

# The Accuracy and Dosimetry of Individualized 3D-Printing Template Assisted I<sup>125</sup> Radioactive Seed Implantation for Recurrent/Secondary Head and Neck Cancer

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## Research article

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# Abstract

**Background:** Individualized 3D-printing template (3D-PT) is developed to facilitate  $I^{125}$  radioactive seed implantation (RSI), 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 of intraoperative needle puncture and post-plan dosimetry of individualized 3D-PT assisted  $I^{125}$  RSI for recurrent/secondary head and neck cancer.

**Methods:** From February 2017 to January 2020, clinical data of 41 patients (mean age,  $58.5 \pm 16.1$  years; 28 males) with recurrent (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 needles [mean, 10.5 (range 3–17) per patient] were inserted. Technical success rate was 100% without major complication. The mean needle's entrance deviation was 0.090 cm (95% Confidence Interval, 0.081–0.098). The mean intraoperative depth and angular of the needle were consistent with that of pre-plan ( $6.23 \pm 0.24$  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 the needle's pre-planned and intraoperative depth and angular were  $0.168 \pm 0.024$  cm and  $1.56 \pm 0.14$  degrees, respectively. The post-plan dosimetry parameters, including D90, D100, V100, V150, V200, conformity index, external index, and homogeneity index, were all well coordinate with pre-planned dosimetry without significant deference (all  $p \geq 0.05$ ).

**Conclusion:** Within the limitation of this study, individualized 3D-PT assisted  $I^{125}$  RSI may be accurate obtaining favorable post-plan dosimetry for patients with recurrent/secondary 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 ( $>100\text{Gy}$ ) directly to the target volume with the advantage of a rapid dose falling-off 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 treatments for head and neck cancers [4, 5].  $I^{125}$  radioactive seed implantation (RSI) may be safely used for recurrent/secondary head and neck cancer as a salvage therapy providing a high local tumor control and preservation of organ functions [6–9].

The challenge is how to deliver the  $I^{125}$  seeds into the target volume accurately per pre-plan, spares the vital organ structure, and obtains focused radiation on the lesion. Owing to the dense critical organs and tissues (e.g. eyes, major vessels, and nerve) in head and neck region, the accuracy of needle puncture during  $I^{125}$  RSI and post-plan dosimetry was extremely critical for patients with head and neck cancer. The needle's deviation between pre-plan and intraoperative puncture may occur even under the image

guidance, which leads to mis-implantation of the  $I^{125}$  seeds and unnecessary radiation and damage to surrounding critical organs/tissues.

Recently, Individualized 3D-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 [8–12]. However, most of the previous studies involving 3D-PT assisted  $I^{125}$  RSI were focused on the efficacy and safety profiles, e.g. local control and survival [6–8, 13]. Only 2 studies involving accuracy of intraoperative needle puncture and dosimetry after  $I^{125}$  RSI were published for head and neck cancer [11, 14]. Indicated by these existed evidence, 3D-PT assisted  $I^{125}$  RSI may provide satisfied accuracy and post-plan dosimetry without additional perioperative complications [8, 11, 14], while cases reported in these studies was limited with small sample sizes. Here, the aim of the study is to evaluate the accuracy of intraoperative needle puncture and post-plan dosimetry of individualized 3D-PT assisted  $I^{125}$  RSI for patients with recurrent/secondary head and neck cancer in our institute.

## Methods

### Study design

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/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/secondary head and neck cancer after surgery; (ii) Progressive/recurrent/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 < 70 or predicted life span < 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 needles inserted and seed implanted, the mean needle's entrance deviation, the depth and angular of the pre-planned and intraoperative needle insertion, and pre-planned and post-plan dosimetry profiles were recorded. Subgroups analysis by cancer type (recurrent/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 conducted. Technical success was defined as successful needle insertion and implantation of  $I^{125}$  seed in the targeted volume per pre-plan/intraoperative plan. The mean needle's entrance deviation was defined as the superficial distance between the pre-planned needle's entrance point and the actual intraoperative needle's entrance point on CT images after fusing the pre-planned and intraoperative CT images into the same coordinate axis on the BT Treatment Planning System (BT-TPS). Then the needle's depth and angular were directly calculated and extracted from the BT-TPS. The needle's depth was defined as the tip of the pre-planned/inserted needle to the template surface when the needle is deemed

