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The dosimetry evaluation of 3D printing non-coplanar template-assisted CT-guided ^{125}I seed stereotactic ablation brachytherapy for pelvic recurrent rectal cancer after external beam radiotherapy

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ABSTRACT

The aim of this study was to investigate the safety and accuracy of computed tomography (CT)-guided ^{125}I seed implantation assisted by a three-dimensional printing non-coplanar template (3D-PNCT) for treating pelvic locally recurrent rectal cancer (LRRC) patients. A total of 13 patients with 18 masses received ^{125}I seed implantation. The dosimetric parameters of pre-implantation and post-implantation were calculated to evaluate the quality of ^{125}I seed implantation. Doses delivered to the organs at risk (OAR) were also calculated. Differences between pre-implantation and post-implantation were compared by the paired *t*-test. The mean number of ^{125}I seeds pre-implantation and post-implantation was 67.1 and 68.8, respectively. The mean values of D_{90} (dose that was delivered to 90% of the target volume), D_{100} (dose that was delivered to 100% of the target volume), V_{100} (the target volume receiving 100% of the prescription dose) and V_{150} (the target volume receiving 150% of the prescription dose) pre-implantation and post-implantation were 136.6 and 135.2 Gy, 63.5 and 71.0 Gy, 90.3% and 90.3% and 62.1% and 62.2%, respectively. Dosimetric outcomes were evaluated quantitatively using the dose volume indices, i.e. coverage index (CI), external volume index (EI) and relative dose homogeneity index (HI). The mean values of those indices pre-implantation and post-implantation were 0.62 and 0.61, 0.31 and 0.33, and 0.31 and 0.31, respectively. The mean doses delivered to OAR pre-implantation and post-implantation for the bladder (D_{2cc}) and bowel (D_{2cc}) were 33.4 and 34.4 Gy, and 58.6 and 61.8 Gy, respectively. The parameters mentioned above fitted well, and no significant difference was found among them. It is concluded that CT-guided ^{125}I seed implantation assisted by 3D-PNCT could be a safe and accurate salvage modality for treating LRRC patients; the ideal pre-prescription dose could be achieved. Also, addition of 3D-PNCT could minimize radiation damage to the surrounding normal tissues.

Keywords: 3D printing non-coplanar template; CT guidance; ^{125}I seed implantation; stereotactic ablation brachytherapy; pelvic locally recurrent rectal cancer; dosimetric evaluation

INTRODUCTION

Over the past few decades, the incidence of locally recurrent rectal cancer (LRRC) has significantly decreased after the introduction of standard treatment modalities composed of neoadjuvant chemoradiotherapy and total mesorectal excision. Despite these advances, local pelvic recurrences still occur in 5–10% of rectal cancer. The median survival time of LRRC is ~10 months. Over 80% of patients suffer from pelvic pain, fecal discharge, tenesmus, bleeding, obstruction and fistulation, resulting in a significant decrease in patients' quality of life. Although inferior to surgery, radical radiotherapy remains a

potentially curative option for inoperable patients. However, not all LRRC patients are eligible to undergo R_0 resection, especially for lateral pelvic wall recurrence. Moreover, it is a major challenge to deliver re-irradiation due to potential toxicities, since up to 80% of LRCC patients received neoadjuvant or adjuvant chemoradiotherapy as initial treatment. Palliative chemotherapy is less advantageous for LRCC patients, with a median overall survival (OS) of 8 months. [1] However, permanent ^{125}I seed interstitial brachytherapy is a potential salvage modality because of its unique physical and clinical characteristics. [2–5]

Stereotactic ablation brachytherapy (SABT) allows the delivery of high radiation doses to a tumor with a rapid radiation dose fall-off into the surrounding normal tissues. SABT has been successfully applied to LRRC treatment under computed tomography (CT) guidance in our institute since 2002. [6–8] Utilization of SABT showed that OS and quality of life of LRRC patients were improved. However, the major challenge in SABT is the arrangement of needles, directly influencing dose distribution and treatment effect. However, under CT guidance, needle placement is strongly dependent on an individual's experience. It may take a long time to train skilled surgeons or interventional radiologists for precise puncture and needle arrangement. Hence, we developed an individualized three-dimensional printing template (3D-PT) with a pre-designed needle orientation and insertion. [9] We have also assessed the possibility of CT-guided ^{125}I seed implantation assisted by a 3D printing non-coplanar template (3D-PNCT) for LRRC patients since 2015. This prospective cohort study analyzed the feasibility, safety and accuracy of CT-guided ^{125}I seed implantation assisted by 3D-PNCT for treating LRRC patients.

MATERIALS AND METHODS

Study subjects

In this prospective cohort study, 13 patients with 18 masses [7 men and 6 women; median age, 57 (range 48–66) years old] were recruited from February to October 2016. Twelve patients received radical surgery and external beam radiation therapy (EBRT), and one received only EBRT. The post-operative pathological results were classified into yp I (one case), yp II (two cases), II (six cases) and III (four cases) according to the tumor–node–metastasis (TNM) classification. The patient who underwent only EBRT was in the clinical TNM stage of cII. All the patients with pathological confirmation were diagnosed as having adenocarcinoma. In terms of treatment strategy, 2, 5, 10 and 2 patients received neoadjuvant EBRT, adjuvant EBRT, adjuvant chemotherapy, and neither adjuvant EBRT nor chemotherapy, respectively.

