Puncture and Dose Accuracies of Navigation-Assisted 3D-Printing Templates Combined with Computed Tomography Guided Radioactive Iodine-125 Seed Implantation in the Treatment of Malignant Tumors

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Abstract

Objective: To preliminarily verify the accuracy of navigation-assisted seed implantation by comparing preoperative and actual differences in puncture characteristics and dosimetry in computed tomography-guided, navigation-assisted radioactive iodine-125 seed implantation using 3D-printed templates for the treatment of malignant tumors.

Methods: A total of 27 tumor patients who were treated with seed implantation under combination guidance in our hospital between December 2018 to December 2019 were enrolled in this study. Navigation needles (n=1–3) were placed in each patient to obtain preoperative and intraoperative puncture information, including angle, depth, insertion point, and tip position; we also investigated the dosimetry parameters in the preoperative and postoperative plans, including D$_{90}$, V$_{100}$, V$_{150}$, V$_{200}$, minimum peripheral dose (MPD), conformal index, external index, and homogeneity index of the target area. The t-tests and nonparametric correlation tests were used for analysis (P<0.05 was considered significant).

Results: The means errors of the angle, depth, insertion point, and tip position were 0.47 ± 0.521°, 0.35 ± 0.238 cm, 1.7 ± 0.99 mm, and 3.1 ± 1.75 mm, respectively. There were no significant differences between the intraoperative and preoperative angles (P = 0.271), but there was a significant difference in depth (P = 0.002). Errors of the angle, depth, and insertion point were larger for the pelvic/retroperitoneal area than for the head and neck/chest wall (P < 0.05). With the exception of MPD, there was no significant difference in dosimetry indices between the postoperative and preoperative plans (P > 0.05). The MPD in the postoperative plan was higher than that in the preoperative plan (mean: 72.1 Gy and 63.8 Gy, respectively; P < 0.05).

Conclusion: Seed implantation under combination guidance showed good accuracy, and the actual intraoperative puncture information and postoperative doses were in good agreement with those in the preoperative plan, thereby demonstrating promising prospects for further development.

Introduction

Radioactive iodine-125 seed implantation (RISI) is being increasing used for the local treatment of tumors [1]. However, as it involves a puncture procedure, which largely depends on the physician's personal clinical experience and level of expertise, the quality of the procedure and treatment effect vary, limiting the further promotion of RISI for clinical use. Three-dimensional-printing template (3DPT) technology is a milestone in the advancement of RISI therapy. With 3DPT guidance, accurate control of the seed needle has been realized, greatly improving adherence to the preoperative plan [2]. Recently, some studies have used an image navigation system (INS) to assist in the treatment of head and neck tumors using seed implantation, achieving good puncture accuracy [3]. This study applied INS and 3DPT to RISI treatment for tumors in various parts of the body to evaluate the puncture and dose accuracies under combination guidance and provide a theoretical basis and data support for the rational selection and optimization of implantation protocols.

1. Methods

1.1 Baseline clinical data

A total of 27 patients with malignant tumors who were treated with INS-assisted, 3DPT-guided, computed tomography (CT)-guided RISI in our department between December 2018 and December 2019 were enrolled in this study. All patients had complete imaging data, preoperative/postoperative plans, and intraoperative data. All treated patients met the indication criteria for radioactive seed implantation [1]: (1) patients who showed relapse after surgery or external radiotherapy or refused surgery or external radiotherapy with a tumor diameter ≤ 7 cm; (2) the pathological diagnosis was clear; (3) there was a suitable puncture path; (4) there was no bleeding tendency or hypercoagulable state; (5) the general physical condition was good (Karnofsky performance status score > 70), radioactive seed implantation could be tolerated; and (6) the expected survival was > 3 months. All patients signed an informed consent form prior to treatment. Table 1 shows the baseline information of the patients, target lesions, and the preoperative plan. The research protocol was approved by the Ethics Committee.
### Table 1
Baseline information of the patients and lesions

