

# The Accuracy of Individualized Three Dimensional-printing Template Assisted I<sup>125</sup> Radioactive Seed Implantation for Recurrent head and Neck Cancer

**Bin Qiu**

Department of Radiation Oncology, Peking University Third Hospital, Beijing,100191, China

<https://orcid.org/0000-0003-1133-5562>

**Yuliang Jiang**

Department of Radiation Oncology, Peking University Third Hospital, Beijing,100191, China

**Zhe Ji**

Department of Radiation Oncology, Peking University Third Hospital, Beijing,100191, China

**Haitao Sun**

Department of Radiation Oncology, Peking University Third Hospital, Beijing,100191, China

**Jinghong Fan**

Department of Radiation Oncology, Peking University Third Hospital, Beijing,100191, China

**Weiyan Li**

Department of Radiation Oncology, Peking University Third Hospital, Beijing,100191, China

**Yuxia Shao**

Department of Radiation Oncology, Peking University Third Hospital, Beijing,100191, China

**Ping Jiang**

Department of Radiation Oncology, Peking University Third Hospital, Beijing,100191, China

**Junjie Wang (✉ anglebin@126.com)**

Department of Radiation Oncology, Peking University Third Hospital, Beijing,100191, China

---

## Research

**Keywords:** 3D-printing, radioactive seed implantation, head and neck cancer, brachytherapy

**Posted Date:** June 30th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-38129/v1>

**License:**  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

# Abstract

**Background:** Individualized three-dimensional-printing template(3D-PT) is developed to facilitate  $I^{125}$  radioactive seed implantation (RSI) for recurrent head and neck cancer, while most of the previous studies were focused on the efficacy and safety profiles, study on the accuracy of  $I^{125}$  RSI is lacking. Therefore, the aim of this study is to evaluate the accuracy involving needle puncture and dosimetry of individualized 3D-printing template (3D-PT) assisted  $I^{125}$  radioactive seed implantation (RSI) for head and neck cancer.

**Materials and Methods:** From February 2017 to January 2020, clinical data of 41 patients (mean age,  $58.5 \pm 16.1$  years; 28 males) with recurrent primary (48.8%)/secondary (51.2%) head and neck cancer underwent individualized 3D-PT assisted  $I^{125}$  RSI under CT guidance in our institute were retrospectively reviewed.

**Results:** A total of 430 [mean, 10.5 (range 3–17) per patient] needles were inserted. Technical success rate was 100% without major complication. The mean entrance deviation was 0.090 cm (95% Confidence Interval, 0.081–0.098), which was significantly larger in patients with primary cancer than patients with secondary cancer ( $0.107 \pm 0.012$  vs.  $0.072 \pm 0.012$  cm,  $p < 0.001$ ). The mean intraoperative depth and angular of the needle were consistent with planned depth and angular ( $6.23 \pm 0.24$  vs.  $6.21 \pm 0.24$  cm,  $p = 0.903$ ;  $83.14 \pm 3.64$  vs.  $83.09 \pm 3.66$  degrees,  $p = 0.985$ , respectively). The mean deviation between planned and intraoperative depth and angular of the needle were  $0.168 \pm 0.024$  cm and  $1.56 \pm 0.14$  degrees, respectively, without significant difference involving cancer type and implantation site ( $p = 0.065$  and  $0.092$ , respectively). The post-plan dosimetry parameters, including D90, D100, V100, V150, V200, conformity index, external index, and homogeneity index, were all well coordinate with planned dosimetry without significant deference (all  $p > 0.05$ ).

**Conclusions:** Individualized 3D-PT assisted  $I^{125}$  RSI may be accurate with consistent planed and post-plan dosimetry for patients with recurrent head and neck cancer, further prospective study is warranted.

## Background

Brachytherapy (BT) is a specific form of radiotherapy (RT) consisting of the precise placement of radioactive sources directly placed into or next to the tumor [1]. Currently, BT has the potential to deliver an ablative radiation dose ( $\geq 100$  Gy) over a short period of time directly to the altered tissue area with the advantage of a rapid fall-off in dose, and consequently, sparing of adjacent organs [2, 3]. BT was recommended by both The Head and Neck Working Group of the European Brachytherapy Group and American Brachytherapy Society as one of the treatment for head and neck cancers, as external beam radiotherapy (EBRT) alone is difficult to spare adjacent normal tissues such as the salivary glands, the mandible, and mastication muscles which sustain undesirable late effects [4, 5].

As the standard option for early stage prostate cancer,  $I^{125}$  radioactive seed implantation (RSI) is also commonly used for recurrent head and neck cancer, providing a high local tumor control and preservation of organ functions [1, 6, 7]. While the deviation between planned and intraoperative needle pass way may occur even under the image guidance of Ultrasound, Computerized Tomography(CT), and Magnetic Resonance Imaging(MRI), leading to the mis-implantation of radiative seeds and unnecessary radiation or damage of surrounding critical organs and tissues. Owing to the dense critical organs and tissues (e.g. eyes, major vessels and nerve) in head and neck region, the accuracy of  $I^{125}$  RSI and post-plan dosimetry was extremely critical for patients with head and neck cancer. Individualized three dimensional-printing template (3D-PT) was developed to facilitate  $I^{125}$  RSI for head and neck cancer in order to improve the accuracy, optimize post-plan dosimetry, and shorten the RSI duration [8-11].

However, most of the previous studies involving 3D-PT assisted  $I^{125}$  RSI were focused on the efficacy and safety profiles, mainly including local control, survival and complications [7, 11-13]. As the mean entrance deviation, planned and intraoperative deviation of needle depth and angular were deemed to represent the accuracy of needle related interventions, only 2 studies involving these parameters were published to described the accuracy of 3D-PT assisted  $I^{125}$  RSI for head and neck cancer [9, 14]. Indicated by existed evidence, 3D-PT assisted  $I^{125}$  RSI may provide satisfied accuracy with consistent planed and post-plan dosimetry without additional complications [9, 11, 14], while cases reported in these studies was limited. Here, the aim of the study is to evaluate the accuracyinvolving needle puncture and dosimetry of individualized3D-PT assisted  $I^{125}$  RSI for patients with recurrenthead and neck cancer in our institute.

