

Technology and Method

Water-filled balloon in the postoperative resection cavity improves dose distribution to target volumes in radiotherapy of maxillary sinus carcinoma

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Abstract

Postoperative radiotherapy is a major treatment for patients with maxillary sinus carcinoma. However, the irregular resection cavity poses a technical difficulty for this treatment, causing uneven dose distribution to target volumes. In this study, we evaluated the dose distribution to target volumes and normal tissues in postoperative intensity-modulated radiotherapy (IMRT) after placing a water-filled balloon into the resection cavity. Three postoperative patients with advanced maxillary sinus carcinoma were selected in this trial. Water-filled balloons and supporting dental stents were fabricated according to the size of the maxillary resection cavity. Simulation CT scans were performed with or without water-filled balloons, IMRT treatment plans were established, and dose distribution to target volumes and organs at risk were evaluated. Compared to those in the treatment plan without balloons, the dose (D_{98}) delivered to 98% of the gross tumor volume (GTV) increased by 2.1 Gy ($P = 0.009$), homogeneity index (HI) improved by 2.3% ($P = 0.001$), and target volume conformity index (TCI) of 68 Gy increased by 18.5% ($P = 0.011$) in the plan with balloons. Dosimetry endpoints of normal tissues around target regions in both plans were not significantly different ($P > 0.05$) except for the optic chiasm. In the plan without balloons, 68 Gy high-dose regions did not entirely cover target volumes in the ethmoid sinus, posteromedial wall of the maxillary sinus, or surgical margin of the hard palate. In contrast, 68 Gy high-dose regions entirely covered the GTV in the plan with balloons. These results suggest that placing a water-filled balloon in the resection cavity for postoperative IMRT of maxillary sinus carcinoma can reduce low-dose regions and markedly and simultaneously increase dose homogeneity and conformity of target volumes.

Key words Maxillary sinus carcinoma, postoperative radiotherapy, dose distribution, water-filled balloon

Carcinoma of the maxillary sinus is rare, accounting for 2% to 3% of all head and neck tumors. Therefore, clinical data regarding the management of this disease have been collected primarily from retrospective studies with small sample sizes at single institutions. These

studies have shown that patients with early stage disease have an excellent chance of cure after surgical resection with clear margins^[1]. However, most patients are diagnosed at advanced stages, with tumor extension through the bony walls of the paranasal sinus, orbit, and anterior skull base. Therefore, the gross tumor may not be completely removed during surgical resection. Thus, postoperative radiotherapy appeared to be very necessary and became one of the major approaches of comprehensive treatment^[2,3]. Nevertheless, many studies have shown that local residue and recurrence were common after postoperative radiotherapy, primarily because of inadequate dose coverage and uneven dose distribution to the tumor-involved region^[4]. Generally, a large irregular cavity is present after maxillectomy.

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Because of dose build-up effects, a lower dose region exists on the surface of an air cavity penetrated by a radiation beam, especially a megavoltage X-ray beam^[5]. The presence of a low-dose region in residual tumor and micrometastases may result in local recurrence. To solve this problem, tissue equivalent bolus compensators were used to fill the resection defects for radiation therapy^[6]. However, similar treatment and dosimetric analyses, especially combined with intensity-modulated radiotherapy (IMRT), have not been reported domestically^[7]. In this study, we used a water-filled balloon with a supporting individual dental stent to fill the postoperative resection defect at the site of locally advanced maxillary sinus carcinoma and then executed an IMRT treatment plan to analyze its impact on dose distribution in the target volumes and normal tissues.

Patients and Methods

Patient characteristics

Three maxillary sinus cancer patients who underwent surgery in Head and Neck Department of Sun Yat-sen University Cancer Center between February 2011 and July 2011 were selected. All patients had stage IVa disease and T4aN0M0 status according to the 2010 American Joint Committee on Cancer (AJCC) classification, had undergone subtotal maxillectomy, and had positive macroscopic surgical margins. Two patients

were women and one was man, and their ages ranged from 36 to 66 years. Two patients had poorly differentiated squamous cell carcinoma and one had adenoid cystic carcinoma. The tumor-involved region and surgical bed were quite different among the three patients. Postoperative cavities in the maxillary sinus were 30–40 mL.