The recurrent LRRC lesions were located at central (3/18), presacral (7/18) and lateral (8/18) pelvis. In addition, seven patients received re-EBRT with concomitant chemotherapy after recurrence, while one patient underwent only re-EBRT after recurrence, one patient received only chemotherapy after recurrence, and four patients received no treatment after recurrence. All the patients received pelvic EBRT, of whom three patients received two-course EBRT and one patient underwent three-course EBRT. The cumulative EBRT doses were 48–134 Gy (dose, 56 Gy) before undergoing ^{125}I seed implantation. The patients' demographic characteristics and clinical data are presented in Table 1.

Table 1. Patients' demographic characteristics

Characteristic	No. of patients (%)
Age, years: median (range)	56 (48–64)
Sex	
Male	7 (53.8%)
Female	6 (46.2%)
Stage	
I	1 (7.7%)
II	2 (15.4%)
III	6 (46.2%)
IV	4 (30.8%)
Pathology	
Adenocarcinoma	13 (100%)
Surgery	
Yes	12 (92.3%)
No	1 (7.7%)
Chemotherapy	
Yes	11 (84.6%)
No	2 (15.4%)
EBRT	
Yes	13 (100%)
No	0
Previous EBRT frequency	
Once	6 (46.1%)
Twice	5 (38.5%)
Three times	2 (15.4%)
Total dose of previous EBRT, Gy: median (range)	56 (48–134)
Recurrent sites (18 masses)	
Central	3 (16.7%)
Pre-sacral	7 (38.9%)
Lateral	8 (44.4%)

The inclusion/exclusion criteria

The inclusion criteria were as follows: (i) pathologically confirmed pelvic LRRC before undergoing ^{125}I seed implantation; (ii) unresectable lesions reviewed by a multidisciplinary team of surgeons, radiation oncologists and medical oncologists, or patients who refused to undergo further EBRT; (iii) patients with a history of receiving pelvic EBRT; (iv) patients in whom the diameter of the lesion was $\leq$5 cm, and the number of recurrent masses was not $>$3; (v) the evaluation of pre-implatation met the requirements of prescribed doses; (vi) patients' expected OS was $>$3 months; and (vii) Karnofsky performance status (KPS) was $\geq$70.

The exclusion criteria were as follows: (i) the recurrent tumor caused fistula formation and bleeding; (ii) patients with severe cardiopulmonary disorders, hypertension and diabetes; and (iii) intolerance to the procedures of spinal or general anesthesia, as well as lumbar puncture. Informed consent was obtained from all the patients, and the Ethics Committee of Peking University Third Hospital (China) approved the study.