## Materials And Methods

### *Study Design*

The retrospective study was approved by our institutional review board and the requirement to obtain written informed consent was waived. The electronic database of our institute was searched and reviewed to identify eligible patients. Patients who underwent 3D-PT assisted  $I^{125}$  RSI under CT guidance for the treatment of recurrent primary/secondary head and neck cancer between February 2017 to January 2020 were included. The indications for 3D-PT assisted  $I^{125}$  RSI were as follows: (i) Residual/Recurrent primary/secondary head and neck cancer after surgery; (ii) Progressive/Recurrent primary/secondary head and neck cancer after EBRT and/or chemotherapy. The contraindications were as follows: (i) Active infection; (ii) The diameter of largest tumor  $> 7$  cm or any active concomitant distant cancer; (iii) Karnofsky Performance Score  $\leq 70$  or predicted life span  $\leq 3$  months; (iv) Approach of  $I^{125}$  RSI deemed not available revealed by preoperative CT/MRI; (v) International normalized ratio  $> 2$ ; and (vi) Pregnancy/mental disorder or any somatic comorbidities of clinical concern.

The technical success rate, number of needle and seed, and the mean entrance deviation, the depth and angular of the planed and intraoperative inserted needles, and planed and post-plan dosimetry profiles were recorded. Subgroups by cancer type (primary/secondary) and implantation site (head/neck, bounded

by the connecting line of the lower margin of the jaw, the mandibular angle, the tip of the mastoid process, superior nuchal line, and the external occipital carina) were further analyzed. Technical success was defined as successful needle insertion and implantation of  $I^{125}$  seed in the targeted tumors per preoperative/intraoperative plan. The mean entrance deviation was defined as the superficial distance between the planned needle entrance point and the actual intraoperative needle entrance point. The depth and angular of the needle were directly calculated and extracted from the BT Treatment Planning System (BT-TPS) after fusing the preoperative and intraoperative CT images into the same coordinate axis. The depth of the needle was defined as the tip of the planned/inserted needle to the template surface when the needle is deemed deep enough/in place during the retrusive implantation. The angular of the needle was defined as the angle between the needle and the horizontal axis when the needle is deemed in place. The planned and post-plan dosimetry parameters, including the prescription dose (PD), seed number, gross tumor volume (GTV), D<sub>90</sub>, D<sub>100</sub>, V<sub>100</sub>, V<sub>150</sub>, V<sub>200</sub>, conformity index (CI), external index (EI), and homogeneity index (HI), were recorded and compared. D<sub>90</sub> and D<sub>100</sub> refer to the dose delivered to the 90% or 100% of GTV, respectively. V<sub>100</sub>, V<sub>150</sub>, and V<sub>200</sub> refer to the percentage of GTV receiving 100% or 150% or 200% of prescription dose, respectively.

### ***Patient Population***

A total of 41 patients (mean age,  $58.5 \pm 16.1$ ; range, 10–87 years) with head and neck cancer were included. Majority of the patients was male ( $n = 28$ , 68.3%). Recurrent primary head and neck cancer ( $n=20$ , 48.8%) included oral carcinoma ( $n=6$ , 14.6%), oropharyngeal cancer ( $n=2$ , 4.9%), laryngocarcinoma ( $n=2$ , 4.9%), thyroid cancer ( $n=2$ , 4.9%), orbital rhabdomyosarcoma ( $n=2$ , 4.9%), and other cancers ( $n= 6$ , 14.6%). Other cancers were consisted of nasopharynx cancer ( $n=1$ , 2.4%), hypopharyngeal carcinoma ( $n=1$ , 2.4%), frontal sinus carcinoma ( $n=1$ , 2.4%), chordoma ( $n=1$ , 2.4%), maxillary sinus carcinoma ( $n=1$ , 2.4%), and parotid gland carcinoma ( $n=1$ , 2.4%). Secondary head and neck cancer ( $n = 21$ , 51.2%) included lymphatic metastasis ( $n = 19$ , 46.3%) derived from lung cancer ( $n = 4$ , 9.8%), esophageal cancer ( $n=3$ , 7.3%), nasopharynx cancer ( $n=3$ , 7.3%), oral carcinoma ( $n=3$ , 7.3%), laryngocarcinoma ( $n=1$ , 2.4%), thymic carcinoma ( $n=1$ , 2.4%), breast cancer ( $n=1$ , 2.4%), cervical cancer ( $n=1$ , 2.4%), and cancer of unknown ( $n=2$ , 4.9%), and 2 patients (4.9%) presented with brain metastasis from lung cancer. All the patients received previous treatments. Implanted tumor was mainly located in the neck region ( $n=22$ , 53.7%, 4 primary cancers and 18 secondary cancers) and 81.8% of the cancer in the neck was secondary cancer, 84.2% of the cancer in the head was primary cancer. The characteristics of the patients are presented in **Table 1**.

### ***$I^{125}$ RSI Procedure***

#### ***Preoperative planning***

Patients all underwent contrast-enhanced CT with 2.5-mm or 5-mm (rarely, for large tumors only) resolution within 2–3 days before RSI. All patients were fixed with a bow cap/vacuum pad in selected suitable gesture according to the lesion location and facilitation for RSI and then marked with

surfacepositioning line. Then the CT images were transferred into the BT-TPS (Beijing Feitian Industries Inc and Beijing University of Aeronautics and Astronautics, Beijing, China). The preoperative plan was then established by defining GTV and adjacent organs at risk (OARs), determining PD according to expert consensus on  $I^{125}$  RSI [15] and clinical experiences gained in our department, commonly 110 to 160Gy, the radioactivity of seeds (usually 0.4–0.7 mCi), and the quantity and distribution of seeds and needles, designing needle puncture pathway, and verifying the dose calculations of the GTV and OARs (e.g., eyes, brainstem, spinal cord, groove for vertebral artery, throat, trachea, and glands). The optimization for D90 of GTV and doses delivered to the OARs was made by the physicists.