Fabrication of water-filled balloons and individual dental stents

A medium-sized balloon with a round bulb and narrow neck was filled with water. The round bulb was used to fill the postoperative cavity, after which water was injected with a syringe through the neck of the balloon according to the volume of the maxillary defect. The balloon neck was subsequently tightened after exhausting the air inside of the balloon. An individual dental stent fabricated by a dentist supported the water-filled balloon and pushed the tongue down and away from the hard palate (Figure 1).

Deposition of water-filled balloons, body position and immobilization, CT scans for radiotherapy

First, patient assumed a supine position, and a water-filled balloon was placed into his resection defect. Then, an individual dental stent was seated into the oral cavity (Figure 2). Next, the patient's head was immobilized by thermoplastic facial mask, and CT scans were performed with the water-filled balloons.

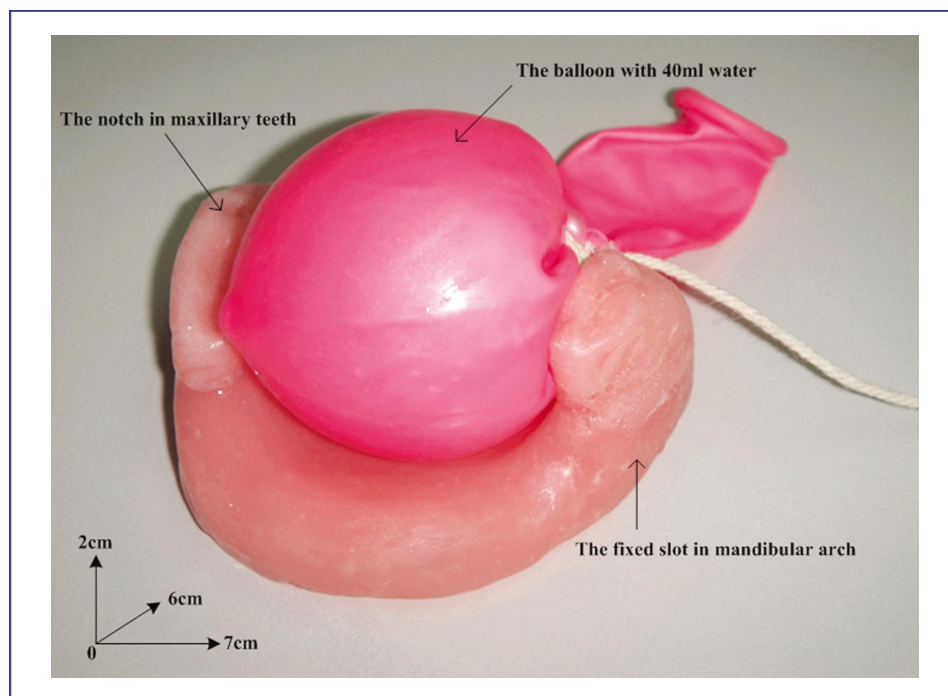


Figure 1. Water-filled balloon and supporting individual dental stent.

Subsequently, after removing the bolus, CT scans were performed once without water-filled balloons using the same immobilization and locating marks.

Image fusion

The two sets of CT images, with and without water-filled balloons, were then transferred to the MONACO planning system to perform image fusion. We delineated target volumes on CT images with water-filled balloons and copied target volume contours to the CT images without balloons. Finally, we made modifications based on the displacement to maintain full agreement of target volume coverage in the two sets of CT images.

Delineation of target volumes and prescription dose

Gross tumor volume (GTV) was determined according to the postoperative CT/MRI findings of disease, including the edges of the resection. The clinical target volume of 60 Gy (CTV₆₀), the region at risk for microscopic disease, was defined as the GTV expanded by 1 cm in three dimensions, including the surgical bed and the preoperative tumor-invading regions (such as the ipsilateral ethmoid sinus, medial and bottom orbital wall, ipsilateral optic canal, sella, ipsilateral cavernous sinus, base of sphenoid bone, clivus, petrous apex, foramina lacerum, pterygoid process, pterygopalatine fossa, ipsilateral hard palate and mandible stump, whole lateral pterygoid muscle, and ipsilateral nasal cavity mucosa). Planning target volume (PTV) was obtained by applying a 3-mm expansion

margin to the GTV and CTV₆₀.

