

Preoperative surgical simulation and validation of the line of resection in anterolateral craniofacial resection of advanced sinonasal sinus carcinoma

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ABSTRACT: *Background.* The purpose of this study was to assess the usefulness and accuracy of preoperative 3D virtual simulation of anterolateral craniofacial resection in cases of advanced sinonasal sinus carcinoma.

Methods. Seven patients with advanced (T4 classification) sinonasal sinus carcinoma who underwent anterolateral craniofacial resection in our hospital between 2011 and 2013 were included in this study. Postsimulation CT images were fused with postoperative CT images and differences between the planned and actual osteotomy were measured in 3 regions of the skull base.

Results. The differences ranged from 0 mm to 5.8 mm (average, 3.1 mm) at the inferior wall of the cavernous sinus, from 0.8 mm to 8.3 mm (average, 3.5 mm) at the inferior wall of the sphenoid sinus, and from 0 mm to 13.6 mm (average, 2.3 mm) in the palatine bone.

Conclusion. Preoperative 3D virtual surgical simulation and postoperative feedback can contribute to training for surgeons. © 2016 Wiley Periodicals, Inc. *Head Neck* 00: 000–000, 2016

KEY WORDS: 3D virtual simulation, validation, craniofacial resection, sinonasal sinus carcinoma, skull base surgery

INTRODUCTION

Malignant tumors of the nasal cavity and sinonasal sinuses are uncommon, comprising 0.2% to 0.5% of all cancer cases and only 3% of malignant head and neck tumors.¹ Almost half (43.9%) of these lesions are localized to the nasal cavity, whereas most others originate in the maxillary (35.9%) or ethmoid (9.5%) sinus. Frontal and sphenoid sinus carcinomas comprise 1.1% and 3.3% of all sinonasal tumors, respectively.²

Among the multiple therapeutic approaches that have been proposed for carcinoma of the nasal cavity and sinonasal sinuses, complete surgical resection followed by postoperative radiotherapy has been associated with the best outcomes.^{3–5} Craniofacial resection of sinonasal carcinoma has been used widely since Ketcham et al⁶ first reported it in 1963, and many authors have reported good results with favorable prognoses and low complication rates for craniofacial resections of malignant skull base tumors.^{7–11} In cases of locally advanced sinonasal sinus carcinoma, especially maxillary sinus and ethmoid sinus

tumors, anterolateral craniofacial resection is an effective treatment, and complete osteotomy can permit en bloc resection with tumor-free margins. Although accurate osteotomy in these regions is associated with a low complication rate and good prognosis, it is often difficult to perform because the surgical field is limited and deep and is easily filled with blood. Successful en bloc tumor resection requires a complex and precise surgical technique, and outcomes of craniofacial resection depend on clinical experience and surgical expertise.

Recent advances in technology have allowed more accurate imaging of the complicated anatomy of the skull base, and several authors have reported on the usefulness of 3D virtual imaging in preoperative surgical simulation. However, because the deep portion of the skull base region is not easily reached during the actual surgery as a result of the proximity of crucial structures, including the cerebrum, the brainstem, the internal carotid artery, and the cavernous sinus, the actual osteotomy in the skull base is sometimes not consistent with the planned osteotomy, and there have been few reports validating the accuracy of surgical simulation in this regard. A means of appropriate feedback that can highlight disparities between a surgical simulation and the actual surgery could help to reduce complication rates and improve prognoses.

In this study, we compared preoperative 3D virtual simulation of anterolateral craniofacial tumor resections with the actual surgeries and examined the differences between

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planned and actual lines of resection (osteotomy) using postsimulation and postoperative CT scans.

PATIENTS AND METHODS

Patients

We retrospectively analyzed clinical and pathological characteristics, including operative data and complications, of 7 patients with locally advanced sinonasal sinus carcinoma (T4 classification) who underwent anterolateral craniofacial resection at the Department of Otorhinolaryngology, Nagoya University Hospital, Nagoya, Japan, between 2011 and 2013. Informed consent was obtained from all patients and this study was approved by the ethics review committee of Nagoya University Hospital. TNM stage was reclassified using the American Joint Committee on Cancer seventh edition criteria.