| Characteristic                  | Number | Proportion(%) |
|--------------------------------|--------|---------------|
| Gender                         |        |               |
| Male                           | 17     | 63.0          |
| Female                         | 10     | 37.0          |
| Age (years old)                | Median 59 (34–84) |               |
| KPS                            | Median 80 (60–90)  |               |
| Primary disease                |        |               |
| SCC of nasopharynx / H & N*    | 9       | 33.3          |
| Colorectal cancer              | 6       | 22.2          |
| Cervical cancer                | 5       | 18.5          |
| Esophageal cancer              | 3       | 11.1          |
| Lung cancer                    | 2       | 7.4           |
| Breast cancer                  | 1       | 3.7           |
| Prostatic cancer               | 1       | 3.7           |
| Sarcoma                        | 1       | 3.7           |
| Position of seed               | 0.0     |               |
| Head and neck                  | 13      | 48.1          |
| Chest wall                     | 1       | 3.7           |
| Pelvic cavity                  | 11      | 40.7          |
| Retroperitoneal & paravertebral | 2     | 7.4           |
| Prescription dose (Gy)         | Median 130 (110–160) |     |
| Activity of seed (mCi)         | Median 0.5 (0.4–0.64) |     |
| Number of navigation needle    |        |               |
| 1                              | 12     | 44.4          |
| 2                              | 5      | 18.5          |
| 3                              | 10     | 37.0          |

*H & N: head and neck

### 1.2 Information on systems, materials, and equipment

(1) Brachytherapy treatment planning system (BTPS): KLSIRPS-3D, Beijing University of Aeronautics and Astronautics, and Beijing Astro Technology. The source data in the planning system were derived from TG 43 and its updated document issued by the American Association of Physicists in Medicine [4, 5]. (2) CT: Brilliance Bigbore CT and Philips. (3) INS: IGS-MO Optical Image Navigation system and Xinbo Medical Technology (Fig. 1). (4) 3DPT: 3D photocuring rapid-prototyping machine printing (Shanghai 3D Union Tech, RS6000), with an accuracy of 0.1 mm, and photocurable resins that comply with the European Communities standards were used as printing materials. (5) I-125 seeds: type 6711_1985, from HTA Co., Ltd, with a half-life of 59.4 days and dose rate constant of 0.965 cGy/(h·U). (6) Radioactive I-125 seed implantation devices: Mick Radio-Nuclear Instruments and Eckert & Ziegler BEBIG.
1.3 Preoperative plan

We performed 3DPT-guided RISI in accordance with published profession standards [6]. INS assistance was applied based on the following aspects:

(1) Positioning and preoperative plan design: CT, with a slice thickness of 2.5 mm, was performed 2 days before operation. The posture (supine/prone/lateral) was selected according to the location of the lesion; the vacuum pad was fixed, and the body surface was marked with a pendulum line. CT data were transmitted to the BTPS for developing a preoperative plan design. The tumor in the target area (gross tumor volume, GTV) and the organs at risk (OAR) within 2 cm around the target area were outlined to set the prescribed dose and seed activity; identify the direction, distribution, and depth of the seed needle; and set up 1–3 navigation needles. The number of seeds was calculated, and the spatial distribution of the seeds was simulated. Through BTPS optimization, GTV $D_{90}$ (when GTV receives 90% of the dose) was adjusted to meet the prescribed dose setting requirements.

(2) Design and production of 3DPT: Personalized digital modeling of the treatment area template in the BTPS and additional information on the alignment axis and puncture characteristics were used to set the printing range of the template. A 3DPT was produced using a 3D photocuring rapid-prototyping machine and medical photocuring resin material. The 3DPT included body surface information, alignment marks, and puncture information with respect to the treatment area of the patients.

(3) Patient reset and INS-assisted 3DPT alignment and fixation: The patient was reset with reference to the positioning mark, and the template was aligned with reference to the positioning mark, template coordinates, and the contour of the patient’s body surface. An optical tracer was placed on the CT rack and the template navigation needle. CT was performed with the image information transmitted to the INS, and image fusion and registration were conducted. The navigation needle was inserted under the guidance of the virtual navigation needle displayed by the INS, and the position of the needle was adjusted in real time so that the position of the virtual navigation needle in the intraoperative image anatomy was consistent with the position of the navigation needle set in the preoperative plan. After insertion of the navigation needle was completed, CT was performed to confirm that the position of the needle was accurate, and fine-tuning was conducted when there was an error. After the navigation needles were correctly calibrated, the 3DPT position was considered accurate.