Dose specifications and treatment delivery for IMRT

We used the same dose-optimizing constraints to do two IMRT treatment plans. The planning gross tumor volume (PGTV) was prescribed to 68 Gy in 30 fractions of 2.27 Gy per fraction given 5 days per week over 42 days, with simultaneous application of 60 Gy to planning clinical target volume (PCTV)^[8]. We determined the 100% isodose line encompassed the PTV. A set of dose limitations were defined for the organs at risk depending on the standard of TD5/5, the dose at which, under standard treatment conditions, less than or equal to 5% of patients experienced serious complications within 5 years after radiation therapy, and the distance of the PTV to the organs at risk. However, in this study, stringent dosimetric constraints of the ipsilateral optic pathway were not employed to obtain better dose distribution. Treatment was administered with a 6-megavoltage (MV) photon from a linear accelerator with a multileaf collimator and a coplanar nine beams technique.

Evaluation criteria

The quality of the treatment plan was assessed with several dosimetric indices.

D₉₈, which can be considered the minimum dose, is the dose to 98% of the target volume; that is, 98% of the target volume receives this dose or higher.

HI, the dose homogeneity index, is defined as



Figure 2. A patient wearing an individual dental stent that supported a water-filled balloon after resection of maxillary sinus carcinoma.

follows: $HI = D_2 - D_{98} / D_{68Gy} \times 100\%$. D_2 , which can be considered the maximum dose, is defined as the dose to 2% of the target volume, indicating that only 2% of the target volume receives this dose or higher. The high-dose gradient is common in IMRT, therefore, the true minimum or maximum dose is typically not reliable. The reason for choosing D_{98} and D_2 to represent the minimum and maximum doses, respectively, is that the calculation of true minimum or maximum dose are more sensitive and stringent constraint than the traditional definition of highest-dose and coldest-dose regions. D_{68Gy} is the prescription dose, which equals to 68 Gy. A lower HI value means a more homogeneous dose distribution in the target volume.

TCI, an index of tumor conformity, is defined as follows: $TCI = \text{PGTV volume covered by the prescribed dose} / \text{PGTV volume}$. A higher TCI value means better conformity. In this study, the percentage volumes of 68 Gy (V_{68Gy}) and 65 Gy (V_{65Gy}) were used instead of the TCI_{68Gy} and TCI_{65Gy} .

For organs at risk, D_1 is the maximal dose of 1% of the normal structure volume. For the temporal lobe and brainstem which were considered to be serial organs, we computed D_1 to represent the maximal dose. We also calculated the maximum dose for pituitary and optic pathways of small volumes, such as the lens, optic nerve, and optic chiasm.

Statistical analysis

Evaluation dose indices of the treatment plans were

compared by the paired *t* test using SPSS13.0 software. Hypothesis testing was two-sided and $P < 0.05$ was considered statistically significant.

Results

Compared to the dose in the treatment plan without balloons, D_{98} delivered to the GTV increased by 2.1 Gy ($P = 0.009$) (Figure 3), HI improved by 2.3% ($P = 0.001$), and V_{68Gy} increased by 18.5% ($P = 0.011$) in the plan with balloons (Table 1). V_{65Gy} values were not significantly different in both plans. Dosimetric endpoints of normal tissues around target regions in both plans were not significantly different ($P > 0.05$) except for the optic chiasm (Table 2, Figure 4). The 68 Gy high-dose regions entirely covered the GTV in the plan with water-filled balloons (Figure 5).