Surgery

We have performed en bloc anterolateral craniofacial resection in cases of locally advanced stage T4 sinonasal sinus carcinoma since 1992. Cervical lymph nodes are evaluated by CT, MRI, and ultrasonography, and therapeutic neck dissection is recommended for patients with N1 to N3 disease, whereas no neck dissection is recommended for those with N0 disease. We do not perform en bloc anterolateral craniofacial resection in patients with involvement of the sphenoidal sinus or clivus, those with distant metastases (eg, to bone, lungs, or liver), those whose general condition is too poor to allow craniofacial resection (ie, worse than performance status 2, as defined by the Eastern Cooperative Oncology Group),¹² or those who choose not to undergo surgical resection. Our surgical strategy for T4 maxillary sinus carcinomas and ethmoid sinus carcinomas is to provide en bloc tumor resection with clean margins while maximizing preservation of normal bony tissues and surrounding soft tissues. Depending on the extent of tumor invasion, we usually plan to perform the osteotomy with a margin of bone of at least 5 mm to achieve en bloc resection with tumor-free margins. The surgical procedure was described in detail in a previous report from our institute¹⁰; therefore, we describe it only briefly here. Head and neck surgeons perform the neck dissection for patients with N1 to N3 tumors and then, using a Weber–Fergusson incision, dissect the left face and cut the coronoid process of the mandible and the zygomatic arch. To ensure complete en bloc removal of the tumor, we resect surrounding tissues, such as the orbit, medial/lateral pterygoid muscle, oral mucosa (with a 10-mm margin), and affected mucosa of the nasal septum tumor-free margins. A left frontotemporal craniotomy is performed, and the anterior and middle cranial bases are exposed epidurally. The anterior clinoid process is removed and optic canal is unroofed. The optic nerve is cut in the optic canal, and then the superior orbital fissure and its cranial nerves are cut. The maxillary nerve is cut at the foramen rotundum. The mandibular nerve is cut at the foramen ovale when larger resection is necessary. Now that the cavernous sinus can be mobilized after these procedures, it is dissected epidurally and retracted posteromedially, making it possible to place a middle fossa osteotomy sufficiently postromedial to reach the posterior

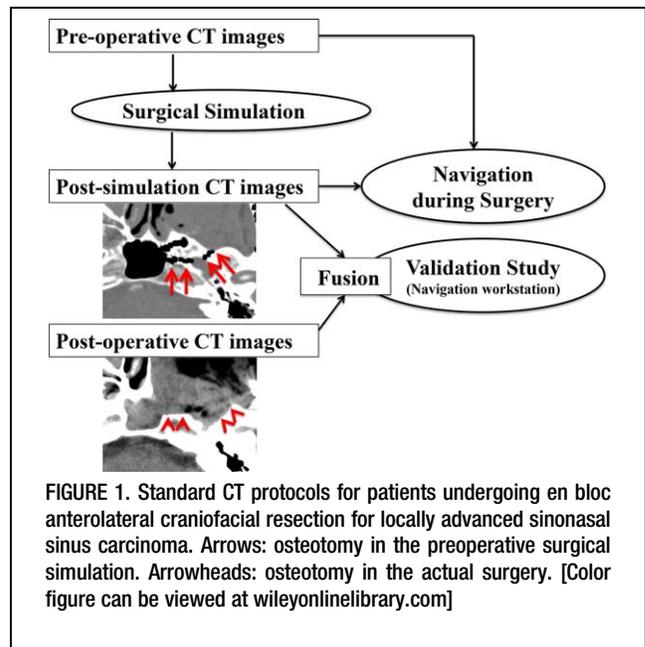
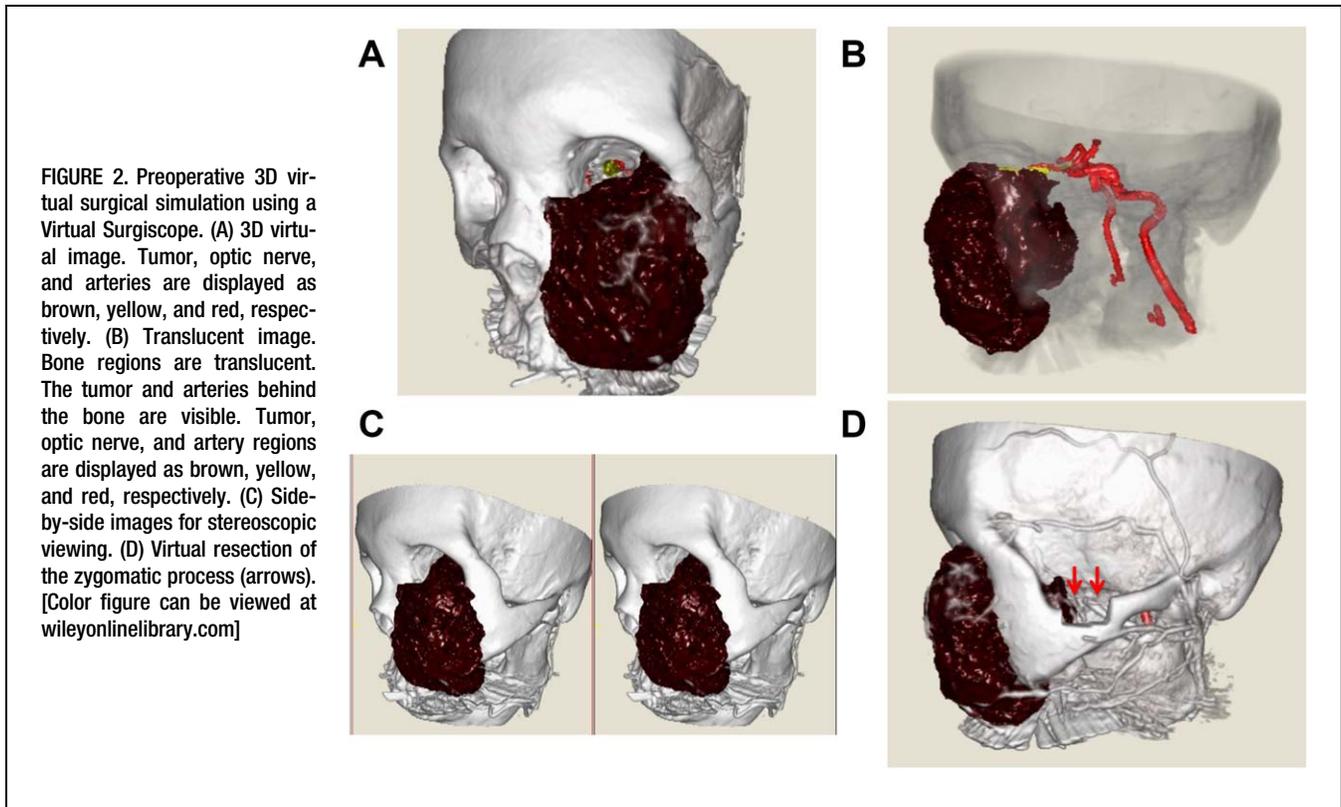