The individualizedplanning data in the BT-TPS was transferred into 3D imaging and reverse engineering software (Beijing Feitian Industries Inc and Beijing University of Aeronautics and Astronautics, Beijing, China) for digital modeling of individualized 3D-PT. The modeling data was then finally optimized with postprocessing in Magics 19.01 software (Materialise Company, Belgium) and the individualized3D-PT was produced by 3D light-cured rapid-forming printer RS6000 (Shanghai Liantai 3D Technology Company, Shanghai, China). The 3D-PT with 3 mm thickness contained individualizedinformation such as body-surface characteristics of the treatment area, localization markers, and entrance hole for 18 gauge needle [16], **Figure 1**.

### ***Intraoperative implantation***

All RSI procedures were performed with local anesthesia under the CT guidance. After skin preparation and sterilization, the 3D-PT was aligned to the therapeutic region according to the outline characteristics, reference line on the 3D-PT, previously marked surfacepositioning line, and positioning laser,**Figure 2A-B**. Then CT was performed to confirm thefitting of 3D-PT exactly in position according to thepreoperative planning and design data in BT-TPS. Malposition between the BT-TPS data and the current CT image was adjusted in real-time, and then 2–3 locking needles (18 gauge) followed by the seed implantation needles (18 gauge) were percutaneously inserted via the pre-designed holes on the 3D-PT, **Figure 2C-D**. After all the needle were deemed in place, the  $I^{125}$  seeds were implanted and delivered using the Mick applicator in a retrusive manner with 0.5/1.0 cm interval according to the preoperative plan and intraoperative re-plan, which was made and executed if necessary, **Figure 2E-H**.

### ***Postoperative verification***

All patients were re-evaluated immediately with CT simulator after  $I^{125}$  RSI to validate the post-plan distribution of the  $I^{125}$  seeds and rule out potential complications. Then, the CT images were transferred to BT-TPS to verify post-plan dosimetry, **Figure 3**. Dosimetry parameters including D90, D100, V100, V150, V200, CI, EI, and HI were evaluated. All RSI procedures were performed in accordance with relevant guidelines and regulations, as also described in published study [7, 12].

### ***Statistical analysis***

Continuous variables were compared using paired t-test between planned data and intraoperative/post-plan data. As 84.2% of the cancer in the head was primary cancer and 81.8% of the cancer in the neck was secondary cancer, subgroups by cancer type and implantation site were further analyzed in multivariate analysis using linear regression model. A 2-sided p-value < 0.05 was considered as statistically significant difference. Statistical analyses were performed using SPSS software (version 26.0; SPSS, Chicago, IL, USA).

## Results

### *Procedure Details*

A total of 428 [mean, 10.4 (range 3–18) per patient] needles were preoperative planned and 430 [mean, 10.5 (range 3–17)] needles were actually inserted. Eight patients (19.5%) underwent intraoperative planning and adjusted the number of inserted needles. All needles were inserted manually in a single attempt, technical success rate was 100%. The mean seeds planned and implanted per patient were 42.6 (range, 11–85) and 44.4 (range, 12–85), respectively. The planned PD was 90–170 (mean,  $136.1 \pm 7.7$ ) Gy and GTV was 1.2–85.2 (mean,  $20.5 \pm 5.1$ ) cm<sup>3</sup>. No major complications (e.g. mis-implantation of radiative seeds, adjacent main arteriovenous or other organ injury) were observed.

### *Accuracy of needle insertion and dosimetry*

Of the 430 needles inserted, the mean entrance deviation was 0.090 cm (95% Confidence Interval, 0.081–0.098; range, 0–0.350 cm). The mean intraoperative depth and angular of the needle were consistent with planned depth and angular ( $6.23 \pm 0.24$  vs.  $6.21 \pm 0.24$  cm,  $p = 0.903$ ;  $83.14 \pm 3.64$  vs.  $83.09 \pm 3.66$  degrees,  $p=0.985$ , respectively). The mean deviation between planned and intraoperative depth and angular of the needle were  $0.168 \pm 0.024$  (range, 0–0.400) cm and  $1.56 \pm 0.14$  (range, 0–7.20) degrees, respectively. The planned and post-plan D90 and D100 were well coordinate ( $160.0 \pm 6.2$  and  $156.3 \pm 9.1$  Gy,  $p = 0.515$ ;  $83.6 \pm 7.1$  and  $80.8 \pm 10.0$  Gy,  $p = 0.662$ , respectively). The planned and post-plan V100, V150, and V200 were  $19.4 \pm 4.8$  and  $19.2 \pm 4.9$ ,  $p = 0.958$ ,  $15.1 \pm 3.8$  and  $14.6 \pm 3.7$ ,  $p = 0.865$ , and  $9.9 \pm 2.8$  and  $9.5 \pm 2.8$ ,  $p = 0.872$ , respectively. The planned and post-plan CI, EI, and HI were  $0.52 \pm 0.04$  and  $0.49 \pm 0.04$ ,  $p = 0.278$ ,  $0.91 \pm 0.20$  and  $1.04 \pm 0.25$ ,  $p = 0.456$ , and  $0.31 \pm 0.14$  and  $0.31 \pm 0.15$ ,  $p = 0.989$ , respectively. **Table 2.**