in place during the retractive seed implantation. The needle's angular was defined as the angle between the pre-planned/inserted needle in place and the horizontal axis. The pre-planned and post-plan dosimetry parameters, including the prescription dose (PD), seed number, gross tumor volume (GTV), D90, D100, V100, V150, V200, conformity index (CI), external index (EI), and homogeneity index (HI) were recorded and compared. D90 and D100 refer to the dose delivered to the 90% or 100% of GTV, respectively. V100, V150, and V200 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 recurrent/secondary head and neck cancer were included. Majority of the patients was male ( $n = 28, 68.3\%$ ). Recurrent head and neck cancer ( $n = 20, 48.8\%$ ) included oral carcinoma ( $n = 6, 14.6\%$ ), oropharyngeal cancer ( $n = 2, 4.9\%$ ), laryngo-carcinoma ( $n = 2, 4.9\%$ ), 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 ( $n = 3, 7.3\%$ ), laryngo-carcinoma ( $n = 1, 2.4\%$ ), 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 brain metastasis ( $n = 2, 4.9\%$ ) derived from lung cancer. Over a half of the target volume was located in the neck region ( $n = 22, 53.7\%$ ). The majority (81.8%) of the target volume in the neck was secondary cancer and 84.2% of the target volume in the head was recurrent cancer. The characteristics of the patients are presented in Table 1. All the patients received previous treatments.

Table 1  
Clinical characteristics of the patients

Item	n (%)
Age (Years)	58.5 ± 16.1
Sex	
Male	28 (68.3)
Female	13 (31.7)
Recurrent 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.	

# I<sup>125</sup> RSI procedure

## Pre-plan

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 suitable gesture according to the lesion location and facilitation for RSI and then marked with surface positioning 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 pre-plan was then established by defining GTV and adjacent organs at risk (OARs), determining PD according to expert consensus on I<sup>125</sup> RSI [15] and clinical experiences gained in our department, commonly 110 to 160 Gy. The radioactivity of I<sup>125</sup> seeds (usually 0.4–0.7 mCi) and the quantity and distribution of the seeds and the needles were determined after designing the 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 were conducted by the physicists.

The individualized pre-plan data in the BT-TPS was then 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. After that, the modeling data was optimized with postprocessing using Magics 19.01 software (Materialise Company, Belgium) and the individualized 3D-PT was finally produced by using 3D light-cured rapid-forming printer RS6000 (Shanghai Liantai 3D Technology Company, Shanghai, China). The 3D-PT with 3 mm thickness contained individualized information such as body-surface characteristics of the target region, localization markers, and entrance hole for 18-gauge needle [16], Fig. 1.

## Intraoperative seed 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 target region according to the outline characteristics, reference line on the 3D-PT, surface positioning line, and positioning laser, Fig. 2A-B. Then CT scan was performed to confirm the exact fitting of 3D-PT in position according to the pre-plan data in BT-TPS. Malposition identified between the pre-plan 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-planned holes on the 3D-PT, Fig. 2C-D. After all the needle were deemed in place, the I<sup>125</sup> seeds were implanted and delivered using the Mick applicator in a retractive manner with 0.5/1.0 cm interval according to the pre-plan and intraoperative re-plan, which was made and executed if necessary, Fig. 2E-H.

## Postoperative verification

All patients were re-evaluated immediately with CT scan after I<sup>125</sup> RSI to validate the post-plan distribution of the I<sup>125</sup> seeds and rule out potential perioperative complications. Then, the CT images were

transferred to BT-TPS to verify post-plan dosimetry, Fig. 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 [6, 7].

## Statistical analysis

Continuous variables were compared using paired t-test between pre-plan data and intraoperative data/post verification data. As 84.2% of the cancer in the head was recurrent cancer and 81.8% of the cancer in the neck was secondary cancer, subgroups analysis by cancer type and implantation site were further conducted 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 pre-planned and 430 [mean, 10.5 (range 3–17)] needles were actually inserted during RSI. Eight patients (19.5%) underwent intraoperative re-plan and adjusted the number of inserted needles. All needles were inserted manually in a single attempt, technical success rate was 100%. The mean seeds pre-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>. Pain (26.8%) and a small amount of bleeding (78%) at puncture site were seen in some of the patients and all were self-healing after RSI. No major perioperative complications (e.g. mis-implantation of radiative seeds, adjacent main arteriovenous or other critical organ damage) were observed.

### Accuracy of needle puncture and post-plan dosimetry

Of the 430 needles inserted, the mean needle's entrance deviation was 0.090 cm (95% Confidence Interval, 0.081–0.098; range, 0–0.350 cm). The mean needle's intraoperative depth and angular were consistent with that of pre-plan ( $6.23 \pm 0.24$  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 needle's pre-planned and intraoperative depth and angular were  $0.168 \pm 0.024$  (range, 0–0.400) cm and  $1.56 \pm 0.14$  (range, 0–7.20) degrees, respectively. The pre-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 pre-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 pre-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.

Table 2  
Analysis of pre-plan and intraoperative/post-plan parameters

Parameter	Pre-plan	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.