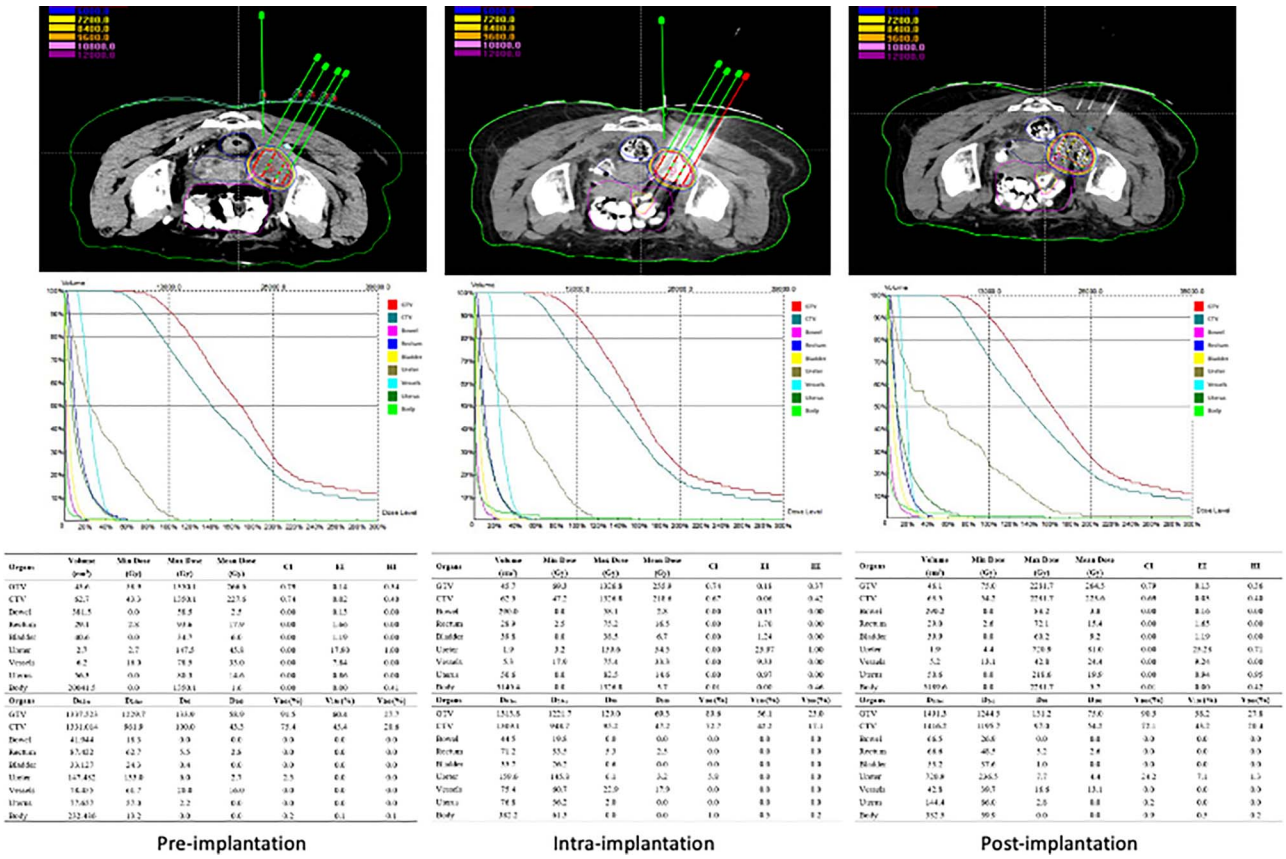

Fig. 1. DVH and dose distribution in pre-implantation, intra-implantation and post-implantation.

Patients' preparation and pre-implantation

The patients received vacuum pads and underwent the supine-to-prone turning procedure. Under CT guidance, the patient's body surface for the center of the mass was marked on the Cartesian coordinate system. The central point was defined as a stable needle insertion site where the stable needle facilitates the fixation of template, skin and lesions. The contrast-enhanced CT scan was performed 2 days before undergoing ^{125}I seed implantation. The CT images were acquired at a slice thickness of 5 mm. The CT images were transmitted to the brachytherapy-treatment planning system (B-TPS; KL-SIRPS-3D V6.0; Beijing ASTRO Information Technology Co. Ltd, Beijing, China). Then, the target volume, organs at risk (OAR) and the gross tumor volume (GTV) were delineated by physicians. The clinical target volume (CTV) was defined as the GTV with a 3–5 mm expansion in three dimensions. In addition, it was attempted to prescribe the dose and total seed activity, design the puncture channels (depth and direction), determine optimal arrangement and positions of needles, and simulate the dose–volume histogram (DVH) to confirm the dose constraints for OAR (Fig. 1).

3D-PNCT

The CT scan images were imported into the 3D-PT module in B-TPS to design an individualized 3D-PT. The 3D-PNCT was fabricated by Materialise Magics software (Leuven, Belgium), a stereolithography-based 3D printing machine and light-cured resins (Fig. 2).

^{125}I seed implantation

The ^{125}I seed implantation is made up of eight steps that are summarized in the following. (i) Patients' preparation and CT guidance: all selected patients received epidural anesthesia and were fixed with a vacuum pad in the supine or prone position depending on the tumor's location. (ii) Pre-implantation: the acquired CT images were transmitted into B-TPS, where the target volume, GTV and OAR were delineated. Meanwhile, the defined prescription doses, the optimal position, orientation and depth of needles were imported into the B-TPS. (iii) Designing templates: 3D-PNCT integrated the information, including patients' demographic characteristics, as well as optimal orientation and depth of needles. (iv) Mounting 3D-PNCT: 3D-PNCT was fixed on the skin and overlapped with the patients' body surface with laser lines via the Cartesian coordinate system, and three stable needles were inserted into the body for 2–3 cm penetration. The CT scan was used to verify the position of the stable needles. In the case of appearance of an error (>2 mm) in the estimated orientation of stable needles, a fine adjustment of the 3D-PNCT position should be carried out until reduction of the mentioned error to <2 mm. In this stage, all needles were inserted into the targets according to the pre-implantation. (v)

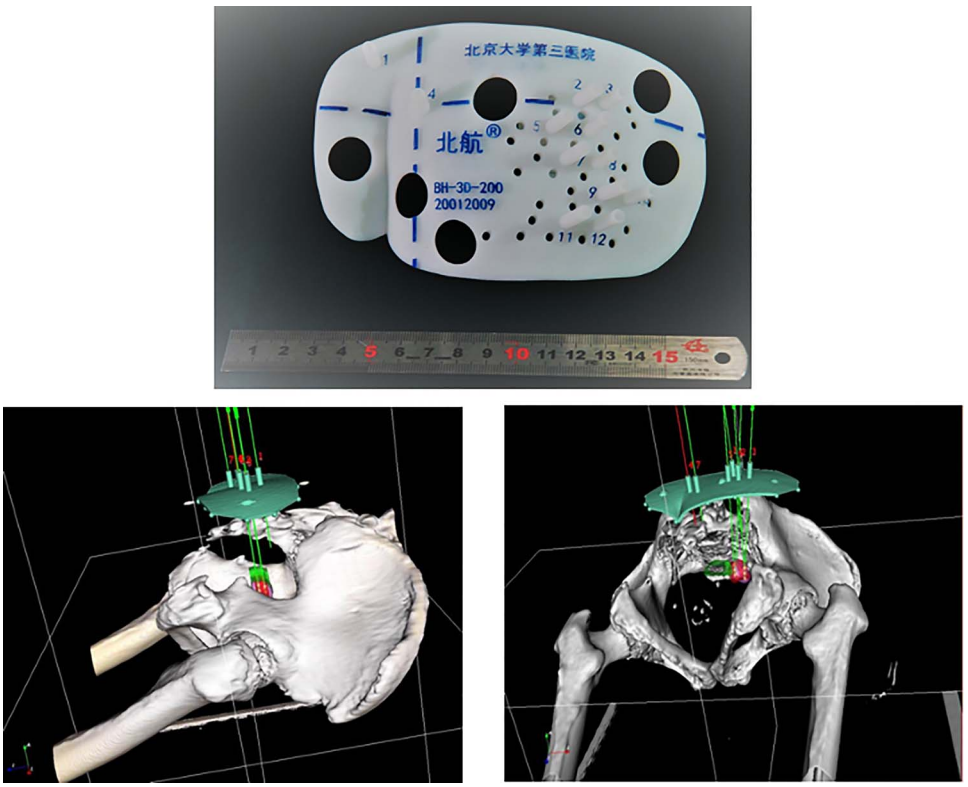

Fig. 2. Models of 3D printing non-coplanar template.