### *Subgroup analysis*

In the univariate analysis, the entrance deviation in patients with primary cancer were significantly larger than patients with secondary cancer ( $0.107 \pm 0.012$  vs.  $0.072 \pm 0.012$  cm,  $p \leq 0.001$ ) and was comparable in patients with implantation in the region of head and that of neck ( $0.089 \pm 0.011$  vs.  $0.090 \pm 0.013$  cm,  $p = 0.938$ ). The mean deviation between planned and intraoperative depth of the needle had no significant difference between patients with primary and secondary cancers ( $0.169 \pm 0.041$  vs.  $0.167 \pm 0.026$  cm,  $p = 0.951$ ) or between patients with implantation in the region of head and that of neck ( $0.152 \pm 0.043$  vs.  $0.182 \pm 0.025$  cm,  $p = 0.224$ ). While the mean deviation between planned and intraoperative

angular of the needle was smaller in patients with primary than secondary cancers ( $1.18 \pm 0.19$  vs.  $1.94 \pm 0.19$  degrees,  $p < 0.001$ ) and also smaller inpatients with implantation in the region of head than that of neck ( $1.25 \pm 0.19$  vs.  $1.84 \pm 0.19$  degrees,  $p < 0.001$ ). **Table 3.**

In the multivariate analysis usinglinear regression modelinvolving both cancer type and implantation site. The linear regression involving entrance deviation had statistical significance ( $F = 17.064$ ,  $p < 0.001$ ) with adjusted  $R^2 = 0.07$ . The entrance deviation in patients with primary cancer were significantly different in patients with secondary cancer( $p < 0.001$ , standardized B = -0.378) and were also significantly different between patients with implantation in the region of head and that of neck ( $p < 0.001$ , standardized B = 0.266). The linear regression involving deviation between planned and intraoperative depth and angular of the needle both had no statistical significance ( $F = 2.748$ ,  $p = 0.065$ ;  $F = 2.398$ ,  $p = 0.092$ , respectively) with adjusted  $R^2 = 0.008$  and 0.006, respectively.

## Discussion

The present study evaluated the accuracy involving needle puncture and dosimetry ofindividualized 3D-PT assisted  $I^{125}$  RSI for recurrent primary/secondary head and neck cancer. As a result, the mean entrance deviation was  $\approx 0.1$  cm. The mean intraoperative depth and angular of the needle were well consistent with planned depth and angular without significant deference. The post-plan dosimetry parameters, including D90, D100, V100, V150, V200, CI, EI, and HI, were also well coordinate with planned dosimetry profiles without significant deference. Therefore, this study indicated that the accuracy of needle puncture was satisfied with consistent planed and postoperative dosimetry profiles of individualized3D-PT assisted  $I^{125}$  RSI for patients with recurrent head and neck cancer.

Since the introduction of 3D-PT in the clinical practice, few studies investigate the accuracy of 3D-PT assisted needle related interventions [14, 17]. As revealed by a non-inferiority randomized clinical trial that enrolled 200 patients for localizing small pulmonary nodules [17], localizer deviation did not significantly differ between the 3D-PT group and CT-guided group (mean, 8.7 vs. 9.6 mm;  $p = 0.36$ ). The mean procedural durations were 7.4 minutes for the template-guided group and 9.5 minutes for the CT-guided group ( $P < 0.001$ ). The mean CT related radiation dose was  $229 \text{ mGy} \times \text{cm}$  in the template-guided group and  $313 \text{ mGy} \times \text{cm}$  in CT-guided group ( $p < .001$ ) [17]. Indicating that the use of the 3D-PT for localization showed efficacy and safety that were not substantially worse than those with the CT-guided alone, while significantly simplifying the procedure and decreasing patient CT related radiation exposure.

For patients with head and neck cancer, the relative stable craniocerebral structure may fascinate the usage of individualized 3D-PT and the deviation of needle puncture during RSI maybe prone to be smaller than that of localizing pulmonary nodules. Ming-Wei Huang et al [14] reported 25 patients with head and neck tumors implanted with  $I^{125}$  radioactive seeds under the assistance of 3D-PT. The mean entrance deviation for all inserted needles was  $1.18 \pm 0.81$  mm varying from  $0.857 \pm 0.545$  to  $1.930 \pm 0.843$  mm at different sites and was significantly smaller in the parotid and maxillary regions (belong to head region), which is significant smaller than that of localizing pulmonary nodules mentioned above and seems

similar to that of reported here (0.81–0.98 mm). In the present study, entrance deviation was also significantly different in patients with implantation in head and neck region and in patients with primary cancer and secondary cancer in multivariate analysis, but was only larger in patients with primary cancer in univariate analysis. Meanwhile, in the study by Ming-Wei Huang et al [14], the mean angular deviation was  $2.08 \pm 1.07$  degrees varying from  $1.85 \pm 0.93$  to  $2.73 \pm 1.18$  degrees at different sites and was significantly larger (indicating less accurate placement) in the sub-mandibular and upper neck area (neck region), than in the other regions (head region), which also seems similar to that reported here ( $1.56 \pm 0.14$  degrees). Interestingly, in the current study, angular deviation was larger in patients with cancer in the neck region than in the head region, and also larger in patients with secondary cancer than primary cancers in univariate analysis. However, in multivariate analysis, both planned and intraoperative deviation of depth and angular have no statistical significance involving both cancer type and implantation site. This may be owing to the influence of other potential factors as  $R^2$  of the linear regression turns out to be  $\approx 0.1$ . Therefore, whether the accuracy of 3D-PT assisted RSI varies by cancer type or implantation site, further high-quality study is needed before conclusion is drawn.