(4) Puncture and seed implantation: After the 3DPT was accurately positioned, the rest of the seed needles were percutaneously punctured to the predetermined depth through a template guide hole. During the puncture process, CT was performed to monitor the needle insertion path, and the needle was fine-tuned, if necessary, to avoid damage to the OAR. After the needle was in place, the seeds were implanted according to the preoperative plan, and CT was performed to confirm the seed distribution. As there may be differences between the actual intraoperative situation and the preoperative plan, intraoperative optimization was carried out if necessary, and the needle insertion path and seed distribution were adjusted in real time to ensure that the dose received by the GTV met the requirements of the preoperative plan.

(5) Postoperative dose evaluation: CT was performed postoperatively, the image was transmitted to the BTPS for dose verification, and the actual doses delivered to the GTV and OAR were evaluated. The technical process is shown in Fig. 2. The postoperative dose quality evaluation complied with the quality evaluation standard defined by the BC (British Columbia) Cancer Research Center [7]. According to the immediate verification of the target area $D_{90}$ and $V_{100}$ (volume when the GTV receives 100% of the prescribed dose), the evaluation results were characterized as excellent, good, fair, and poor.

1.4 Collection and comparison of treatment parameters

(1) Puncture information: In the BTPS, the images taken after the intraoperative navigation needle was in place were fused with the preoperative plan images, and rigid registration for the bone was performed. In the fusion image, both the virtual and actual puncture characteristics with respect to the preoperative plan were displayed. The angle and depth of the puncture before and during the operation were compared, and the absolute value of the difference was taken as the error value. Meanwhile, the straight-line distances between the two puncture points on the body surface and between the two tip positions were recorded.

(2) Dosimetry information: In the BTPS, every dosimetry parameter from the preoperative and postoperative plans was recorded and compared, including GTV $D_{90}$, $V_{100}$, $V_{150}$ (volume when the GTV receives 150% of the prescribed dose), $V_{200}$ (volume when the GTV...
receives 200% of the prescribed dose), and minimum peripheral dose (MPD; the minimum dose received at the edge of the GTV) in the target area. With regards to the conformal index (CI) \[8\], \(\text{CI} = \left( \frac{V_{T,\text{ref}}}{V_T} \right) \times \left( \frac{V_T}{V_{T,\text{ref}}} \right)\), where \(V_T\), \(V_{T,\text{ref}}\), and \(V_{\text{ref}}\) are the volume of the target area, the volume of the target area receiving the prescribed dose, and the total volume (cm\(^3\)) contained in the prescribed dose, respectively. The optimal CI was 1, which indicated that the prescribed dose covered the target area but the received dose outside the target area was lower than the prescribed dose. A larger CI indicated that the volume inside the target area receiving the prescribed dose was larger, whereas the volume outside the target area receiving the prescribed dose was smaller. In terms of the external index (EI) \[9\], \(\text{EI} = \left( \frac{V_{\text{ref}}}{V_{T,\text{ref}}} \right) / V_T \times 100\%\). The optimal EI was 0, which suggested that the dose tissues outside the target area received less than the prescribed dose. A higher EI implied that the volume of the prescribed dose received outside the target area was larger. Regarding the homogeneity index (HI) \[9\], \(\text{HI} = \left( \frac{V_{T,\text{ref}}}{V_{T,1.5\text{ref}}} \right) / V_{T,\text{ref}} \times 100\%\), where \(V_{T,1.5\text{ref}}\) is the volume (cm\(^3\)) of the target area receiving 150% of the prescribed dose. The ideal optimal HI was 100%. A higher HI suggested a more uniform dose distribution in the target area. As the location of the lesions was scattered and the adjacent OAR varied, this study was not designed to compare OAR doses.

(3) Other treatment information: In the BTPS, other preoperative and postoperative treatment parameters were collected and compared, including GTV and the numbers of needles and seeds.

**1.5 Statistical methods**

For comparisons between groups, a Shapiro-Wilk test was first used to verify whether the data in each group were normally distributed. A \(P\) value > 0.05 indicated that the data conformed to a normal distribution. For normally distributed data, a \(t\)-test (including paired and independent sample \(t\)-tests) was used for comparison, and the \(t\)-value was used to describe the test value. For non-normally distributed data, a nonparametric test was adopted for comparison (Wilcoxon test for correlated samples and Mann-Whitney U test for independent samples), and the \(z\)-value was used to describe the test value. \(P\)-values \(\leq 0.05\) were considered as statistically significant, and the statistical software used was SPSS 25 (IBM Corporation).