## Subgroup analysis

In the univariate analysis, the needle's entrance deviation in patients with recurrent cancer were significantly larger than patients with secondary cancer ( $0.107 \pm 0.012$  vs.  $0.072 \pm 0.012$  cm,  $p < 0.001$ ) 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 needle' pre-planned and intraoperative depth had no significant difference between patients with recurrent 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 needle' pre-planned and intraoperative angular was smaller in patients with recurrent cancers than with secondary cancers ( $1.18 \pm 0.19$  vs.  $1.94 \pm 0.19$  degrees,  $p < 0.001$ ) and also smaller in patients 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.

Table 3  
Subgroup analysis of pre-plan and intraoperative parameter deviation (univariate analysis)

Parameter	Cancer type		p value	Implantation site		p value
	Recurrent	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

In the multivariate analysis using linear regression model including both cancer type and implantation site. The linear regression of needle's entrance deviation had statistical significance ( $F = 17.064$ ,  $p < 0.001$ ) with adjusted  $R^2 = 0.07$ . The needle's entrance deviation were significantly different between patients with recurrent cancers and patients with secondary cancers ( $p < 0.001$ , 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 of deviation between pre-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 of intraoperative needle puncture and post-plan dosimetry of individualized 3D-PT assisted  $I^{125}$  RSI for recurrent/secondary head and neck cancer. As a result, the mean needle's entrance deviation was  $< 0.1$  cm. The mean needle's intraoperative depth and angular were well consistent with pre-plan without significant deference. The post-plan dosimetry parameters, including D90, D100, V100, V150, V200, CI, EI, and HI, were also well coordinate with pre-plan without significant deference. Therefore, this study indicated that the accuracy of needle puncture and post-plan dosimetry was satisfied for individualized 3D-PT assisted  $I^{125}$  RSI in patients with recurrent/secondary head and neck cancer.

Since the introduction of 3D-PT in the clinical practice, few studies investigate the accuracy of needle puncture during 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 assisted 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 3D-PT assisted group and 9.5 minutes for the CT-guided group ( $P < 0.001$ ). The mean CT related radiation dose was 229 mGy × cm in the 3D-PT assisted group and 313 mGy × cm in CT-guided group ( $p < .001$ ) [17]. Indicating that the use of the 3D-PT for placement of pulmonary localizer 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, needle's entrance deviation was also significantly different in patients with implantation in head and neck region and in patients with recurrent cancer and secondary cancer in multivariate analysis, but was only larger in patients with recurrent 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, needle's 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 recurrent cancers in univariate analysis. However, in multivariate analysis, both needle's pre-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  $< 0.1$ , which means little weightiness. 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 that of pre-plan and ranged from 122 Gy to 198 Gy (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 pre-plan and post-plan dosimetric data (e.g. V150, V200, CI, EI, and HI) was not reported in their study. In a study by Ji Z et al [16] comparing the dose distributions of post-plan data with pre-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 pre-plan ones, and average post-plan V200 and minimum peripheral dose of GTV were larger than the pre-plan 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 pre-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 pre-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 pre-plan for 3D-PT assisted RSI without significant deference.

The present study has several limitations. First, this was a retrospective study and therefore prone to potential 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 needle's depth and angular was calculated after fusing the pre-plan and intraoperative CT images into the same coordinate axis on BT-TPS, suffered from potential fusion error. However, this is the only way to compare pre-plan data with intraoperative data. Fourth, in subgroup analysis for implantation site, further refined subregion classification, 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. 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 obtaining favorable post-plan dosimetry for patients with recurrent/secondary 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, 3D-printing templates

## Declarations

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### Competing interests:

The authors declare that they have no conflict of interest.

### Ethics approval:

The retrospective study was approved by Peking university Third Hospital Medical Science Research Ethics Committee and the requirement to obtain written informed consent was waived.

### Consent to participate:

Not applicable.

### Consent for publication:

Not applicable.

### Availability of data and materials:

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

### Code availability:

Not applicable.