The position and arrangement of needles in the targets were confirmed via CT scan images. (vi) Importing CT images into B-TPS to optimize the dose distribution of the target. (vii) Performing ^{125}I seed implantation according to the pre-implantation using a Mick-gun. The number of ^{125}I seeds implanted ranged from 19 to 192 (median 69) with specific activity of 0.5–0.7 mCi (median 0.7 mCi). (viii) The dose was evaluated for the post-implantation (Fig. 3).

Special considerations for ^{125}I seed implantation of pelvic LRRC patients

The ^{125}I seed implantation of pelvic LRRC patients requires more accurate positioning and operation due to the complicated anatomy of the pelvis. Additionally, the sacrum sometimes blocks the pathway of needles. When a main orientation is blocked, the applied implantation pathways are not perpendicular to the axis of the body. In such a situation, the transverse image of needles is a point in successive CT images rather than a line perpendicular to the axis, causing difficulty in its identification. With the assistance of 3D-PNCT, the procedure is more efficient and safer than traditional freehand placement of implants. To find out the shortest needle pathway, the transgluteal or transinguinal approach is selected, for either lateral recurrence or presacral/-central recurrence. A pathway perpendicular to the axis of the body aspect is mainly designed for the above-mentioned situations when the sacrum blocks the pathway of needles. Figure 4 illustrates such special situations for pre-sacral recurrence. The epidural anesthesia is highly essential for the process since the pain cannot be tolerable under local infiltration anesthesia for nerves in the pelvis which are densely distributed.

Evaluation of dosimetric parameters after implantation

CT examinations were performed immediately after ^{125}I seed implantation. Images were then imported into B-TPS. The dosimetric parameters, including distribution of ^{125}I seeds, tumor volume, D_{90} (dose that was delivered to 90% of the target volume), D_{100} (dose that was delivered to 100% of the target volume), V_{100} (the target volume receiving 100% of the prescription dose) and V_{150} (the target volume receiving 150% of the prescription dose) were calculated. Dosimetric outcomes were evaluated quantitatively using the dose volume indices, i.e. coverage index (CI), external volume index (EI) and relative dose homogeneity index (HI). [10, 11] The radiation doses delivered to OAR of D_{5cc} (the exposure radiation dose of the 5 cm^3 volume) and D_{2cc} (the exposure radiation dose of the 2 cm^3 volume) for both bladder and bowels were recorded.

After undergoing ^{125}I seed implantation, all patients were instructed to lie in a horizontal position without a pillow for 6 h. Radiographic examinations of pelvis and chest were performed after 24 h to explore migration of seeds. The puncture procedure-related acute toxicities were detected. The flowchart of ^{125}I seed implantation is shown in Fig. 3.