**2. Results**

Navigation-assisted 3DPT combined with CT-guided RISI can be successfully completed according to the established technical procedures. A total of 52 navigation needles were used in 27 patients (mean: 2 ± 1). The preoperative and intraoperative needle angles ranged between 72.5–111.1° and 73.9–109.9°, respectively, and the absolute value of the difference between the two groups was 0–1.7°. The preoperative and intraoperative needle depths ranged between 2–11 cm and 2–11.8 cm, respectively, and the absolute value of the difference between the two groups was 0–0.89 cm. Table 2 lists the results of the comparison between the two groups. In addition, the range, median, and mean value of error of the needle insertion point for the two groups were 0–3.9 mm, 1.3 mm, and 1.7 ± 0.99 mm, respectively, and those of the needle tip were 0–0.88 mm, 2.9 mm, and 3.1 ± 1.75 mm, respectively. The range and mean value of the needle depth in the head & neck and chest wall were 2–6.6 cm and 3.4 ± 1.08 cm, respectively, and those in the retroperitoneal & paravertebral and pelvic part were 4.3–11.8 cm and 5.8 ± 1.71 cm, respectively. The results of a Mann-Whitney U test showed that there was significant difference in needle depth between the two groups (\(P = 0.000\)). If divided into two groups by position, the error of the retroperitoneal & paravertebral and pelvic cavity were significantly larger than those of the head & neck and chest wall (Table 3), and the differences in angle, depth, and insertion point were statistically significant (\(P < 0.05\)).
Table 2
Comparison of the preoperative and intraoperative needle angle and depth

| Parameter     | Preoperative | Intraoperative (actual) | Absolute value of error | Shapiro-Wilk significance (Pre/Intra)* | Normal distribution | Test value (z) | P (Wilcoxon) |
|---------------|--------------|-------------------------|-------------------------|----------------------------------------|---------------------|----------------|--------------|
| Angel (degree) | 90 ± 5.47    | 90.7 ± 5.35             | 0.35                    | 0.47 ± 0.521                           | No                  | -1.1           | 0.271        |
| Depth (cm)    | 4 ± 1.78     | 4.4 ± 1.81              | 0.3                     | 0.35 ± 0.238                           | No                  | -3.172         | 0.002        |

*Pre: Preoperative; Intra: Intraoperative

Table 3
Comparison of the navigation needle error between different body parts

| Parameter                  | Head & neck and chest | Retroperitoneal & paravertebral and pelvic | Shapiro-Wilk significance (HNC/RPP)* | Normal distribution | Test value (t/z) | P (Independent-t/Mann-Whitney U) |
|----------------------------|------------------------|--------------------------------------------|--------------------------------------|--------------------|------------------|-----------------------------|
| Angle error (degree)       | 0-1.7                  | 0-1.4                                      | 0.000/0.068                          | No                 | -2.739           | 0.006                       |
| Depth error (cm)           | 0-0.62                 | 0-0.89                                    | 0.041/0.172                          | No                 | -2.298           | 0.022                       |
| Insertion point error (mm) | 0-2.6                  | 0-3.9                                      | 0.000/0.073                          | No                 | -3.01            | 0.003                       |
| Tip error (mm)             | 1.5-4.0                | 0-8.8                                      | 0.064/0.541                          | Yes                | -1.755           | 0.092                       |