### 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.

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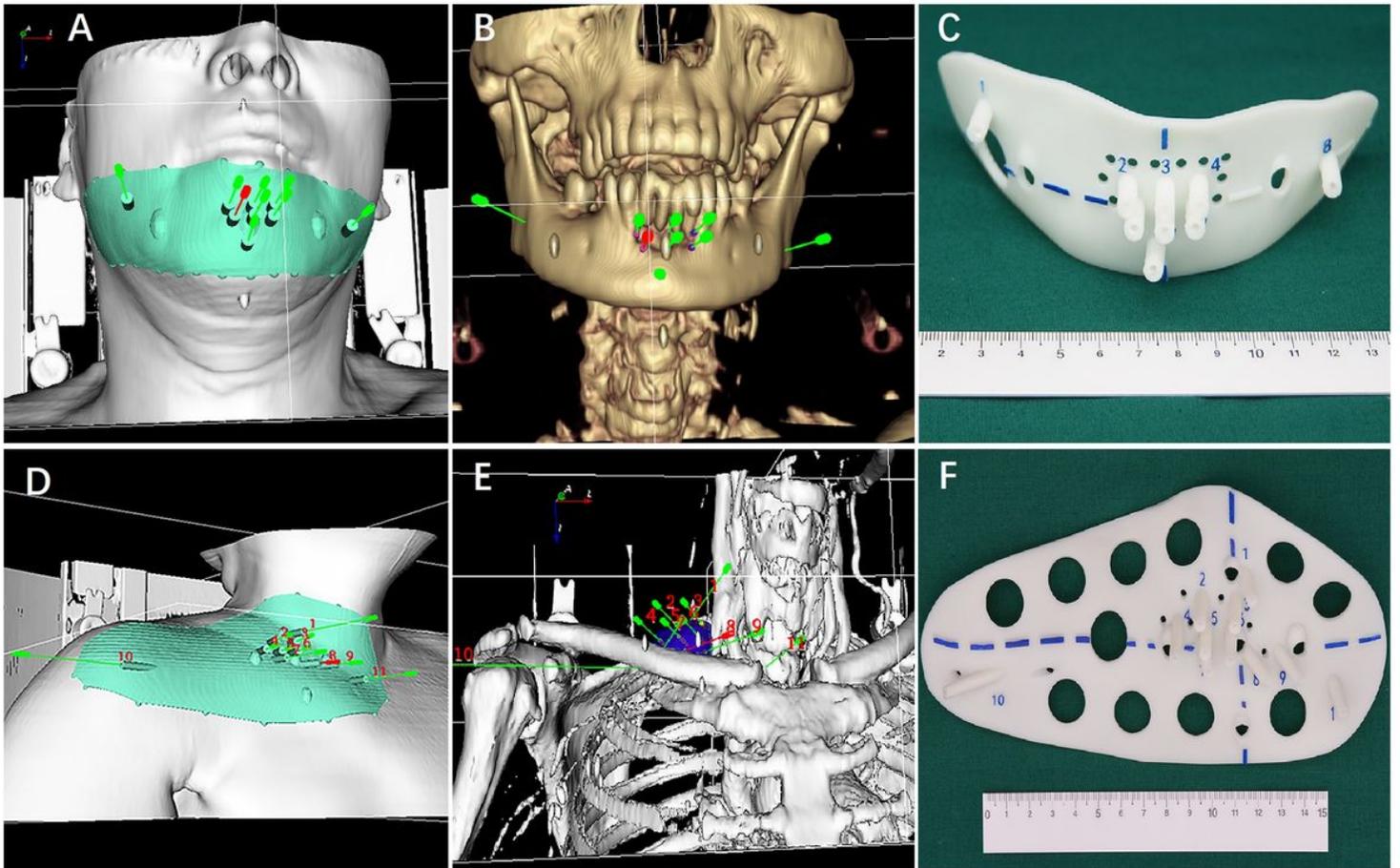
Not applicable.