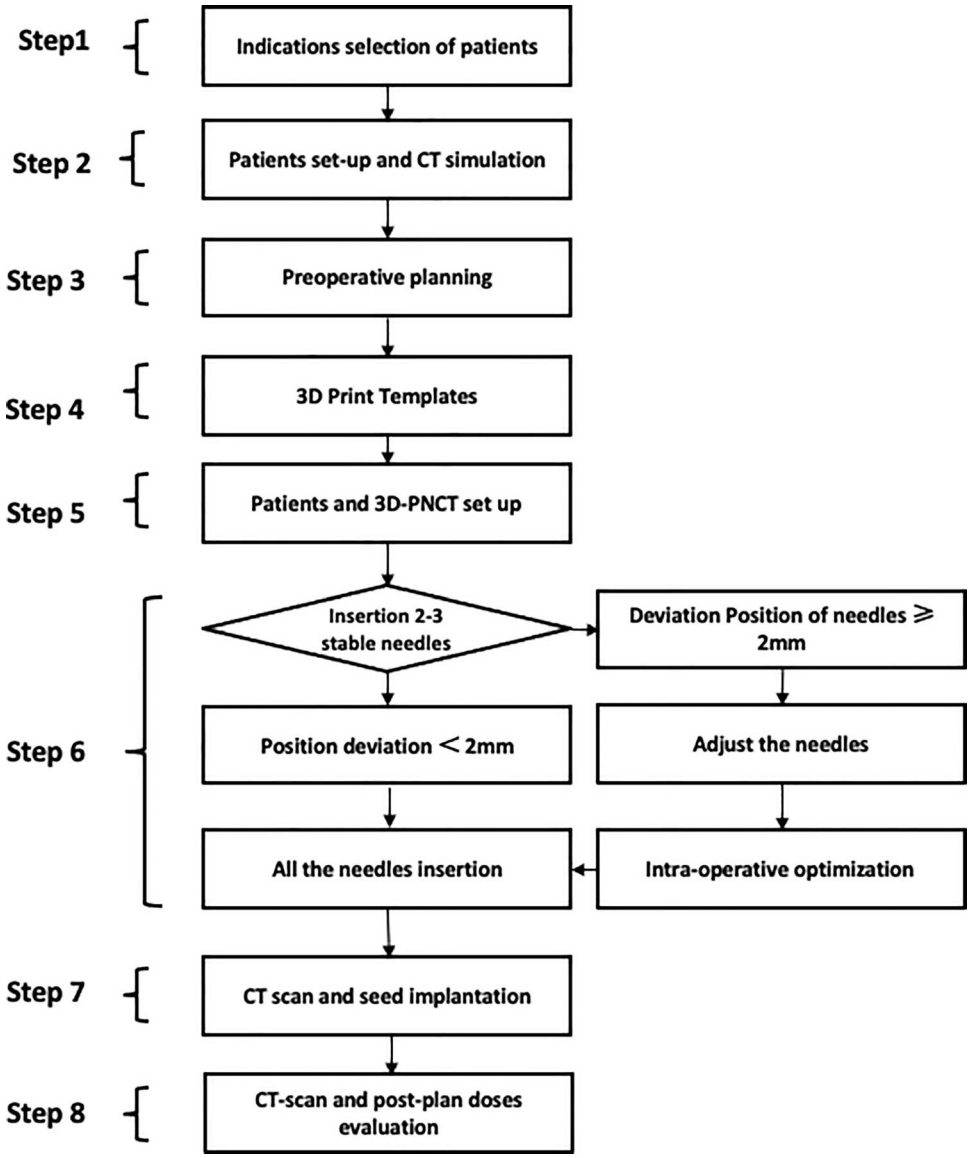

Fig. 3. Workflow of ^{125}I seed implantation.

Definition of endpoints

The prospective primary endpoint was defined to assess the matching degree of parameters between pre-implantation and post-implantation. The dosimetric parameters included D_{90}, D_{100}, V_{100}, V_{150} as well as the above-mentioned indices (CI, EI and HI). These parameters and indices were calculated to evaluate the quality of ^{125}I seed implantation. Additionally, the radiation doses delivered to OAR of D_{5cc} and D_{2cc} for both the bladder and bowel were calculated. The secondary endpoints were major perioperative complications.

Follow-up

Patients were followed up with contrast-enhanced CT imaging or magnetic resonance imaging (MRI) examinations along with carcinoembryonic antigen (CEA), as a tumor marker, every 3 months during the first 2 years. The toxicity was assessed on the basis of Common Terminology Criteria for Adverse Events (CTCAE; ver. 4.03) presented by the National Cancer Institute (Bethesda, MD, USA). [12]

Statistical analysis

All statistical analyses were performed using SPSS 22.0 software (IBM, Armonk, NY, USA). The coincidence of planning metrics between pre-implantation and post-implantation was evaluated by paired *t*-test. A P value <0.05 was considered statistically significant.

RESULTS

The median tumor volume was 25.4 ml (range 2.4–83.5 ml). The mean number of puncture needles was 15.8 ± 8.4 (range 5–39) and

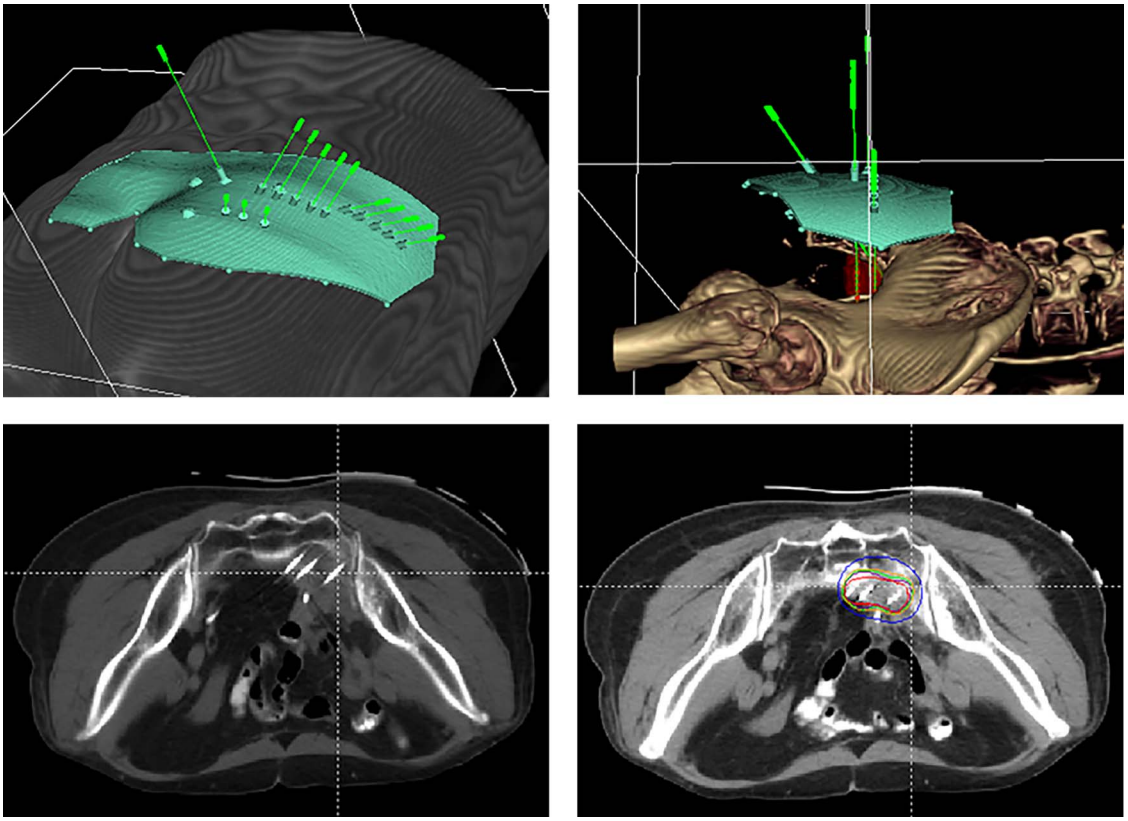

Fig. 4. Needle pathway designed for the presacral recurrence.