FIGURE 1. Standard CT protocols for patients undergoing en bloc anterolateral craniofacial resection for locally advanced sinonasal sinus carcinoma. Arrows: osteotomy in the preoperative surgical simulation. Arrowheads: osteotomy in the actual surgery. [Color figure can be viewed at wileyonlinelibrary.com]

side of the pterygoid plates. Osteotomies are performed on the anterior cranial base both anterior and posterior to the olfactory groove. The anterior osteotomy is connected and continued to the osteotomy on the root of the nose. The posterior osteotomy is continued on the osteotomy on the planum sphenoidale. Through the opening of the planum sphenoidale plus the posteromedial middle fossa osteotomy, the inferior wall of the sphenoid sinus is cut, reaching the upper pharynx. After cutting of the hard palate and sphenoid floor, the tumor is resected en bloc. We generally conduct the osteotomy using a drill with a width of 2 to 3 mm. After en bloc resection of the tumor, plastic surgeons reconstruct the defect in the cranial base using a rectus abdominis myocutaneous free flap and occasionally with a temporoparietal galeal flap. We evaluate tumor margins in all cases and recommend that all patients begin postoperative radiotherapy (50 to 60 Gy in 2-Gy fractions at 5 fractions per week to the tumor bed) within 8 weeks after tumor resection. For patients with positive margins or extranodal spread, we recommend cisplatin-based chemoradiotherapy as an adjuvant treatment.

CT protocol

Figure 1 shows the standard CT protocol for patients undergoing en bloc anterolateral craniofacial resection for locally advanced sinonasal sinus carcinoma at our hospital. The CT scan is performed from the top of the head to the mandible (64-row multidetector Toshiba Aquilion scanner, Toshiba, Japan; slice thickness 0.5 mm; 120 kV; field of view 240 mm; 1 sec/rot; HP 21; SD 3; 1 mm*32). Preoperative CT images are obtained within 2 weeks of the planned surgery and are used in the surgical simulation and the intraoperative navigation system. Post-simulation CT images are obtained after 3D virtual surgical simulation, and postoperative CT images are obtained at 6 months postoperatively. The postsimulation CT images can be transferred to the navigation system, and it is technically possible for surgeons to analyze the



differences between the surgical simulation and the actual surgery.