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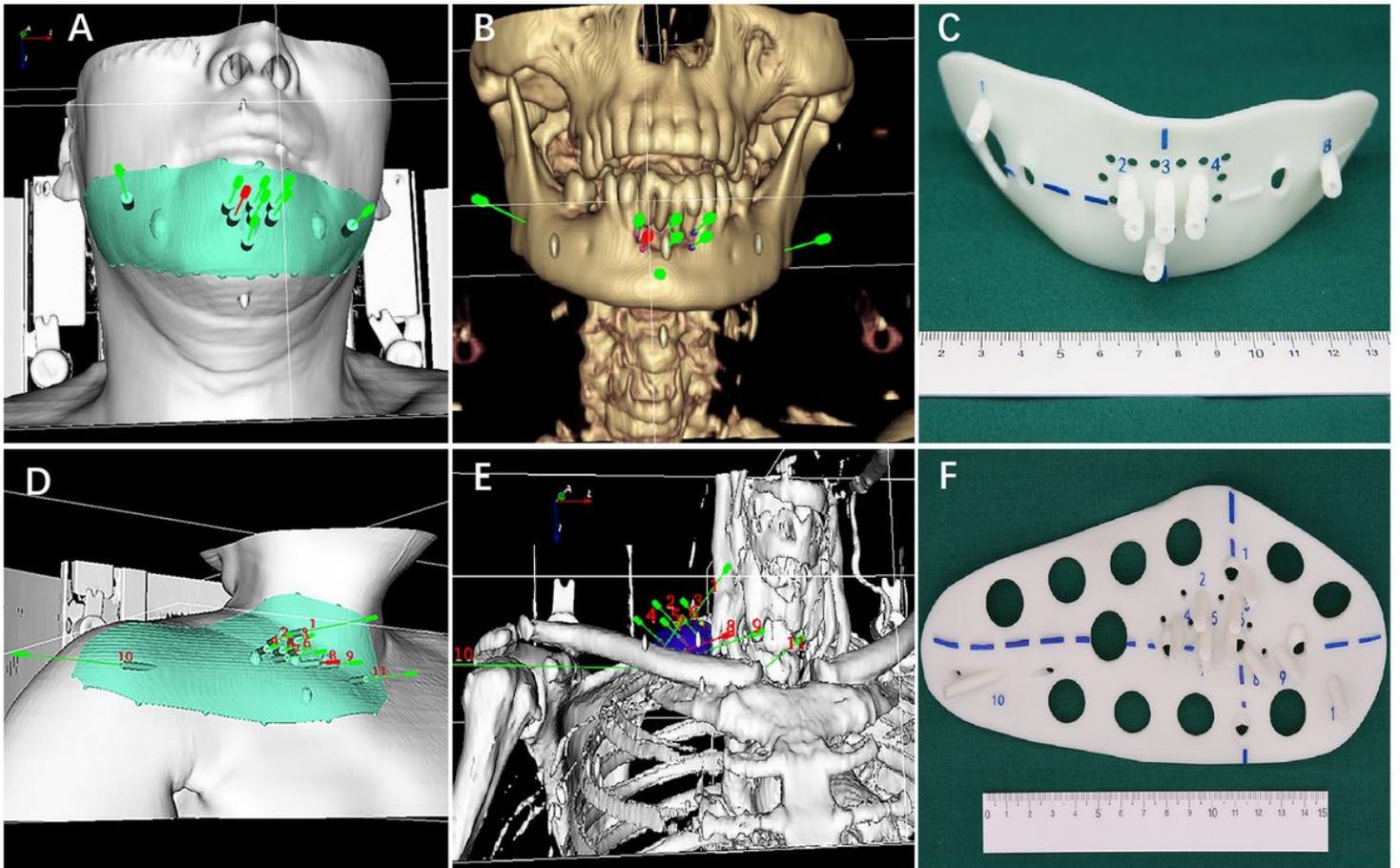
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## Figures