the mean number of seeds was 67.1 ± 45.1 (range 23–196) for pre-implantation. The mean number of needles was 16.2 ± 8.2 (range 5–38) and the mean number of seeds was 68.8 ± 42.7 (range 29–192) for post-implantation. There was no significant difference between pre-implantation and post-implantation ($P > 0.05$). The values of dosimetric parameters (D_{90}, D_{100}, V_{100} and V_{150}), CI, EI and HI for CTV of pre-implantation were consistent with those of post-implantation ($P > 0.05$) (see Tables 2 and 3).

Moreover, the dosimetric parameters of the bladder and bowels fitted well in both pre-implantation and post-implantation, and there was no significant difference ($P > 0.05$) (Table 4). The mean D_{5cc} of the bladder in pre-implantation and post-implantation was 22.7 ± 20.2 and 24.7 ± 15.9 Gy, respectively ($P = 0.640$). The mean D_{2cc} of the bladder in pre-implantation and post-implantation was 33.4 ± 27.4 and 34.4 ± 21.8 Gy, respectively ($P = 0.851$). The mean D_{5cc} of the bowel in pre-implantation and post-implantation was 44.3 ± 22.9 and 47.7 ± 30.0 Gy, respectively ($P = 0.707$). The mean D_{2cc} of the bowel in pre-implantation and post-implantation was 58.6 ± 28.8 and 61.8 ± 39.0 Gy, respectively ($P = 0.790$).

The median follow-up time was 8.2 months (range 2.5–11.2 months). Only one patient suffered from grade 4 chronic skin/mucosal toxicity (1/18, 5.6%). The patient had received two-course EBRT, as neoadjuvant for 30 Gy/10f and salvage for 55 Gy/30f at the first recurrence. The majority of adverse events were of lower grades (≤2) and well tolerated (Table 5). There were two cases with acute pain, one case with chronic pain, one case with acute, chronic urinary toxicity, one case with chronic urinary toxicity, one case with acute gastrointestinal toxicity and one case with chronic gastrointestinal toxicity; in addition, one patient suffered from both chronic skin and mucosal toxicity. The incidence of acute grades 1–2 gastrointestinal toxicity was 22.2% (4/18) and the incidence of chronic grades 1–2 gastrointestinal toxicity was 27.8% (5/18).

DISCUSSION

For patients with pelvic LRRC, surgical resection, chemotherapy, EBRT and intraoperative high-dose rate brachytherapy could be utilized with consideration of their advantages and limitations. [13–18] There are three patterns of LRRC in the pelvic location, namely central recurrence, sacral recurrence and lateral recurrence. The resectable LRRC was defined as an ability to remove all tumors with an R_0 margin. When LRRC includes the lateral pelvic side wall or sacrum, it is hard to achieve R_0 resection, typically leading to an unfavorable clinical outcome. Interstitial brachytherapy can be an alternative modality in the treatment of LRRC patients who cannot undergo radical resection or are not indicated for EBRT again. ^{125}I seed implantation, as low dose rate interstitial brachytherapy, is conducted with the guidance of imaging methods and percutaneous puncture, and associated with minimal invasion. The guidelines published by the US National Comprehensive Cancer Network (NCCN) recommended

Table 2. Comparing dosimetric and volumetric parameters (D_{90}, D_{100}, V_{100} and V_{150}) between pre-implantation and post-implantation in 18 lesions

n	D_{90} of pre-plan (Gy)	D_{90} of post-plan (Gy)	D_{100} of pre-plan (Gy)	D_{100} of post-plan (Gy)	V_{100} of pre-plan (%)	V_{100} of post-plan (%)	V_{150} of pre-plan (%)	V_{150} of post-plan (%)	V_{200} of pre-plan (%)	V_{200} of post-plan (%)
1	154.6	152.4	75.7	104.0	90.0	90.0	58.9	52.4	27.5	27.1
2	119.5	116.3	31.0	41.6	90.0	90.0	67.3	65.6	40.9	40.6
3	153.4	151.0	88.0	95.9	90.0	90.0	64.5	59.1	37.8	35.7
4	153.6	150.9	44.6	89.3	90.0	90.0	62.0	59.8	39.3	37.5
5	121.9	101.1	54.4	53.0	90.0	90.0	57.0	63.5	24.4	33.5
6	136.6	130.2	51.5	32.8	90.2	88.9	63.2	63.9	34.6	37.6
7	113.0	106.5	44.5	41.4	90.0	90.0	65.3	62.6	39.8	37.7
8	138.7	90.2	47.5	40.1	90.0	90.0	62.3	72.4	25.8	55.4
9	138.8	126.6	56.9	65.8	90.0	90.0	64.4	62.2	36.3	36.1
10	112.4	129.4	68.2	84.2	89.9	90.0	71.2	51.6	54.1	36.2
11	133.0	124.2	55.7	52.5	91.4	91.7	60.5	64.7	28.0	42.1
12	130.7	175.5	86.5	95.8	90.3	98.9	61.8	88.1	39.1	63.3
13	137.4	187.4	85.2	80.5	92.2	94	71.4	85.5	35.8	75.6
14	153.6	113.3	81.9	67.6	95.5	87.9	82.8	68.2	69.1	55.6
15	150.8	166.9	92.4	93.9	90.2	94.5	64.1	65.4	38.5	41.5
16	133.6	115.7	33.7	62.8	83.3	82.2	39.9	46.3	13.8	16.6
17	159.8	148.7	83.5	74.4	93.4	89.3	58.9	41.2	24.7	18.3
18	117.4	147.6	61.2	102.3	88.2	88.7	42.9	46.6	25.2	24.5
Mean ± SD	136.6 ± 15.4	135.2 ± 26.5	63.5 ± 19.7	71.0 ± 23.5	90.3 ± 2.4	90.3 ± 3.3	62.1 ± 9.6	62.2 ± 12.2	35.3 ± 2.4	39.7 ± 15.0
P value	0.821		0.098		0.913		0.988		0.208	