Discussion

Some studies reported that total dose of postoperative radiotherapy was correlated to local control of maxillary sinus cancer. For patients with positive margins, the target dose should purportedly be more than 66–74 Gy for tumor control^[9]. The prescription was determined using α/β value of related tissue and the estimating doses using iso-effect formalisms based on linear-quadratic relationships, yielding 68 Gy in 30 fractions of 2.27 Gy as biologically equivalent to 70 Gy

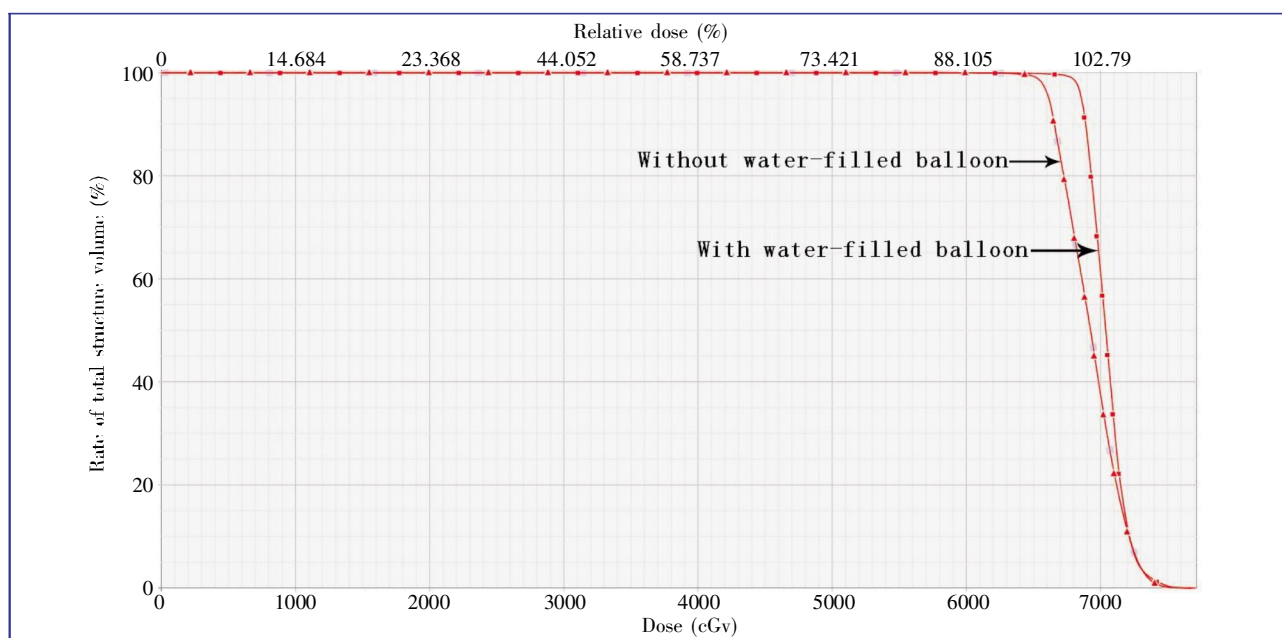


Figure 3. Dose-volume histogram of the gross tumor volumes with and without water-filled balloons. Filling the maxillary cavity with a water-filled balloon not only increased the minimum dose in gross tumor volume but also increased the volume covered between 65 and 68 Gy.

Table 1. Dosimetric endpoints of the target gross tumor volumes in treatment plans with and without water-filled balloons			
Dosimetric endpoint	Without balloon	With balloon	P
D ₉₈ (cGy)	5902.6 ± 760.1	6117.2 ± 747.1	0.009
V _{68Gy} (%)	78.0 ± 2.9	96.5 ± 5.7	0.011
V _{65Gy} (%)	99.2 ± 1.3	99.2 ± 1.4	0.965
HI (%)	12.0 ± 1.4	9.7 ± 1.5	0.001

D₉₈, the dose delivered to 98% of the gross tumor volume; V_{68Gy}, the percentage volumes of 68 Gy; V_{65Gy}, the percentage volumes of 65 Gy; HI, homogeneity index.