*HNC: Head & neck and chest; RPP: Retroperitoneal & paravertebral and pelvic

Table 4 summarizes the comparison of dosimetry parameters between the preoperative and postoperative plans. With the exception of MPD, the other parameters were similar in both groups, and there was no significant difference (P > 0.05). The MPD in the postoperative plan was higher than that in the preoperative plan (mean: 72.1 Gy and 63.8 Gy, respectively; p = 0.029). The actual number of seeds used after the operation was higher than that planned before the operation (mean: 61.4 and 59.7, respectively; p = 0.031). The volume of the target area (GTV) in the postoperative plan was larger than that in the preoperative plan (mean: 41.3 cm³ and 40.2 cm³, respectively; P = 0.005). In terms of the postoperative dose quality evaluation, the results were excellent in 18 cases (67%), good in 6 cases (22%), fair in 2 cases (7%), and poor in 1 case (4%). Of the 2 cases with fair evaluation quality, one case involved the head and neck and the other involved the pelvic area with postoperative D₉₀s of 128.4% (166.9 Gy/130 Gy) and 87.7% (131.5 Gy/150 Gy) of the prescribed dose, respectively. The one case with poor evaluation quality was a pelvic case, and the postoperative D₉₀ was 79.8% of the prescribed dose (103.7 Gy/130 Gy).
Table 4
Comparison of dosimetry parameters between the preoperative and postoperative plans

| Parameter | Preoperative | Postoperative | Shapiro-Wilk significance (Pre/Intra)* | Normal distribution | Test value | P(Paired-t/Wilcoxon) |
|-----------|--------------|---------------|----------------------------------------|---------------------|------------|-----------------------|
|           | Range | Median | Mean | Range | Median | Mean |                         |                     |                        |
| GTV (cm³) | 10.1-137.1 | 33.6 | 40.2 ± 28.19 | 10.3-137.1 | 33.5 | 41.3 ± 27.90 | 0.001/0.001 | No | -2.813 | 0.005 |
| Needle    | 8–35 | 13 | 15.2 ± 6.48 | 7–35 | 14 | 14.9 ± 6.63 | 0.009/0.01 | No | -1.378 | 0.168 |
| Seed      | 26–135 | 54 | 59.7 ± 24.23 | 26–135 | 59 | 61.4 ± 24.30 | 0.021/0.012 | No | -2.154 | 0.031 |
| D₉₀(Gy)   | 109.6-163.7 | 139.3 | 141.0 ± 15.21 | 103.7-167.4 | 145.3 | 141.9 ± 17.13 | 0.077/0.027 | No | -0.762 | 0.446 |
| MPD(Gy)   | 23.5-92.4 | 60.5 | 63.8 ± 20.59 | 45.2-104.0 | 71.3 | 72.1 ± 16.71 | 0.135/0.539 | Yes | -2.307 | 0.029 |
| V₁₀₀(%)   | 85.1-99.7 | 93.2 | 93.8 ± 3.62 | 87.3-100 | 94.5 | 94.2 ± 3.68 | 0.128/0.12 | Yes | -0.41 | 0.685 |
| V₁₅₀(%)   | 34.5-89.8 | 69.2 | 70.4 ± 13.11 | 37.3-94.1 | 68.2 | 70.0 ± 14.61 | 0.217/0.508 | Yes | 0.214 | 0.832 |
| V₂₀₀(%)   | 14.6-77.6 | 38.5 | 41.0 ± 17.42 | 18.4-74.1 | 37.5 | 41.3 ± 15.92 | 0.037/0.012 | No | -0.521 | 0.603 |
| CI        | 0.4–0.8 | 0.60 | 0.58 ± 0.131 | 0.4–0.9 | 0.59 | 0.59 ± 0.155 | 0.094/0.059 | Yes | -0.289 | 0.775 |
| EI(%)     | 9–99 | 31.5 | 45.6 ± 31.21 | 6.3–152 | 27.7 | 47.5 ± 37.79 | 0.001/0.002 | No | -0.445 | 0.657 |
| HI(%)     | 9-61.9 | 25.9 | 24.9 ± 12.17 | 3.4–57.1 | 28.3 | 26.3 ± 13.55 | 0.034/0.406 | No | -0.747 | 0.455 |