As for dosimetry profile, in the above study of Ming-Wei Huang et al [14], the D90 was larger than the planned PD and ranged from 122Gy to 198Gy (mean  $163.8 \pm 22.6$ Gy), which seems higher than that reported here (range, 90–170; mean,  $136.1 \pm 7.7$  Gy). The V100 was larger than 95% and the V150 was less than 50% in all patients and other planned and post-plan dosimetric data was not reported and compared in their study. In a study by Ji Z et al [16] comparing the dose distributions of post-plan data with preoperative plan for 3D-PT assisted RSI, a total of 14 patients with malignant tumors (majority located in pelvic cavity) were enrolled. The average post-plan D90, V100, and V150 were smaller than the planned ones, and average post-plan V200 and minimum peripheral dose of GTV were larger than the planned ones, however, there was no statistical difference in any these parameters between the two groups except for V100 ( $p=0.027$ ). Sun et al [18] compared the dosimetric data between preoperative plan and post-plan verification in 3D-PT assisted CT-guided RSI for thorax movement tumors. All of the included dosimetry parameters changed slightly, while the difference was also not statistically significant (all  $p > 0.05$ ). Yansong Liang et al [13] reported the dosimetric accuracy of 3D-PT assisted  $I^{125}$  RSI for the treatment of cervical lymph node metastasis in 15 patients. There was also no significant difference for all the parameters (D90, V90, V100, and V150) between preoperative plan and post-plan verification (all  $p > 0.05$ ). Similarly, as also revealed in the current study, the post-plan dosimetry was completely meet the requirements of the preoperative plan involving 3D-PT assisted RSI without significant deference.

The present study has several limitations. First, this was a retrospective study and was therefore prone to selection bias. Second, the absence of a control group limits evaluation of the superiority of 3D-PT assisted CT-guided RSI over bare-handed CT-guided RSI. Third, the depth and angular of the needle was calculated after fusing the preoperative and intraoperative CT images into the same coordinate axis in the current study, instead of same CT image, suffered from potential fusion error. However, this is the only way to compare preoperative plan with intraoperative data. Fourth, in subgroup analysis for implantation site, further refined subregion classification instead of head and neck, e.g. the parotid and masseter

region, maxillary and paranasal region, the retromandibular region, and submandibular and upper neck region, was not applied in the present study, limited by the power of statistics in such small group of patients and with 53.7% of the cancers located in the neck. Finally, there was dilemma in grouping the tumors located at the boundary of head and neck region (submandibular and upper neck area), which may stretch over both head and neck region and were mainly classified according to location of the lesion center, leading to potential distraction of the results.

## Conclusion

Within the limitation of this study, individualized 3D-PT assisted  $I^{125}$  RSI may be accurate with consistent planned and post-plan dosimetry for patients with recurrent head and neck cancer, further prospective study is warranted.

## Abbreviations

BT, brachytherapy

CT, Computerized Tomography

CI, conformity index

EBRT, external beam radiotherapy

EI, external index

GTV, gross tumor volume

HI, homogeneity index

RT, radiotherapy

RSI, radioactive seed implantation

MRI, Magnetic Resonance Imaging

OARs, organs at risk

PD, prescription dose

TPS, Treatment Planning System

3D-PT, three-dimensional-printing template

## Declarations

- **Ethics approval and consent to participate:** The retrospective study was approved by our institutional review board and the requirement to obtain written informed consent was waived.
- **Consent for publication:** Not applicable.
- **Availability of data and materials:** No additional unpublished data are available.
- **Competing interests:** Not applicable.
- **Funding:** This paper was supported by National Key Research and Development Plan of China (Grant No. 2019YFB1311300) to JJ W.
- **Authors' contributions:** BQ, PJ and JJ W conceived and designed the study. BQ, ZJ, HT S, JH F, WY L, and YX S performed the data collection and are responsible for statistical analysis. BQ and PJ wrote the paper. JJ W reviewed and edited the manuscript. All authors read and approved the manuscript.
- **Acknowledgements:** Not applicable.
- **Authors' information (optional):** Not applicable.

## References

- [1] Chargari C, Deutsch E, Blanchard P, Gouy S, Martelli H, Guerin F, et al. Brachytherapy: An overview for clinicians. CA Cancer J Clin. 2019;69:386-401.
- [2] Skowronek J. Current status of brachytherapy in cancer treatment - short overview. J Contemp Brachytherapy. 2017;9:581-9.
- [3] Nath R, Bice WS, Butler WM, Chen Z, Meigooni AS, Narayana V, et al. AAPM recommendations on dose prescription and reporting methods for permanent interstitial brachytherapy for prostate cancer: report of Task Group 137. Med Phys. 2009;36:5310-22.
- [4] Kovacs G, Martinez-Monge R, Budrukkar A, Guinot JL, Johansson B, Strnad V, et al. GEC-ESTRO ACROP recommendations for head & neck brachytherapy in squamous cell carcinomas: 1st update - Improvement by cross sectional imaging based treatment planning and stepping source technology. Radiother Oncol. 2017;122:248-54.
- [5] Takacs-Nagy Z, Martinez-Monge R, Mazeron JJ, Anker CJ, Harrison LB. American Brachytherapy Society Task Group Report: Combined external beam irradiation and interstitial brachytherapy for base of tongue tumors and other head and neck sites in the era of new technologies. Brachytherapy. 2017;16:44-58.
- [6] Davis BJ, Horwitz EM, Lee WR, Crook JM, Stock RG, Merrick GS, et al. American Brachytherapy Society consensus guidelines for transrectal ultrasound-guided permanent prostate brachytherapy. Brachytherapy. 2012;11:6-19.
- [7] Ji Z, Jiang Y, Tian S, Guo F, Peng R, Xu F, et al. The Effectiveness and Prognostic Factors of CT-Guided Radioactive I-125 Seed Implantation for the Treatment of Recurrent Head and Neck Cancer After External

Beam Radiation Therapy. Int J Radiat Oncol Biol Phys. 2019;103:638-45.

[8] Wang J, Chai S, Wang R, Zheng G, Zhang K, Huo B, et al. Expert consensus on computed tomography-assisted three-dimensional-printed coplanar template guidance for interstitial permanent radioactive (125)I seed implantation therapy. J Cancer Res Ther. 2019;15:1430-4.