Surgical simulation

The 3D virtual surgical simulations are performed with the Virtual Surgiscope, which uses a volume rendering method to generate the 3D virtual environment from CT images.¹³ The Surgiscope allows the surgeon to view anatomic structures from various viewpoints and directions. Key anatomic structures can be rendered in different colors by extracting these regions from the CT images in advance. Figure 2A shows a set of 3D virtual images generated from CT images. Translucent images (Figure 2B) are generated by changing the opacity parameters of the volume rendering method. A stereoscopic view is rendered by generating side-by-side images, as shown in Figure 2C. Resections are simulated by changing the intensities of the targeted tissues in the CT images. Figure 2D shows an example of a virtual resection of the zygomatic process.

Important anatomic structures, including arteries, the optic nerve, and the tumor, are segmented semiautomatically on the CT images before the surgical simulation. When these regions are displayed in different colors in the 3D virtual images (Figure 2A), the positional relationships of the structures can be confirmed and the line of resection can be determined. Translucent images (Figure 2B) are useful for identifying anatomic structures and tumor regions behind the bone. Once the line of resection is determined, a simulated osteotomy can be performed using the virtual resection function (Figure 2D). We usually set a width of 2 to 3 mm for the virtual tumor resection during the surgical simulation to match the planned dimensions of the actual surgery. The virtual osteotomy is

performed using the stereoscopic view (Figure 2C), which is also useful for greater understanding of the complex bony structures of the anterolateral craniofacial region. Repeated virtual resections are possible in the system such that the optimal line of resection might be predicted.

Navigation

We use a Vector Vision Compact Navigation System (BrainLAB, Germany) to determine the positional relationship between tumor and normal tissue.^{14,15} The system allows neuronavigation according to surface-based registration or point-based registration using 6 adhesive fiducial markers.^{16,17} Patients undergo preoperative CT scans with the fiducial markers attached to the scalp, and the position of these markers in the CT scans, along with real-space position data measured by an infrared camera, are used for registration. Before the surgery, preoperative CT images and postsimulation CT images were imported into this system. During surgery, we determine the exact position and angulation of our planned osteotomy by measuring the distance from bony landmarks, such as the zygomatic arch or tooth, and, as necessary, by using a navigation system with the planned osteotomies already entered. When the pointer is directed at the skull base region during surgery, the screen of this system displays the corresponding positions on axial, coronal, and sagittal images, and the precise position is confirmed.

Validation of resection lines

We fused postsimulation CT images with postoperative CT images in order to quantify the differences between surgical simulations and actual surgeries.

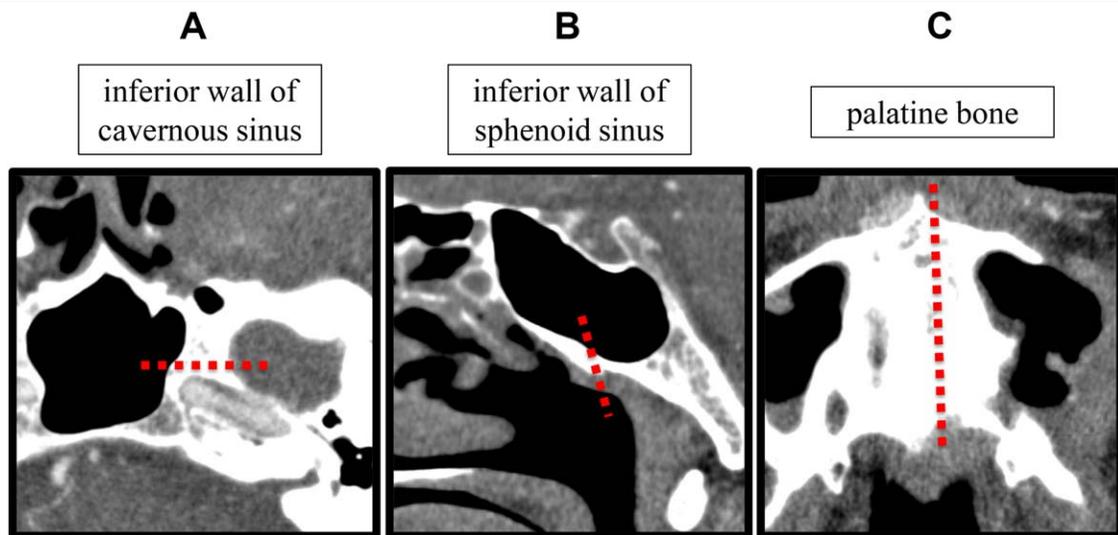


FIGURE 3. The main osteotomy lines for en bloc craniofacial resection of advanced sinonasal sinus carcinoma. (A) Inferior wall of cavernous sinus. (B) Inferior wall of sphenoid sinus. (C) Palatine bone. [Color figure can be viewed at wileyonlinelibrary.com]