*Pre: Preoperative; Intra: Intraoperative

3. Discussion
Although the BTPS enables doctors to develop more rational treatment plans before the operation, if the position of the seed needle is not accurate in the actual operation, it is often difficult for the actual postoperative dose to meet the expectations of the preoperative plan, thus affecting follow-up treatment. The ultimate goal of both 3DPT and INS technologies is to enable more accurate insertion of the seed needle according to the preoperative plan. In terms of the 3DPT, a number of related studies have shown that it has good accuracy, with the postoperative dose meeting the requirements of the preoperative plan [2, 6, 10]. INS is another solution for puncture intervention technology. This technology fuses and registers CT, magnetic resonance, or positron emission tomography images obtained before the operation with intraoperative real-time images. During the operation, the position of the puncture needle is tracked in real time by a tracer (optical or magnetic positioning) to locate the lesion on the fusion image, thereby guiding the operator to perform the puncture [11]. Owing to its real-time, dynamic, and visible characteristics, INS is widely used in biopsy, ablation, and other puncture-related operations [12–14]. However, the combination of the two techniques for RISI and its application in the treatment of tumors in many parts of the body have rarely been reported in this country and abroad. The current data showed that the accuracy of INS-assisted 3DPT-guided RISI treatment was good.
According to different positioning principles, INS mainly includes magnetic and optical positioning and navigation [15]: (1) Magnetic positioning and navigation are chiefly to fix the sensor coil on the tracked device (such as the puncture device). When the sensor coil moves relative to the magnetic field emitter, it produces different intensity currents, and then locates the tracked device through the current signal. (2) Optical positioning and navigation are primarily used to fix the tracer on the CT machine and tracked device, and the infrared camera is used to directly detect the position of the tracer. Compared with magnetic positioning, optical positioning is faster in data transmission and has higher accuracy. The disadvantage is that there can be no obstruction between the optical camera and tracked device, and the position of the needle tip cannot be tracked. Optical positioning and navigation were adopted in this study, but the optical positioning and navigation tracer was large and occupied a large space after being fixed to the seed needle. Furthermore, RISI is a multi-needle operation, so it is impossible to equip all seed needles with tracers. Therefore, 1–3 navigation needles were set for each case in this study. By tracking, guiding, and controlling the navigation needles, we accurately set the 3DPT position, reduced the number of times of adjustment of 3DPT position and CT confirmation, and preliminarily obtained the accuracy data of INS with 3DPT-guided puncture, which could be used as a reference for follow-up multi-needle guidance.

Based on the data in this study, the needle accuracy under INS with 3DPT was good, and the mean errors of the angle, depth, insertion point, and tip were 0.47 ± 0.521°, 0.35 ± 0.238 cm, 1.7 ± 0.99 mm, and 3.1 ± 1.75 mm, respectively. Thus, the mean error of the angle was < 1°, and the mean error of distance was approximately 3 mm. Compared with the previous studies on 3DPT and/or INS assisted brachytherapy (the average tip error was 0.86-7 mm, and the average angle error was 1.9–5.6°), the accuracy of our study was similar or even better [3, 16–18]. Good accuracy contributes to reducing the times of CT scan confirmation and shortening the operation time. For angle comparison, the preoperative and intraoperative angles were not statistically different (P = 0.271), but the intraoperative depth was slightly greater than the preoperative depth (4.4 ± 1.81 cm and 4.3 ± 1.78 cm, respectively; P = 0.002). The reasons for the errors were considered to be changes in skin contour and thickness caused by anesthesia, template alignment issues, and an unsatisfactory fit between the template and body surface. In terms of the treatment site, angle, depth, and insertion point errors in the pelvic/retroperitoneal region were larger than those in the head and neck/chest wall (P < 0.05). In addition to the abovementioned reasons, these errors were possibly attributed to the fact that longer insertion paths led to greater errors (the difference in insertion depth between the two groups was statistically significant, P < 0.05). Moreover, the stability of tissues and organs in the head and neck/chest wall treatment area was better than that in the pelvic/retroperitoneal region. This prompted us to focus on the accuracy of needle insertion and perform multiple CT scans to confirm if it was necessary in areas where the treatment location was deep and the tissue was soft and prone to change.