Table 2. The dose in normal tissues in treatment plans with and without water-filled balloons			
Normal tissues	Without balloon	With balloon	P
Ipsilateral lens, D _{max} (cGy)	1093.5 ± 397.6	1153.5 ± 366.4	0.665
Ipsilateral optic nerve, D _{max} (cGy)	7356.4 ± 229.9	7401.5 ± 204.3	0.340
Optic chiasm, D _{max} (cGy)	7049.6 ± 797.6	7139.6 ± 818.6	0.018
Pituitary, D _{max} (cGy)	6668.1 ± 844.0	6807.8 ± 982.2	0.566
Brain stem, D ₁ (cGy)	5188.9 ± 167.0	5221.8 ± 183.2	0.249
Ipsilateral temporal lobe, D ₁ (cGy)	7006.5 ± 436.3	7098.9 ± 483.2	0.166

D_{max}, maximal dose; D₁, maximal dose of 1% of the normal structure volume.

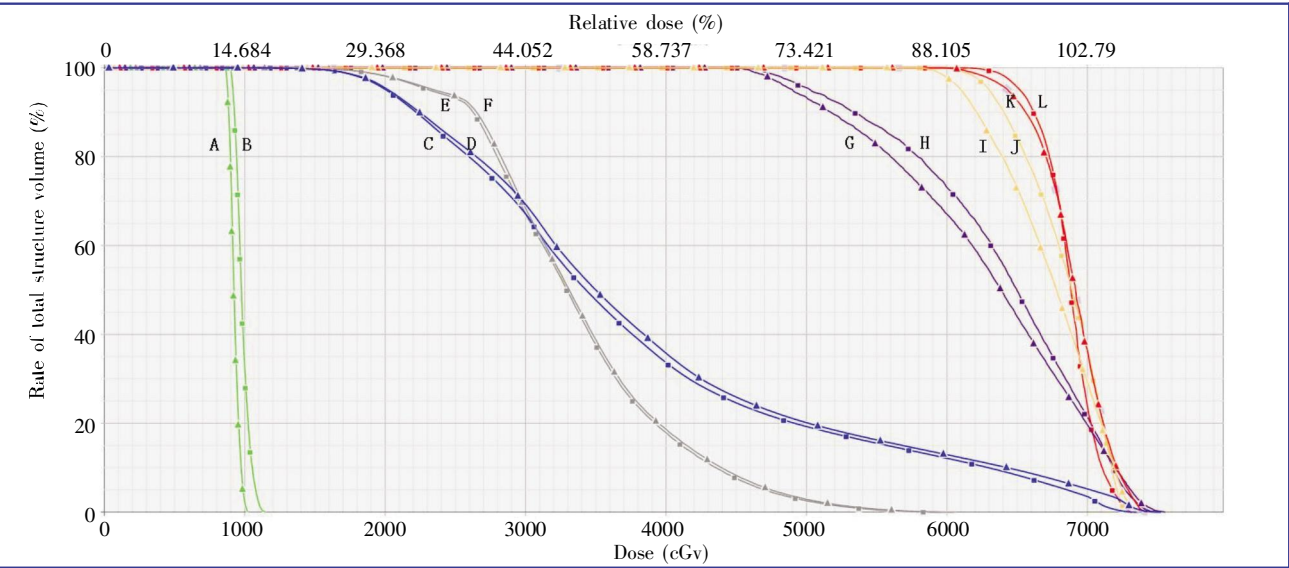


Figure 4. Dose-volume histogram of the organs at risk with and without water-filled balloons. A, ipsilateral lens (without balloon); B, ipsilateral lens (with balloon); C, ipsilateral temporal lobe (without balloon); D, ipsilateral temporal lobe (with balloon); E, optic chiasm (without balloon); F, optic chiasm (with balloon); G, brain stem (without balloon); H, brain stem (with balloon); I, pituitary (without balloon); J, pituitary (with balloon); K, ipsilateral optic nerve (without balloon); L, ipsilateral optic nerve (with balloon). Curves of normal tissues around target regions in both plans were approximately coincided except for slight difference in the brain stem, pituitary and optic pathways. Depositing a water-filled balloon in the maxillary cavity mildly increased the radiation dose to neighboring organs.

with 2 Gy per fraction. Likewise, 65 Gy was biologically equivalent to 66 Gy^[10]. The study results indicated that

the application of balloons increased the minimum dose (D₉₈) delivered to the GTV, improved HI, and increased