[9] Zhang GH, Lv XM, Wu WJ, Wu ZY, Zheng L, Huang MW, et al. Evaluation of the accuracy of computer-assisted techniques in the interstitial brachytherapy of the deep regions of the head and neck. Brachytherapy. 2019;18:217-23.

[10] Huang MW, Liu SM, Zheng L, Shi Y, Zhang J, Li YS, et al. A digital model individual template and CT-guided 125I seed implants for malignant tumors of the head and neck. J Radiat Res. 2012;53:973-7.

[11] Jiang Y, Ji Z, Guo F, Peng R, Sun H, Fan J, et al. Side effects of CT-guided implantation of (125)I seeds for recurrent malignant tumors of the head and neck assisted by 3D printing non co-planar template. Radiat Oncol. 2018;13:18.

[12] Chen Y, Jiang Y, Ji Z, Jiang P, Xu F, Zhang Y, et al. Efficacy and safety of CT-guided (125)I seed implantation as a salvage treatment for locally recurrent head and neck soft tissue sarcoma after surgery and external beam radiotherapy: A 12-year study at a single institution. Brachytherapy. 2020;19:81-9.

[13] Liang Y, Wang Z, Zhang H, Gao Z, Zhao J, Sui A, et al. Three-dimensional-printed individual template-guided (125)I seed implantation for the cervical lymph node metastasis: A dosimetric and security study. J Cancer Res Ther. 2018;14:30-5.

[14] Huang MW, Zhang JG, Zheng L, Liu SM, Yu GY. Accuracy evaluation of a individualised 3D-printing individual template for needle guidance in head and neck brachytherapy. J Radiat Res. 2016;57:662-7.

[15] Wang J, Zhang F, Guo J, Chai S, Zheng G, Zhang K, et al. Expert consensus workshop report: Guideline for three-dimensional printing template-assisted computed tomography-guided (125)I seeds interstitial implantation brachytherapy. J Cancer Res Ther. 2017;13:607-12.

[16] Ji Z, Jiang Y, Guo F, Sun H, Fan J, Zhang L, et al. Dosimetry verification of radioactive seed implantation for malignant tumors assisted by 3D printing individual templates and CT guidance. Appl Radiat Isot. 2017;124:68-74.

[17] Zhang L, Wang L, Kadeer X, Zeyao L, Sun X, Sun W, et al. Accuracy of a 3-Dimensionally Printed Navigational Template for Localizing Small Pulmonary Nodules: A Noninferiority Randomized Clinical Trial. JAMA Surg. 2019;154:295-303.

[18] Sun HT, Jiang YL, Ji Z, Guo FX, Peng R, Fan JH, et al. [3D printing non-coplanar template-assisted 125-iodine seed implantation for thorax movement tumor: individual template design method]. Zhonghua Yi Xue Za Zhi. 2019;99:3699-702.

# Tables

**Table 1.** Clinical Characteristics of the Patients

Item	n (%)
Age (Years)	58.5 ± 16.1
Sex	
Male	28 (68.3)
Female	13 (31.7)
Primary cancer	20 (48.8)
Oral carcinoma	6 (14.6)
Oropharyngeal cancer	2 (4.9)
Laryngo-carcinoma	2 (4.9)
Thyroid cancer	2 (4.9)
Orbital rhabdomyosarcoma	2 (4.9)
Others	6 (14.6)
Secondary cancer	21 (51.2)
Lymphatic metastasis	19(46.3)
Cerebral metastasis	2 (4.9)
Previous treatment	
Chemoradiotherapy	14 (34.1)
Surgery	7 (17.1)
Radiotherapy	6 (14.6)
Chemotherapy	5 (12.2)
Surgery + Chemoradiotherapy	5 (12.2)
Surgery + Radiotherapy	4 (9.8)
Implanted tumor site	
Head	19 (46.3)
Neck	22 (53.7)

Plus-minus data = mean ± standard deviation; number in parentheses = percentage of patients.

**Table 2. Analysis of planned and intraoperative/post-plan parameters**

Parameter	Planned	Intraoperative/post-plan	p value
Depth of needle	6.21 ± 0.24	6.23 ± 0.24	0.903
Angular of needle	83.09 ± 3.66	83.14 ± 3.64	0.985
D90	160.0 ± 6.2	156.3 ± 9.1	0.515
D100	83.6 ± 7.1	80.8 ± 10.0	0.662
V100	19.4 ± 4.8	19.2 ± 4.9	0.958
V150	15.1 ± 3.8	14.6 ± 3.7	0.865
V200	9.9 ± 2.8	9.5 ± 2.8	0.872
CI	0.52 ± 0.04	0.49 ± 0.04	0.278
EI	0.91 ± 0.20	1.04 ± 0.25	0.456
HI	0.31 ± 0.14	0.31 ± 0.15	0.989

D90 and D100 refer to the dose delivered to the 90% or 100% of gross tumor volume and V100, V150, and V 200 refer to the percentage of gross tumor volume receiving 100% or 150% or 200% of prescription dose, respectively; CI, Conformity index; EI, External index; HI, Homogeneity index.