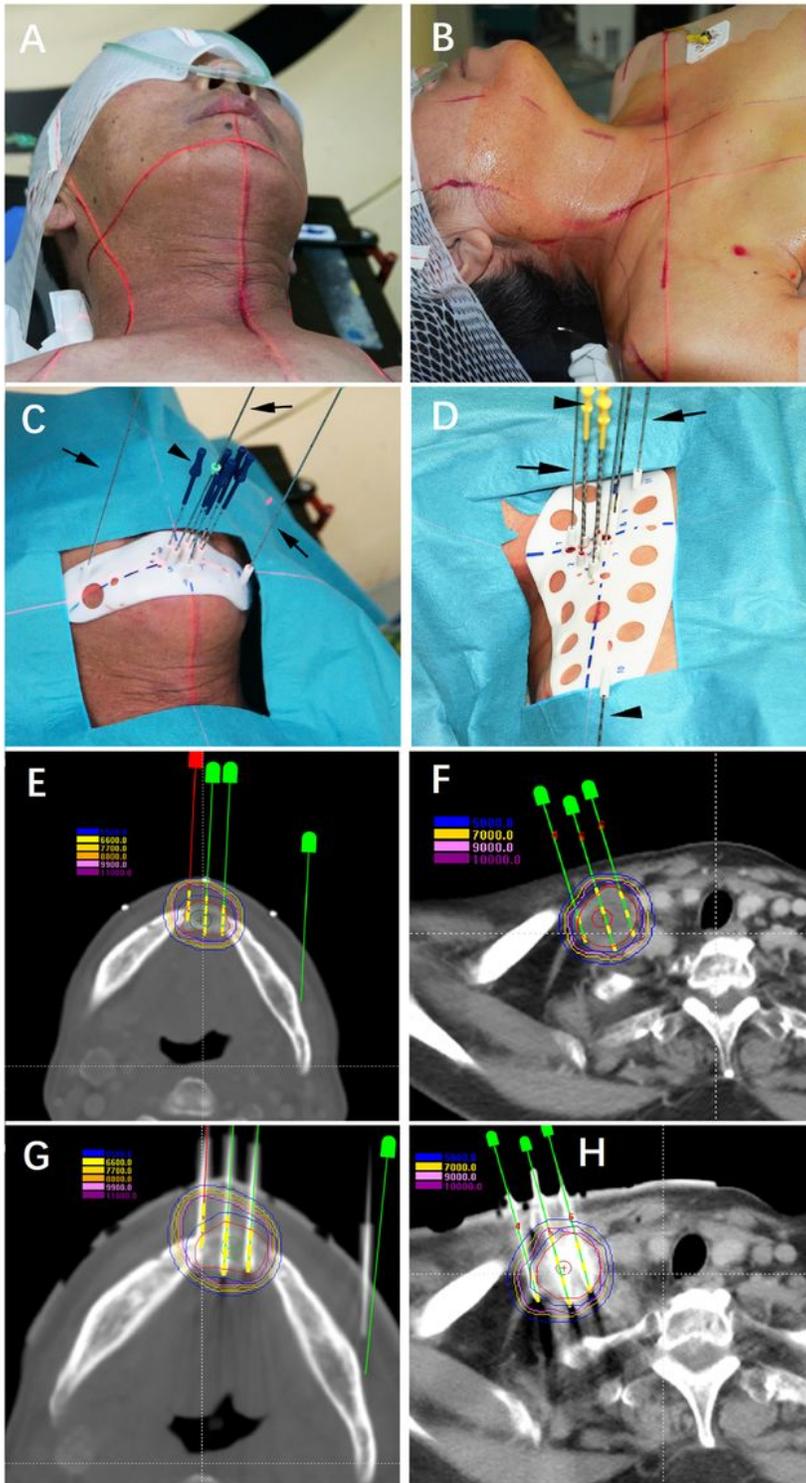
**Figure 1**

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



**Figure 1**

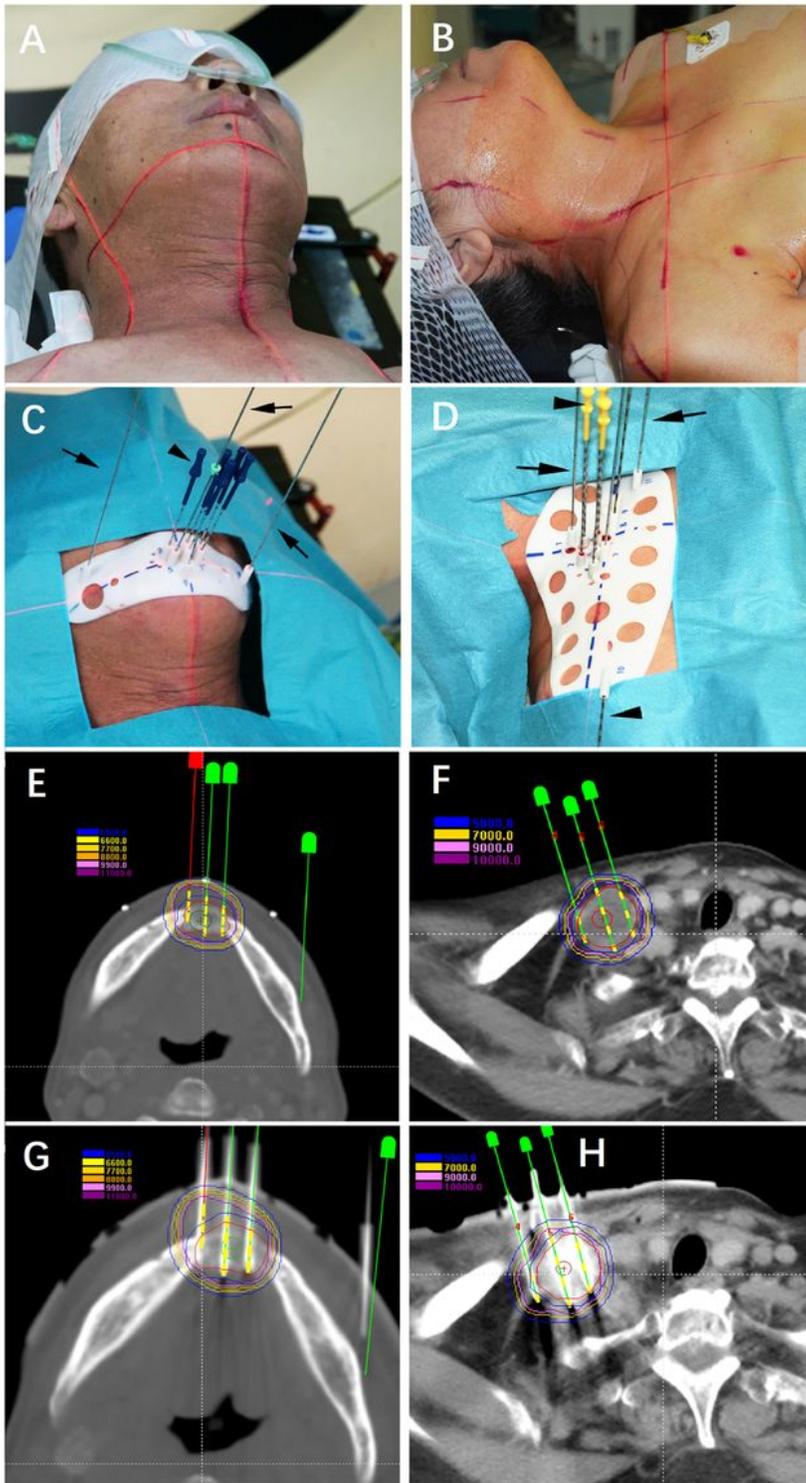
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**Figure 2**