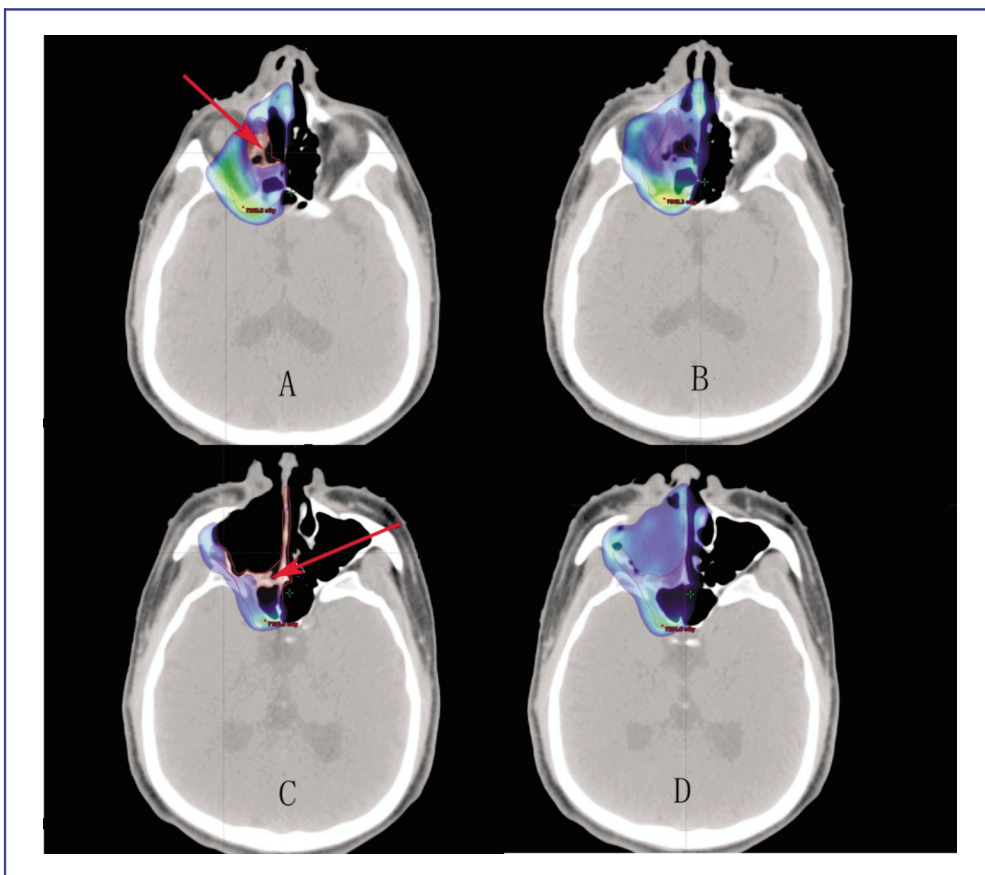


Figure 5. The coverage of 68 Gy at the ethmoid and maxillary sinuses in the treatment plans without (A, C) or with a water-filled balloon (B, D). As indicated by red arrows, significant underdosage regions of the gross tumor volume (GTV) were found in the ethmoid sinus and posteromedial wall of the maxillary sinus in the plan without water-filled balloons. In contrast, the 68 Gy dose entirely covered the GTV in the plan with water-filled balloons, as indicated by the blue regions.

TCI_{68Gy} , but did not affect TCI_{65Gy} . Dose distributions displayed in each CT scan showed good agreement with calculations (Figure 5). Thus, the deposition of a water-filled balloon within a resection defect yielded more target volumes at the 65 to 68 Gy dose level (Figure 3). Moreover, highly conformal high-dose coverage of target volumes in three-dimensions was achieved with this technique. Dose homogeneities were also improved. The doses affecting the optic pathways were slightly elevated in both plans (Table 2, Figure 4), mainly due to the advanced stage of the tumors (T4), and the tumors were physically close to the optic pathways. Many scholars in other countries opted to sacrifice ipsilateral optical pathway structures to obtain better dose coverage. Thus, strict dose constraints were not defined for the ipsilateral optic pathway, which resulted in high-dose radiation to a large volume overlapping the ipsilateral optical pathway. The deposition of a water-filled balloon also increased the radiation dose to the superior and posterior walls of the maxillary sinus and to the neighboring optic chiasm.

