase of 20% or more in the total diameter of surviving target lesions (arterial phase-contrast enhancement) or the appearance of new lesions. SD indicates that the reduction did not reach the level of PR or that the increase did not reach the level of PD.

**Pain relief and quality of life assessment**

The Visual Analog Scale (VAS) score was used to assess pain levels before the operation and 1, 3, and 6 months after the operation. A score of 0 points represented no pain and 10 points represented the most severe pain. The Karnofsky performance status (KPS) score [Table 2] was used to assess the general condition of the patients.

**Data analysis**

The SPSS 17.0 statistical analysis software (SPSS Inc, Chicago, Illinois -- IL United States of America) was used to analyze the data. Variance analysis was used for the VAS and KPS scores which were repeatedly measured before the operation and 1, 3, and 6 months after the operation.

**RESULTS**

**Clinical benefit rate**

Of the 18 lesions evaluated for the outcome of local radioactive $^{125}$I seed treatment, 15 had achieved successful implantation in a single attempt, meeting the TPS requirements. Two lesions failed to meet the TPS requirements, for which more seeds were added. In the postoperative plan, GTV (D90) and CTV (D90) were 129.9 ± 25.8 Gy and 87.8 ± 16.3 Gy, respectively; rectal D2cc, D1cc, and D0.1cc were 26.5 ± 33.7 Gy, 31.5 ± 39.8 Gy, and 46.1 ± 55.3 Gy, respectively. Bladder D2cc, D1cc, and D0.1cc were 10.5 ± 15.2 Gy, 12.2 ± 17.6 Gy, and 16.2 ± 23.9 Gy, respectively; adjacent D2cc, D1cc, and D0.1cc were 43.5 ± 30.3 Gy, 52.4 ± 32.6 Gy, and 73.0 ± 41.0 Gy, respectively. The lesions were followed up for 6 months, after which an evaluation of the 6 month postoperative lesion was conducted. The evaluation at the end of the follow-up period showed that the CR rate of the lesions was 20% (3/15), the PR rate was 53.3% (8/15), the SD rate was 20% (3/15), and the PD rate was 6.6% (1/15). The total response rate (CR + PR) was 73.3% (11/15), and the pain relief rate was 86.6% (13/15). No serious complications, such as massive hemorrhage, pelvic abscess, intestinal fistula, or intestinal perforation, were found [Table 3].

**Karnofsky performance status score changes**

The KPS scores at the preoperative stage and at the 1, 3, and 6 months patient follow-ups were 53.3 ± 6.2, 59.3 ± 7.0, 70.0 ± 6.5, and 63.3 ± 4.9, respectively, suggesting that the postoperative performance status scores were significantly increased compared with those before the operation. This difference was statistically significant ($P < 0.05$); [Figure 2].

**NRS score changes**

The NRS scores of the 15 patients before operation and 1, 3, and 6 months after the operation were 6.80 ± 1.65, 2.00 ± 1.41, 1.80 ± 1.32, and 2.26 ± 1.10, respectively, suggesting that the NRS score at each time point was significantly lower compared with that before the operation. This difference was statistically significant ($P < 0.05$); [Figure 3].

**Complications**

No serious complications, such as pelvic hematoma, abscess, intestinal injury, bladder injury, nerve injury, or infection, occurred after the operation. The short-term complications mainly included the following: (1) local numbness during the operation in two patients, which was relieved by adjusting the position of the implantation needle. (2) Hemorrhage in one patient, revealed postoperatively upon the reexamination.

**Table 2: Karnofsky performance status scoring system**

| Patient's general condition                                      | Value |
|-----------------------------------------------------------------|-------|
| Normal, without symptoms and signs                              | 100   |
| Able to perform regular activities, with mild symptoms and signs| 90    |
| Barely able to perform normal activities, with certain symptoms and signs | 80    |
| Able to live independently, without the ability to perform normal activity or work | 70    |
| Sometimes needs help, but most of the time can take care of themselves | 60    |
| Frequently needs help                                          | 50    |
| Unable to live independently, needs special care                | 40    |
| Unable to live independently at all                            | 30    |
| Seriously ill, needs hospitalization and active treatment       | 20    |
| Critically ill, near death                                     | 10    |
| Dead                                                            | 0     |