Notes: D_{90}, dose to 90% of the target volume; D_{100}, dose to 100% of the target volume; V_{100}, the target volume receiving 100% of prescription dose; V_{150}, the target volume receiving 150% of prescription dose.

^{125}I seed implantation as a salvage modality of brachytherapy for LRRC patients who are ineligible for R_0 surgery or re-EBRT. [19] However, it is hard to achieve the accuracy of ^{125}I seed implantation with pre-implantation distribution of needles when ^{125}I seed implantation is delivered under CT guidance.

A pre-loaded ^{125}I seed implantation combined with a transperineal template-guided prostate biopsy is the clinical standard for early-stage prostate cancer. The arrangement and direction of needles could be determined with the assistance of a 3D printed coplanar template, and there was no OAR interference with the track of the needles.

In 2002, Wang *et al.* proposed the CT-guided ^{125}I seed implantation for recurrent head and neck carcinomas, lung carcinoma, recurrent pelvic carcinomas and spinal cord metastatic carcinoma. [20] CT simulation connected to B-TPS for real-time optimization of intraoperative doses was presented in 2012. The preliminary clinical outcomes of LRRC patients who underwent CT-guided ^{125}I seed implantation showed that it is a safe and effective salvage option. [18, 21] D_{90} and V_{100} are independent prognostic factors for ^{125}I seed implantation of pelvic LRRC patients, in which D_{90} >140 Gy and V_{100} >90% in the post-operative implantation are associated with a better local control and a longer OS. [22]

Part of the significant advantages of CT-guided ^{125}I seed implantation is related to two-dimensional (2D) and 3D visualization. During ^{125}I seed implantation, both GTV and OAR could be visualized simultaneously. Thus, the position of a needle inserted into the target could be monitored, and penetration of needles into normal tissues surrounding blood vessels, colon, small intestines, bone, etc. could be minimized. However, the efficacy of CT-guided ^{125}I seed implantation is often questionable.

Chai *et al.* presented a template plane with a stabilization system under CT guidance for lung cancer treatment with ^{125}I seed implantation. [23] The verified quality in two groups was 92% and 39%, respectively, and the difference was statistically significant (P = 0.003). The disadvantages of the 3D printing template-assisted ^{125}I seed implantation can be attributed to the rib interference, lung aspiration and target movement. Zhang *et al.* proposed a 3D-PT to improve the accuracy of targeting and positioning of seed implantation in head and neck carcinomas. [24–27] However, there was no CT-guided interventional procedure and no information about isodose distribution on the templates. The consistency of dosimetric parameters between pre-implantation and post-implantation was unavailable.

Ji *et al.* introduced a 3D-PT applicable for various types of cancer. [28] A total of 14 patients with 16 sites were treated with an individualized 3D-PT. Compared with pre-operative implantation, the mean values of V_{100}, D_{90} and V_{150} decreased, while the mean values of V_{200} and MPD (peripheral matching dose) increased in post-operative implantation. Nevertheless, there was no significant difference between the two groups except for V_{100} ($P < 0.05$). The differences in CI, EI and

Table 3. Comparing the quality evaluation parameters (CI, EI and HI) between pre-implantation and post-implantation in 18 lesions with recurrence of rectal cancer

n	CI of pre-plan	CI of post-plan	EI of pre-plan	EI of post-plan	HI of pre-plan	HI of post-plan
1	0.74	0.78	0.20	0.14	0.34	0.42
2	0.77	0.73	0.15	0.21	0.25	0.27
3	0.73	0.73	0.20	0.20	0.28	0.34
4	0.71	0.74	0.24	0.20	0.31	0.33
5	0.76	0.68	0.17	0.29	0.37	0.29
6	0.62	0.63	0.40	0.37	0.30	0.28
7	0.68	0.65	0.29	0.34	0.27	0.30
8	0.78	0.60	0.14	0.44	0.31	0.20
9	0.69	0.66	0.27	0.32	0.28	0.31
10	0.47	0.55	0.84	0.57	0.21	0.43
11	0.67	0.59	0.33	0.5	0.34	0.29
12	0.42	0.29	0.16	0.17	0.32	0.12
13	0.34	0.41	0.55	0.62	0.23	0.09
14	0.35	0.33	0.16	0.23	0.20	0.22
15	0.67	0.73	0.31	0.28	0.29	0.31
16	0.71	0.67	0.15	0.18	0.52	0.44
17	0.60	0.71	0.51	0.23	0.37	0.54
18	0.50	0.52	0.44	0.60	0.45	0.48
Mean ± SD	0.62 ± 0.14	0.61 ± 0.14	0.31 ± 0.18	0.33 ± 0.16	0.31 ± 0.08	0.31 ± 0.12
P value	0.517		0.528		0.964	

Notes: CI, conformal index; EI, external index; HI, homogeneity index.