125I radioactive seed implantation for patients with recurrent head and neck cancer. A-B: Patients were fixed with a bow cap in suitable gesture and marked with surface positioning line; C-D: individualized 3D-printing template (3D-PT) was aligned to the target region according to the outline characteristics, reference line on the 3D-PT, surface positioning line, and positioning laser. Then the locking needles (arrow) followed by the implantation needles (arrowhead) were percutaneously inserted via the pre-

designed holes on the 3D-PT. E-F: intraoperative plan and appropriate additional needle was added; G-H: 1125 seeds were implanted.



**Figure 2**

1125 radioactive seed implantation for patients with recurrent head and neck cancer. A-B: Patients were fixed with a bow cap in suitable gesture and marked with surface positioning line; C-D: individualized 3D-printing template (3D-PT) was aligned to the target region according to the outline characteristics,

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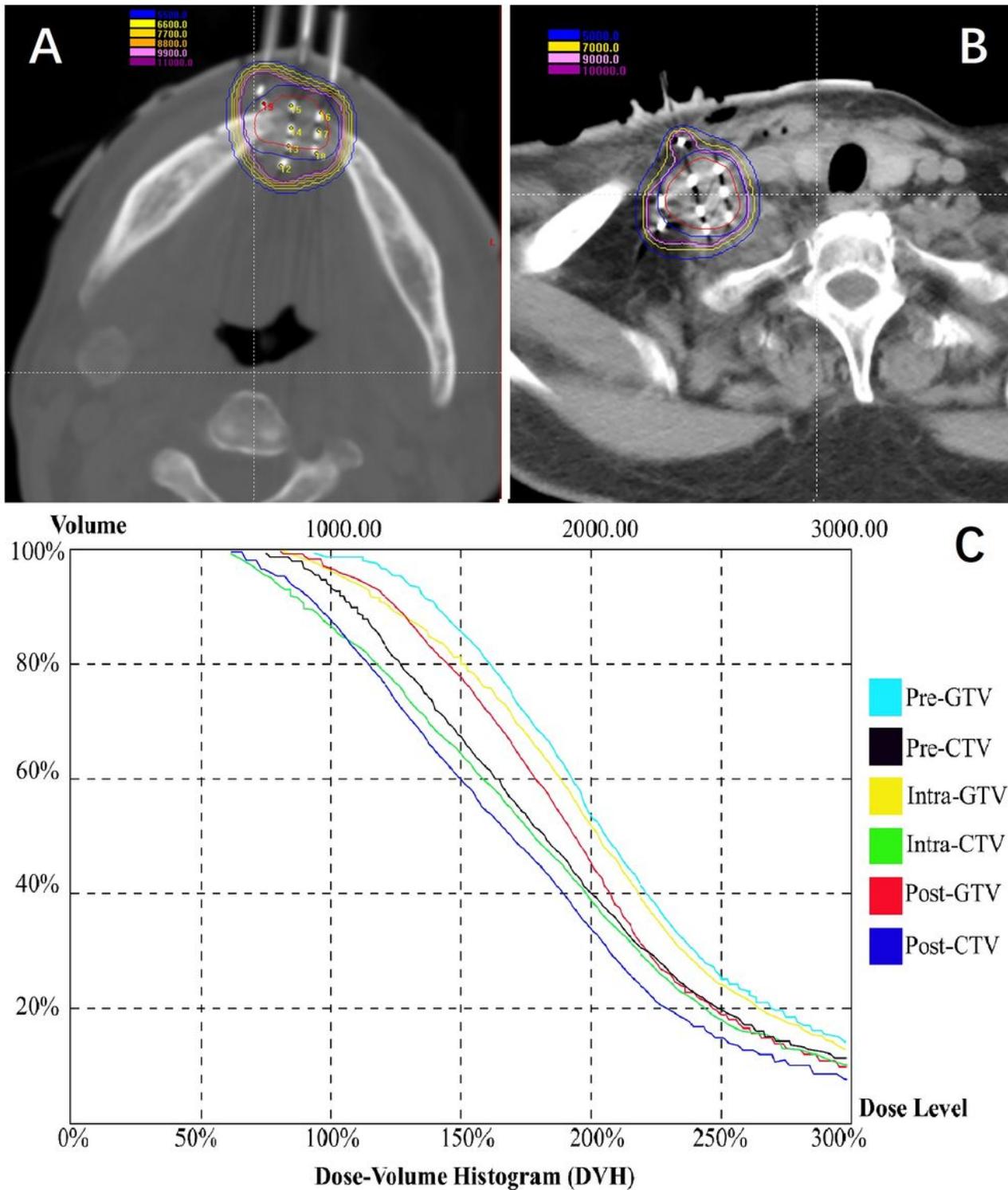