Both sets of images were obtained as digital imaging and communications in medicine data and the image fusion was performed automatically, without manual correction, using iPLAN software (BrainLab). Figure 3 shows the primary osteotomy for en bloc craniofacial resection of advanced sinonasal sinus carcinomas. We evaluated this osteotomy at 3 locations: the inferior wall of the cavernous sinus (Figure 3A), the inferior wall of the sphenoid sinus (Figure 3B), and the palatine bone (Figure 3C).

We compared the line of the osteotomy determined during the preoperative surgical simulation with that of the osteotomy performed during the actual surgery (see Figure 4). We measured 3 points at the inferior wall of the cavernous sinus, 2 points at the inferior wall of the sphenoid sinus, and 3 points at the palatine bone.

The mean value of the differences was regarded as the measured value.

RESULTS

Seven patients, all men, with a mean age at surgery of 62.3 years (range, 53–69 years) and advanced (T4 classification) sinonasal carcinoma were included in our evaluation. Table 1 shows the clinical characteristics of the patients. The median duration of follow-up was 19 months (range, 10–52 months). Five patients had maxillary sinus carcinomas and 2 had ethmoid sinus carcinomas. The histological diagnosis was squamous cell carcinoma in all 7 cases. Five tumors were classified as T4a and 2 as T4b. Two tumors were N1, and 5 were N0. The M classification was M0 in all 7 cases, and all patients presented with

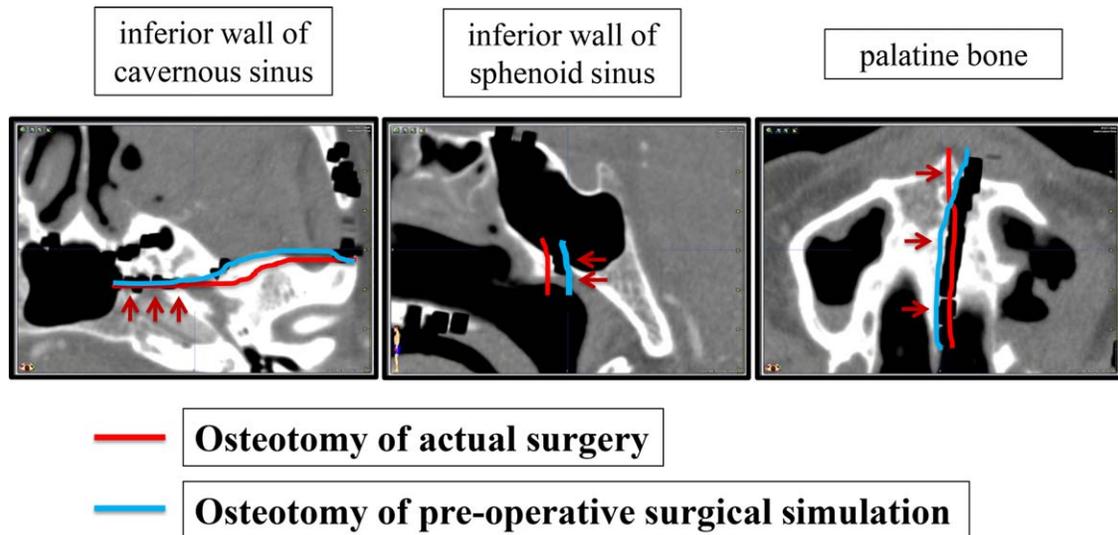


FIGURE 4. Comparison (average measured distance) between the lines of osteotomy in the surgical simulation and the actual surgery. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1. Clinical characteristics of the 7 cases.

Case #	Age, y	Sex	Primary site	T	N	M	Preoperative treatment	Operation time, min	Blood loss, mL	Complication	Margin	Follow-up, mo	Status at last follow-up	Recurrent area
1	61	Male	Maxillary	4a	0	0	RT: 40 Gy	933	2250	Local infection	Negative	52	NED	No
2	69	Male	Maxillary	4a	0	0	Chemo: CF 1	850	2095	Cerebral infarction, pseudoaneurysm	Negative	10	DOD	Neck, Rouviere node
3	62	Male	Ethmoidal	4a	0	0	Chemo: CF 2	991	14,875	No	Negative	36	AWD	Liver
4	61	Male	Maxillary	4a	1	0	Chemo: CF 1	798	1090	No	Negative	34	NED	No
5	62	Male	Maxillary	4a	1	0	Chemo: CF 1	687	1749	No	Negative	17	DOD	Neck, scalp, contrary maxillary sinus
6	53	Male	Ethmoidal	4b	0	0	Chemo: CF 2	934	6415	No	Negative	25	NED	No
7	68	Male	Maxillary	4b	0	0	Chemo: CF 1	893	585	No	Negative	19	NED	No