Table 4. Comparing exposure of radiation doses to the bladder and bowel between pre-implantation and post-implantation in 13 patients with recurrence of rectal cancer

n	Bladder D_{5cc}	Bladder D_{5cc}	Bladder D_{2cc}	Bladder D_{2cc}	Bowel D_{5cc}	Bowel D_{5cc}	Bowel D_{2cc}	Bowel D_{2cc}
	pre-plan (Gy)	post-plan (Gy)	pre-plan (Gy)	post-plan (Gy)	pre-plan (Gy)	post-plan (Gy)	pre-plan (Gy)	post-plan (Gy)
1	29.4	25.4	36.7	35.6	32.1	57.8	42.5	72.3
2	49.3	54.4	66.7	65.5	74.3	27.2	93.0	31.5
3	11.0	11.0	18.7	20.5	50.9	70.5	70.1	93.8
4	73.2	36.9	102.0	55.0	43.4	103.8	61.0	138.8
5	12.3	15.9	15.2	18.6	27.3	0.8	39.4	1.5
6	19.8	43.5	30.9	69.1	64.3	71.6	83.8	93.4
7	0.0	0.0	0.0	0.0	42.2	69.3	52.1	85.8
8	20.3	23.3	35.5	42.4	61.1	72.0	70.9	88.6
9	20.8	34.1	27.1	42.5	77.6	38.6	103.5	47.2
10	1.2	0.0	1.4	0.0	51.6	24.2	73.0	37.3
11	12.8	18.3	16.3	24.0	3.9	3.5	6.2	5.7
12	34.0	26.3	40.4	32.7	7.0	46.2	11.7	64.4
13	11.1	31.4	43.0	40.8	39.7	34.2	54.1	42.5
Mean ± SD	22.7 ± 20.2	24.7 ± 15.9	33.4 ± 27.4	34.4 ± 21.8	44.3 ± 22.9	47.7 ± 30.0	58.6 ± 28.8	61.8 ± 39.0
p-value	0.640		0.851		0.707		0.790	

Notes: bladder D_{5cc} (exposure radiation dose of 5 cm^3 bladder volume), bladder D_{2cc} (exposure radiation dose of 2 cm^3 bladder volume), bowel D_{5cc} (exposure radiation dose of 5 cm^3 bowel volume), bowel D_{2cc} (exposure radiation dose of 2 cm^3 bowel volume).

Table 5. Assessment of toxicity according to the Common Terminology Criteria for Adverse Events (CTCAE; ver. 4.03)

	Pain		Skin/mucosal		GU		GI		Total	
Grade	≤2	≥3	≤2	≥3	≤2	≥3	≤2	≥3	≤2	≥3
Acute toxicities										
Cases	2	0	0	0	1	0	1	0	4	0
Percentage (%)	11.1	0	0	0	5.6	0	5.6	0	22.2	0
Chronic toxicities										
Cases	1	0	1	1	2	0	1	0	5	1
Percentage (%)	5.6	0	5.6	5.6	11.1	0	5.6	0	27.8	5.6

Notes: GU, genitourinary system; GI, gastrointestinal system.

HI between the two groups were not statistically significant ($P > 0.05$). These results indicated that the newly proposed treatment modality might improve the accuracy of ^{125}I seed implantation.

The feasibility and accuracy of CT-guided ^{125}I seed implantation assisted by 3D-PNCT for pelvic LRRC patients were investigated by comparing dosimetric parameters between pre-implantation and post-implantation. There were no significant differences among dosimetric parameters, and the doses delivered to the bladder and small intestines were well controlled. Nevertheless, significant dose-based differences between pre-, intra- and post-implantation in the bladder and bowel in several patients were observed. One reason was the movement of the bladder and bowel itself, which might suggest less adhesion between the bowel and the pelvic wall. Another reason might be the status of the empty stomach and epidural anesthesia during ^{125}I seed implantation. Adverse events were generally of lower grades (≤2) and well tolerated. The incidence of acute grades 1–2 gastrointestinal toxicity was 22.2% (4/18), and the incidence of chronic grades 1–2 gastrointestinal toxicity was 16.7% (3/18). The CT-guided ^{125}I seed implantation assisted by 3D-PNCT could achieve the ideal target dose distribution as designed by pre-implantation and limit the radiation doses to OAR. The present study revealed a favorable clinical outcome with fewer side effects. The local control and other results concerning the efficacy of this method will be assessed in the subsequent research when the follow-up time is sufficient.

Careful planning before seed implantation, precise positioning of seeds during operation and quality control of the workflow are vital to achieve successful ^{125}I seed implantation. The limitation of our study was the single-center experience with a small sample size. A long-term follow-up with a large cohort of patients, and randomized multicenter studies are warranted to confirm our findings.

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CONFLICT OF INEREST

The authors declare that there are no conflicts of interest.

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