**Table 3. Subgroup analysis of planned and intraoperative parameter deviation (univariate analysis)**

Parameter	Cancer type		p value	Implantation site		p value
	Primary	Secondary		Head	Neck	
Entrance deviation	0.107 ± 0.012 cm	0.072 ± 0.012 cm	0.001	0.089 ± 0.011 cm	0.090 ± 0.013 cm	0.938
Depth deviation	0.169 ± 0.041 cm	0.167 ± 0.026 cm	0.951	0.152 ± 0.043 cm	0.182 ± 0.025 cm	0.224
Angular deviation	1.18 ± 0.19 degrees	1.94 ± 0.19 degrees	0.001	1.25 ± 0.19 degrees	1.84 ± 0.19 degrees	0.001

## Figures

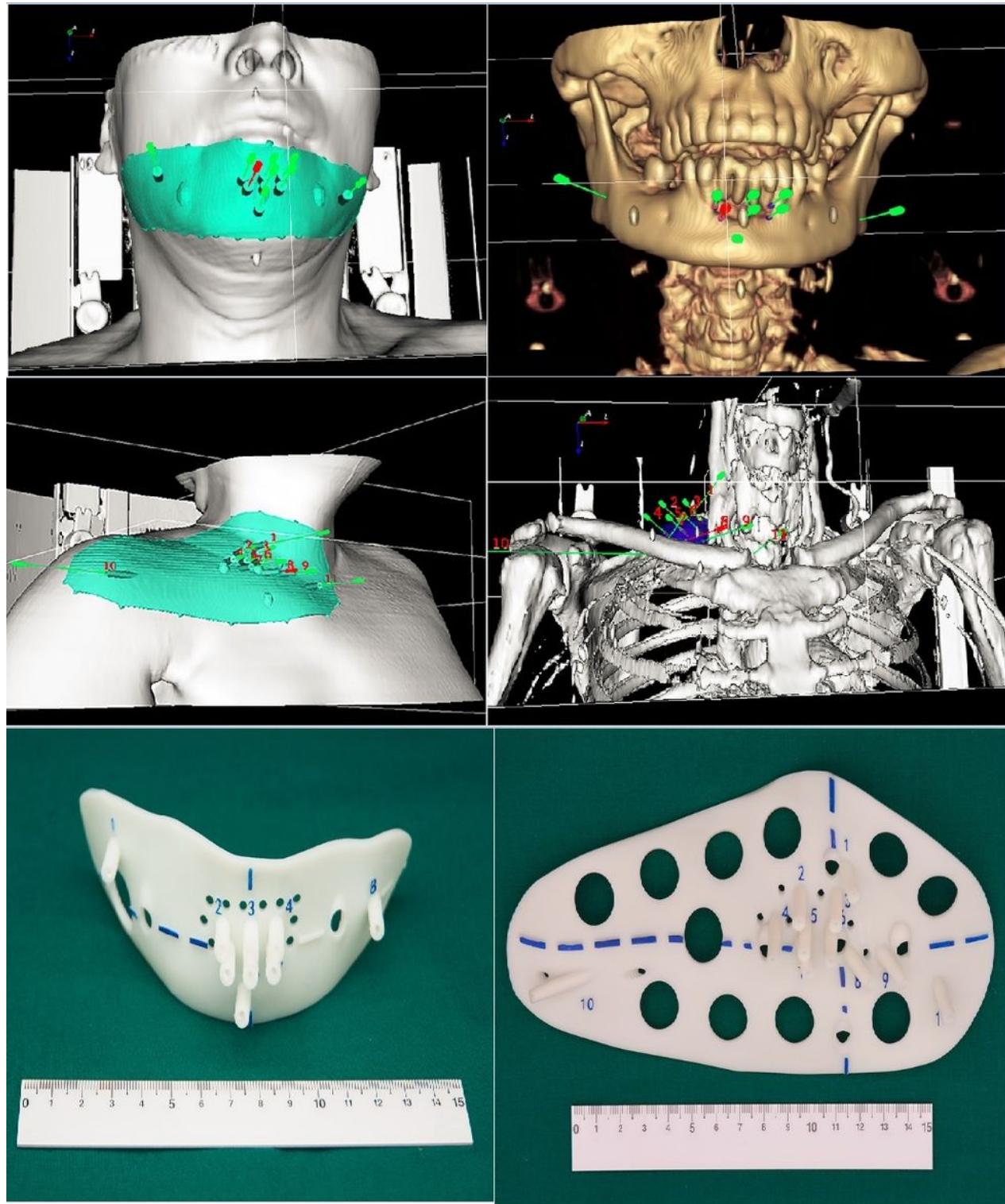
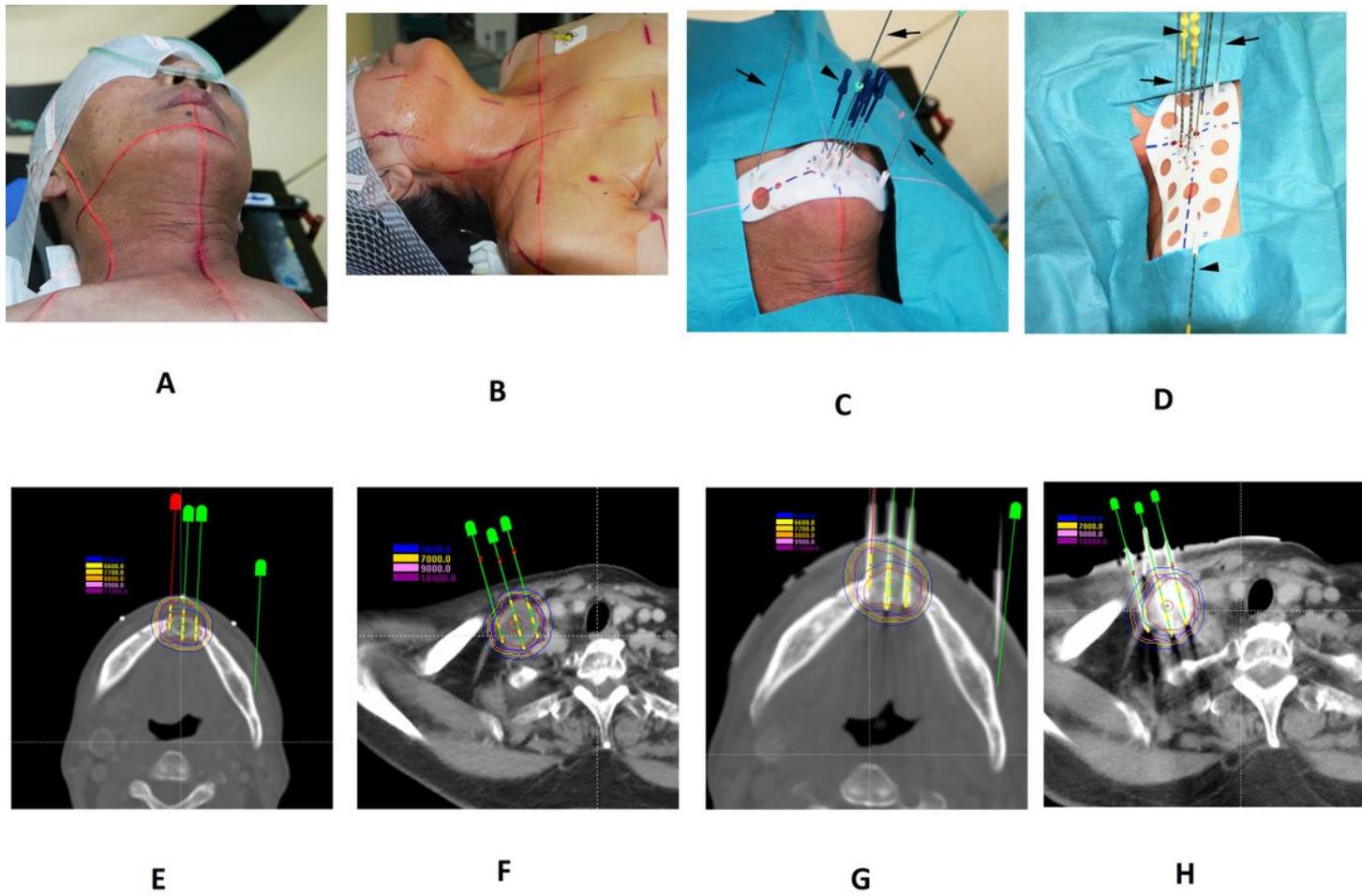