We analyzed dose distribution in the target volumes and organs at risk in each CT slice and found that, in the plan without water-filled balloons, significant underdosage regions of the GTV existed in the ethmoid sinus, posteromedial wall of the maxillary sinus, and

surgical margins of hard palate, whereas hot spots existed in the temporal lobe outside the target volume. In contrast, in the plan with water-filled balloons, dose distribution in each CT slice was much more consistent, and underdosage regions were entirely covered by the dose of 68 Gy (Figure 5). Conventional radiotherapy was delivered with an isocentric anterior and lateral or bilateral wedged beam arrangement, lowering upper bound of lateral beam to protect contralateral vision resulted in underdosage in the posterior ethmoid and the upper corner of the maxillary sinus. In some studies, maxillary cancer patients had tumor residue after completing the total dose of 70 Gy of conventional radiotherapy, and 80% of the residue was located at posteromedial wall (infrastructure) of the maxillary sinus^[11]. Chinese researchers solved this problem by using simultaneous interstitial brachy radiotherapy and local integrated boost radiotherapy^[12].

In recent years, IMRT and three-dimensional conformal radiotherapy (3D-CRT) have become the dominant radiotherapy techniques because of advances in radiotherapy equipments. Mock *et al.*^[13] designed conventional and conformal radiotherapy as well as IMRT treatment plans for 5 patients with maxillary sinus cancer and observed that both 3D-CRT and IMRT

techniques decreased the dose to non-target tissues by 62% to 65% compared with conventional treatment modalities without comprising the dose to target. However, the maxillary sinus consists of many head facial bones and air cavities and is in close proximity to many critical structures. Furthermore, the leaf width of the multileaf collimator also has an impact on target dose coverage^[14]. For these reasons, the dose distribution actually would not satisfy the needs as described in theory.

Studies at Memorial Sloan-Kettering Cancer Center in which modern radiotherapy techniques were applied in the postoperative nasal cavity for paranasal sinus cancer indicated that cribriform plate involvement, an integral part of ethmoid sinus, was also a prognostic factor of local relapse in univariate and multivariate analyses^[15]. In the IMRT plan without water-filled balloons, a significant underdosage region in the ethmoid sinus was observed despite not employing stringent dosimetric constraints for ipsilateral vision (Figure 5). It was reported that patients with infrastructural involvement had significantly higher survival rates compared to patients with suprastructural involvement^[16,17]. According to the 2010 AJCC clinical staging system, only advanced stage tumors involve suprastructures of the maxillary sinus. Surgical procedures in supramaxillary regions are technically difficult because of complex anatomy. Thus, increasing the local dose of radiation for patients with suprastructural involvement is expected to result in better local disease control.

There are several advantages of using water-filled balloons to fill resection defects. Water density is

approximately 1 g/cm³, and water-filled balloons, with good elasticity and conformality, are soft enough to prevent tissue injury and are easy to set up for daily radiation treatments. Thus, water is the best available tissue-equivalent bolus. Acrylic resin is an alternative filler because it has a similar density to water; however, it is a solid material that will likely cause patients discomfort when used. The individual dental stents used in this study also had several advantages. They provided a template to confine the water-filled balloon within the orofacial defect; maintained the balloon in repeatable position; and pushed the tongue and a part of the mandibular, oral mucous membrane away from radiation field, consequently sparing the oral mucous membrane and preserving taste for patients^[18]. On the other hand, the disadvantage of the water-filled balloon technique is that accurate, repeatable positioning of water-filled balloons cannot be ensured from day to day.

In conclusion, we show here that using water-filled balloons to fill maxillary resection defects in maxillary sinus cancer patients undergoing postoperative IMRT improved high-dose coverage of target volumes and reduced low-dose regions, especially in the supramaxillary and ethmoid sinus. Thus, this approach is expected to increase the local disease control rate. Water-filled balloons are easy to use for daily radiation treatments and soft enough to prevent tissue injury. Therefore, this method is recommended for wide use in clinical treatment of postoperative maxillary sinus cancer.

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