Abbreviations: RT, radiotherapy; Gy, Gray; NED, no evidence of disease; Chemo, chemotherapy; CF, cisplatin and 5-fluorouracil; DOD, death of disease; AWD, alive with disease.

untreated primary tumors. One patient received preoperative radiotherapy before anterolateral craniofacial resection and 6 received cisplatin and 5-fluorouracil chemotherapy. The operative time ranged from 687 minutes to 991 minutes and intraoperative blood loss ranged from 585 mL to 14,875 mL. All 7 tumors had negative resection margins.

There were no perioperative mortalities. Two patients developed surgical complications after craniofacial resection: 1 had rupture of a pseudoaneurysm of the ophthalmic artery with epidural hemorrhage and cerebral infarction, and left the hospital with hemiparesis, and the other developed local infection requiring debridement and resection of the exposed area of the zygomatic bone under local anesthesia. Three patients had tumor recurrence, 1 with metastasis to the node of Rouviere and recurrence in the neck, 1 with liver metastases as the sole site of recurrence, and 1 with neck recurrence and metastases to the scalp and the contralateral maxillary sinus.

Table 2 shows the results of the comparison between postsimulation and postoperative CT images; a plus sign (+) indicates excess resection versus the preoperative plan and a minus sign (-) indicates deficient resection versus the preoperative plan.

On the axial view of the inferior wall of the cavernous sinus, the distance between the simulated line of resection and the actual line of resection ranged from 0 mm to 5.8 mm (average, 3.1 mm). In the sagittal view of the inferior wall of the sphenoid sinus, the distance between the simulated line of resection and the actual line of resection

ranged from 0.8 mm to 8.3 mm (average, 3.5 mm). Notably, the sagittal views of the inferior wall of the sphenoid sinus showed that the actual lines of osteotomy were anterior to those determined during the surgical simulations. In the axial views of the palatine bone, the distance between the simulated line of resection and the actual line of resection ranged from 0 mm to 13.6 mm (average, 2.3 mm). The postoperative CT images confirmed that we had completely resected the greater wing of the sphenoid and the root of the pterygoid process in all cases.

Figure 5A (postsimulation) and Figure 5B (postoperative) show the CT images from a representative case. In this patient, the distance between the virtual line of resection and the actual line of resection was 1.5 mm (average) at the inferior wall of the cavernous sinus, 1.7 mm (average) at the inferior wall of the sphenoid sinus, and 1.7 mm (average) at the palatine bone. In this case, the resection was performed as planned and there were no complications during the perioperative period.

DISCUSSION

Accurate osteotomy at the inferior wall of the cavernous sinus, the sphenoid sinus (nasopharynx), and the palatine bone is essential for successful en bloc resection of advanced sinonasal sinus carcinoma. No previous study has examined the distances between the virtual lines of resection and the actual lines of resection for en bloc anterolateral craniofacial resection of advanced sinonasal carcinoma. Most authorities agree that, if possible, wide

TABLE 2. Results of comparison between postsimulation and postoperative CT images.

Case #	Inferior wall of cavernous sinus			Inferior wall of sphenoid sinus			Palatine bone		
1	-4.7	-4.1	-5.8	-7.9	-8.3	0	+5.1	+3.3	
2	-4.4	-2.6	+3.9	-1.0	-0.8	0	-3.2	-4.7	
3	-2.3	-2.6	-3.0	-1.8	-2.0	-13.6	+4.3	0	
4	-3.2	-2.2	0	-1.8	-6.4	0	0	-1.2	
5	-1.6	-0.7	-2.2	-1.7	-1.7	0	-3.7	-1.5	
6	+5.7	+5.0	+3.5	-5.1	-2.9	-1.9	-1.9	-1.1	
7	+2.9	+2.2	+2.6	-3.8	-3.5	-2.0	0	-1.2	
Average		3.1			3.5			2.3	

Note: All units are in millimeters.