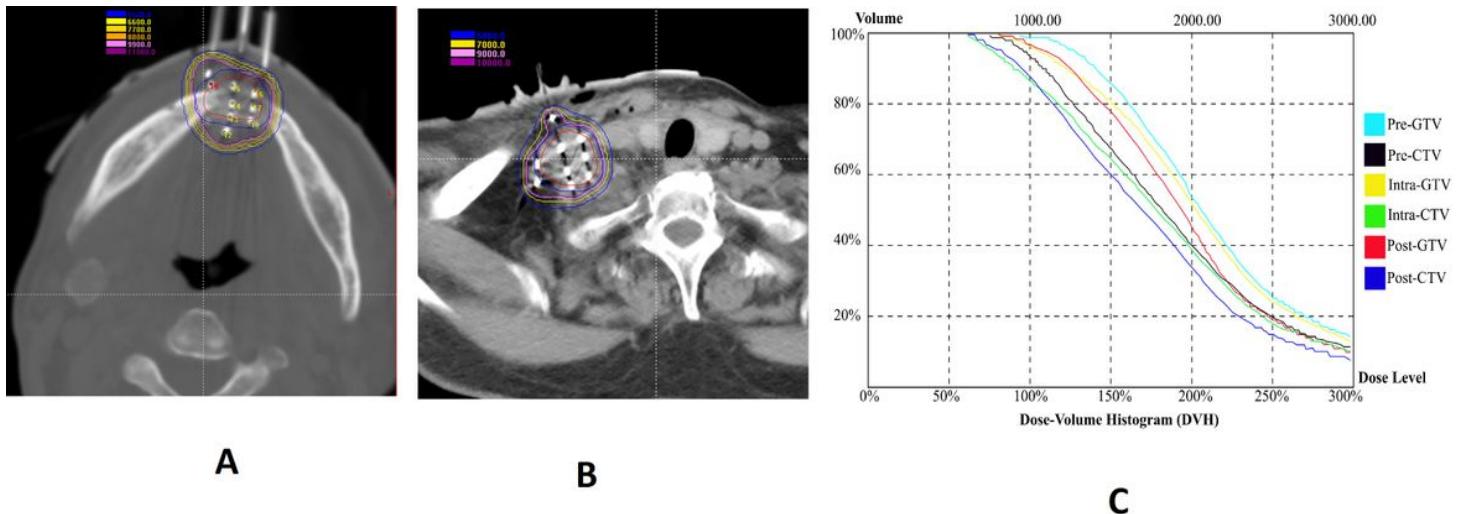
Figure 1

A-D:Digital modeling of individualized 3D-printing template (3D-PT) in patient with recurrent head and neck cancer and simulated needle pass way; E-F: The 3D-PT of head and neck with 3 mm thickness contained information such as body-surface characteristics of the treatment area, localization markers, and entrance hole for 18-gauge needle.



**Figure 2**

I125 radioactive seed implantation for patients with recurrent head and neck cancer. A-B: Patients were fixed with a bow cap in selected suitable gesture and marked with surfacepositioning line; C-D: individualized 3D-printing template (3D-PT) was aligned to the therapeutic region according to the outline characteristics, reference line on the 3D-PT, previously marked surfacepositioning line and positioning laser, and locking needles (arrow) followed by the implantation needles (arrowhead) were percutaneously inserted via the pre-designed holes on the 3D-PT. E-F: Preoperative plan; G-H: I125 seeds were implanted.



**Figure 3**

Patients were re-evaluated immediately with CT simulator after I125radioactive seed implantation. A-B: Validation of post-plan distribution of the I125 seeds; C: The dose-volume histogram of preoperative plan, intraoperative plan, and post-plan in the presented patient with neck cancer; Abbreviations: Pre-GTV, preoperative planned gross tumor volume; Pre-CTV, preoperative planned clinical target volume; Intra-GTV, intraoperative planned gross tumor volume; Intra-CTV, intraoperative planned clinical target volume; Post-GTV, post-plan gross tumor volume; Post-CTV, post-plan clinical target volume.