Figure 3

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

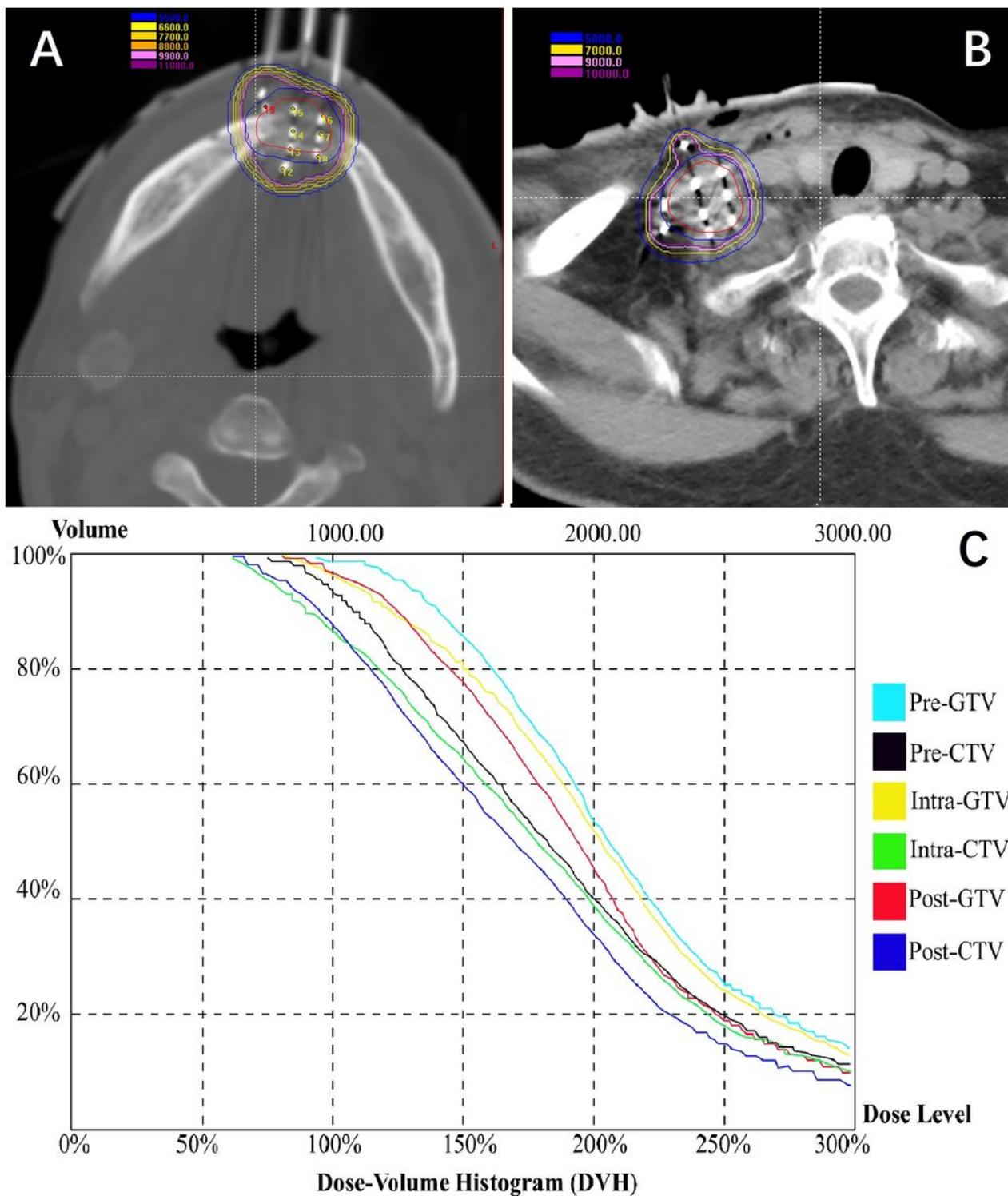


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