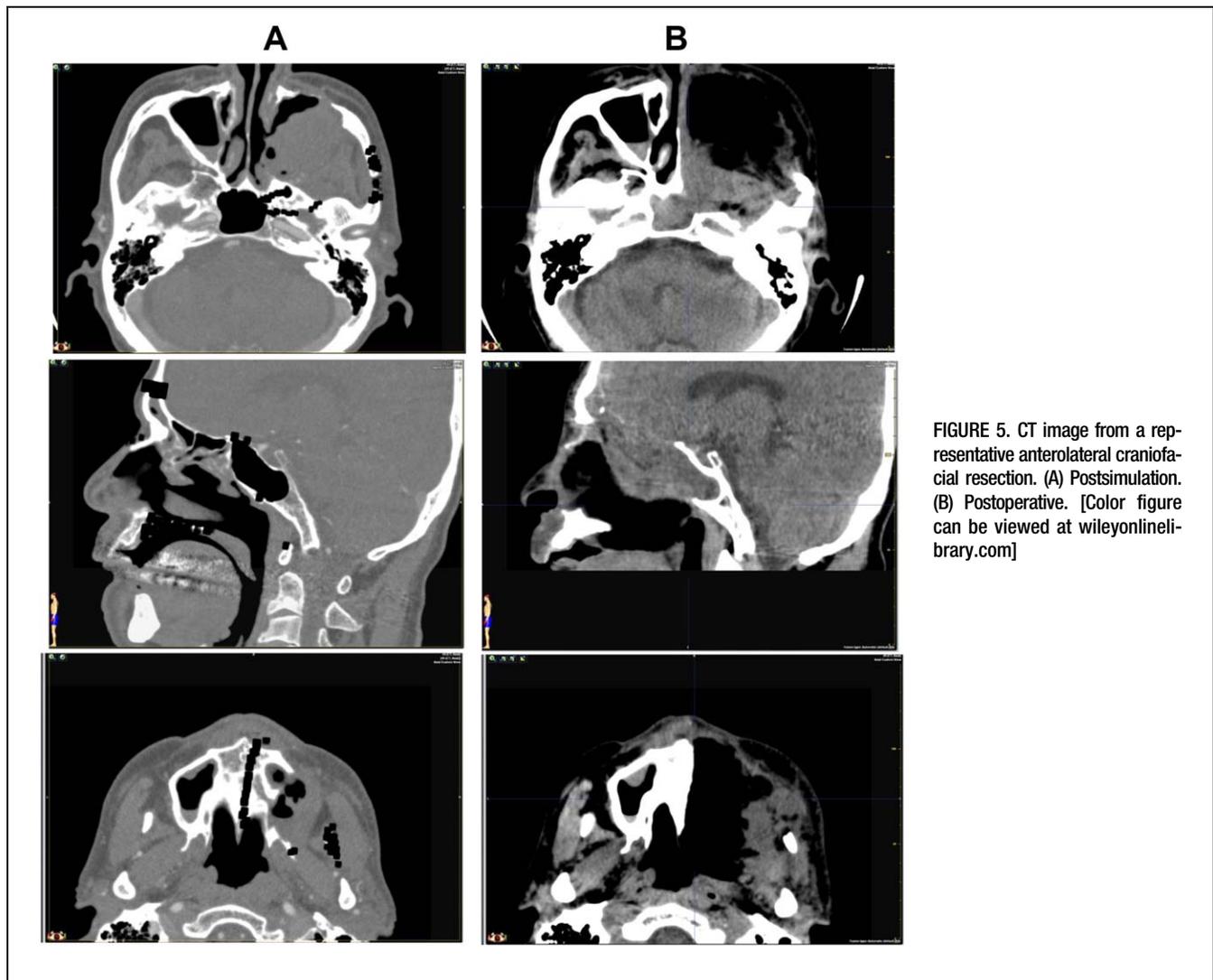


FIGURE 5. CT image from a representative anterolateral craniofacial resection. (A) Postsimulation. (B) Postoperative. [Color figure can be viewed at wileyonlinelibrary.com]

en-bloc resection of the tumor with tumor-free margins is the most important goal. Several reports have shown that a positive surgical margin is a risk factor for poor survival outcomes in patients with malignant skull base tumors.^{18,19} For advanced (T4 classification) sinonasal sinus carcinomas, anterolateral craniofacial resection is effective, and, if possible, the surgery should be performed as quickly as possible. Although the requirement for neoadjuvant chemotherapy remains controversial, neoadjuvant chemotherapy is occasionally administered to minimize the tumor size and to prevent the formation of an unresectable tumor. Outcomes after single-modality therapy are generally poor; therefore, the postoperative period is generally considered the optimal timing for radiotherapy relative to surgery.^{3,20}