By comparing the preoperative and postoperative dosimetry parameters in this study, we revealed that most of them were not significantly different, suggesting that the postoperative dose could better meet the requirements of the preoperative plan. The only dosimetry index with a significant difference was MPD, which was alternatively expressed as D_{100} (when GTV receives 100% of the dose). MPD in the postoperative plan was higher (P < 0.05), indicating that the error in this study did not result in a reduction in dose to the target area. The reason may be that we replanted seeds in the patients whose immediate postoperative CT scans showed unsatisfactory seed distribution. This also explains why the number of seeds in the postoperative plan was higher than that in the preoperative plan, and the difference was statistically significant (P = 0.031). Moreover, the GTV in the postoperative plan was larger than that in the preoperative plan (P = 0.005), which was possibly related to intraoperative and postoperative bleeding, edema, and inflammatory reactions. Immediate postoperative CT allows for real-time observation of seed distribution. For patients with poor seed distribution, the timely replanting of seeds could effectively prevent a cold spot of the dose in the target area [1]. The postoperative D_{90} of the three cases with fair and poor evaluation quality did not reach 90% and 80% of the prescribed dose, respectively, suggesting that RISI is an operation-dependent treatment, and there remain a few cases that have difficulty in meeting expectations in the actual operation. It is believed that the accuracy of treatment will be improved with further proficiency and experience with the procedure. Many studies have analyzed the dose accuracy of RISI guided by 3DPT, the results indicate that the dose accuracy was good [2, 10, 19, 20], however, there was no analysis of needle path error in each study. Whether INS combined with 3DPT guidance is really better than 3DPT guidance alone still needs to be further studied.

The limitations of this study are as follows: (1) the technical development time was slightly short, and the sample size was small; (2) it was limited to comparisons between treatment plans, and further observation and follow-up is needed for subsequent clinical effects; (3) due to the small number of cases and scattered treatment sites, effective comparison of the dose distribution to endangered organs in different parts was not available; and (4) the combination and process of INS with 3DPT remain in the initial
stages and need to be further explored and improved. In a follow-up study, we will further accumulate cases and conduct in-depth and detailed research.

4. Conclusion

The combination of INS and 3DPT technologies for RISI treatment showed good accuracy and feasibility and exhibited good quality with regard to completion of the implantation plan. Errors in the actual needle insertion during the operation were smaller than that before the operation. The actual $D_{90}$ in the target area, CI, and dose uniformity all met the design requirements of the preoperative plan. In a follow-up study, we will expand the number of cases, refine the study, and clarify the efficacy and safety of this approach based on clinical data.

List Of Abbreviations

RISI: Radioactive Iodine-125 Seed Implantation
3DPT: Three-Dimensional Printing Template
INS: Image Navigation System
CT: Computed Tomography
BTPS: Brachytherapy Treatment Planning System
GTV: Gross Tumor Volume
OAR: Organs at Risk
BC: British Columbia
MPD: Minimum Peripheral Dose
CI: Conformal Index
EI: External Index
HI: Homogeneity Index
H & N: Head and Neck
HNC: Head & neck and Chest
RPP: Retroperitoneal & Paravertebral and Pelvic
Pre: Preoperative
Intra: Intraoperative

Declarations

Ethical Approval and Consent to participate

The study protocol was approved by Peking University Third Hospital Medical Science Research Ethics Committee [M2019243]. All patients signed an informed consent form prior to treatment.

Consent for publication
All authors agree to publish the study in this journal.

**Availability of supporting data**

The supporting data used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Competing interests**

There is no competing interest disclosure from any authors.

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**Authors' contributions**

Junjie Wang was the guarantor of integrity of the entire study, who was responsible for the study concepts and design. Junjie Wang and Zhe Ji carried out literature research, manuscript editing and manuscript preparation. Zhe Ji, Yuliang Jiang, Fuxin Guo and Jinghong Fan carried out the clinical treatment and collected the clinical data. Zhe Ji and Haitao Sun carried out the treatment planning design. Zhe Ji, Yuliang Jiang and Haitao Sun carried out the data statistical analysis and interpretation. Fuxin Guo and Jinghong Fan assisted with revising the manuscript.

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Figures
Figure 1

INS composition. a. CT position and optical tracer for needle position; b. optical sensing device; c. image registration and real-time display system; and d and e. the real-time operator-guided operation.

Figure 2
Flowchart of INS-assisted 3DPT-guided RISI. a. Preoperative plan (navigation needle setup); b. Navigation-guided insertion of the navigation needle; c. Seed needles inserted when the navigation needle was in place; d. Preoperative images fused with the intraoperative images to measure the errors (angle, insertion point, and tip) of the navigation needle; e. Preoperative plan; f. 3DPT and CT guided seed needles insertion; g. Seed implantation; e. Dose verification.