KPS=Karnofsky performance status

**Table 3: Clinical benefits in patients**

| Tumor remission | n=11 cases |
|-----------------|------------|
| CR              | 3          |
| PR              | 8          |
| SD              | 3          |
| PD              | 1          |
| RR (%)          | 73.3       |

CR=Complete response, PR=Partial response, SD=Stable disease, PD=Progressive disease, RR=Response rate

**Figure 2:** KPS at each stage. KPS: Karnofsky performance status. **$P<0.05$, ***$P<0.01$**
of the puncture needle passage, which gradually disappeared after hemostasis and symptomatic and supportive treatment. The treatment-related toxicities in patients are summarized in Table 4. Only one patient developed level 2 diarrhea, and one patient showed level 2 hemoglobin decline.

DISCUSSION

Recurrent or metastatic malignant pelvic tumors are clinically common. The recurrence rate of cervical cancer within 3 years after surgery or radiotherapy is over 70%. This is dominated by pelvic recurrence, which accounts for over 60% of cases.[6] The recurrence rate after rectal cancer surgery exceeds 40%,[7] with poor prognosis, especially in patients with large masses (with diameter >4 cm). The treatment approaches for recurrent malignant pelvic tumors include repeated surgery, chemotherapy, and radiotherapy. However, surgery is invasive and causes intractable pain, discomfort with lower abdominal bearing down, bladder and/or rectal fistulas, and other complications, which drastically reduces the patient’s quality of life. The response rate of regional or systemic chemotherapy is relatively low.[8] In cases where external irradiation is used, patients are unable to tolerate the side effects of radiation, which include sustaining injury in the surrounding intestinal canals and other important organs, thus limiting the application. Reirradiation of the previously irradiated area is also dangerous because the risk of complications may significantly increase.[9]

Interstitial implantation of radioactive seeds for the treatment of tumors involves directly implanting radioactive nuclides into or around tumors, which destroy the tumor cells by continuously releasing radiation. Radioactive seeds show a good curative effect on tumors.[10] The gamma ray of 125I radioactive seeds is therapeutic, with a strong ability to destroy tumor DNA. The 125I seeds have a long half-life of approximately 59.6 days, which enhance the high-dose, long-duration, and short-distance cumulative irradiation of the target area. It causes little damage to the surrounding normal tissues[10] and overcoming the limitation of traditional external radiation.[10] Continuous low-dose irradiation affects the tumor’s tissue damage repair, cycle redistribution, reoxygenation, and repopulation and increases its radiosensitivity.[11] It has a definite clinical effect, causes little trauma and has few complications in the treatment of malignant solid tumors, and has been widely used in their treatment.[12,13] A patient’s quality of life could be improved with 125I seed implantation.[14] Sharma et al.[15] performed 125I seed implantation in patients with recurrent and malignant pelvic tumors after radiotherapy, with a local control rate of up to 67%. In addition, 125I seed implantation has a good effect in controlling local pain. Wang et al.[16] treated twenty patients with locally recurrent rectal cancer by seed implantation within a close range, with a pain relief rate of 85% (17/20) and local control rate (CR + PR) at the 2-month follow-up of up to 75%.

The overall response rate (CR + PR) in this study was 73.3% (11/15), and the pain relief rate was 86.6% (13/15). No serious complications, such as massive hemorrhage, pelvic abscess, intestinal fistula, or intestinal perforation, were found. The complications were mainly pain caused by the stimulation of the pelvic nerve plexus during the operation, intraoperative hemorrhage, and a local burning sensation, among other factors, which were relieved after symptomatic treatment. The needle insertion route for pelvic tumors should avoid bones, major blood vessels, nerves, organs, and other structures based on the preoperative TPS; therefore, the TPS should be further verified and improved according to each unique situation during the operation, and the seed spacing should be as uniform as possible. Subsequent seed implantation therapy or external radiotherapy can be supplemented for patients with significant postoperative “cold areas.”

CONCLUSIONS

CT-guided 125I seed implantation is safe and effective in the treatment of recurrent and malignant pelvic tumors, with little trauma and a high clinical benefit rate. It can be used as one of the treatment approaches to reduce local tumor burden and improve the quality of life in tumor patients.

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Conflicts of interest
There are no conflicts of interest.
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