For the inferior wall of the cavernous sinus, conducting an accurate osteotomy can provide a wide view of the sphenoid sinus and help to prevent serious bleeding from the internal carotid artery or the cavernous sinus. Saito et al¹⁰ reported that management of the cavernous sinus during en bloc resections of malignant skull base tumors can be expected to provide good results after craniofacial tumor resection, and we have similarly reported 5-year overall and disease-free survival rates of 62.7% and

52.6%, respectively, in 40 patients with T4 maxillary sinus carcinomas.²¹

Regarding the nasopharynx, the line of osteotomy at the inferior area of the sphenoid sinus tended to be more anterior in the actual surgeries than in the surgical simulations in the present series. Accurate osteotomy around the inferior wall of the sphenoid sinus is difficult because the surgical field is limited and narrow as a result of restricted frontal lobe retraction, which impedes direct visualization and location of the resection line. Moreover, carrying the osteotomy backward at this location may lead to damage of the clivus and the brainstem, with potentially fatal complications. Finally, the location of the osteotomy around the palatine bone is mainly dependent on the extent of tumor invasion into the nasal cavity and nasal septum.

The benefits of surgical planning using 3D CT imaging have been reported since 1980,^{22–24} but only the introduction of 3D visualization systems that integrate various imaging data has allowed preoperative surgical simulation to come into widespread use in clinical settings for procedures, such as neurovascular decompression, clipping of intracranial aneurysms, or skull base surgery.^{25–29} Because complete en bloc resection of a skull base tumor

requires an accurate osteotomy and a high level of expertise, cadaver dissection is sometimes useful for providing a deeper understanding of the complex structures of the skull base and for practicing difficult surgical techniques.³⁰ However, cadaver dissections involve economic and temporal restrictions, and the results are not applicable to individual patients. Virtual surgical simulations based on composite models created from a patient's own imaging studies overcome these limitations, and the usefulness of these technologies as educational tools for skull base and middle ear surgeries has been established.^{31–33}

An accurate osteotomy can ideally be performed based solely on planning during the surgical simulation, but it is sometimes difficult to confirm the positional information for all of the structures in the skull base because of the proximity of surrounding structures, such as the brain and orbit. Use of a navigation system provides an additional means for improving the safety of craniofacial resections.^{34,35} We use a navigation system for all skull base surgeries to help ensure that we have accurate positional information, and 3D virtual neuronavigation using 3D virtual images generated during the preoperative surgical simulation is useful to more clearly delineate the complicated 3D structures in the skull base.³⁶

Although the safety of craniofacial resection has improved, severe complications and mortality are still encountered at times. Of the 7 patients in our series, 6 left the hospital in good condition. However, 1 patient experienced rupture of a pseudoaneurysm of the ophthalmic artery and cerebral infarction on postoperative day 7, and another had an intraoperative hemorrhage with continuous blood loss after craniotomy, mainly from the epidural space and the skull base venous plexus, totaling 14,875 mL in spite of continuous hemostatic efforts of various types (electrocautery, hemostatic cotton, fibrin glue, tenting of the dura mater, head-up position, and blood transfusion). Although the preoperative simulation and validation cannot resolve all types of surgical complications, we believe that valid preoperative surgical simulations and accurate procedures could help to further reduce the risk of certain complications (eg, avoiding injury of vital structures, such as carotid arteries and clivus/brain stem), and that they might also allow for shorter operative times during the actual surgeries.

In this study, it is important to note that all actual osteotomies in the inferior area of the sphenoid sinus were more forward than the osteotomies of the preoperative surgical simulation. This is probably because surgeons tended to avoid placing the osteotomy at the inferior wall of the sphenoid sinus posteriorly, which might lead to fatal damage to the clivus and brainstem, as described above. Moreover, it must be taken into consideration that the exact point of the osteotomy was not usually visible, and even the navigation probe could not be reached appropriately because both the anatomic characteristics and existence of the tumor did not allow surgeons to use a straight corridor to reach the point from the surgical window of the planum sphenoidale; rather, it forced them to use angled chisels or other instruments. This knowledge of surgeons' tendency to place the osteotomy anteriorly is important for improving the accuracy of the osteotomy. Especially when the tumor extends

posteriorly, a more precise osteotomy would be necessary to prevent local recurrence in the posterior area.

Several authors have investigated the radicality of resection for patients with head and neck carcinoma treated with surgery and postoperative radiotherapy and concluded that free surgical margins (ranging from 3 mm to 5 mm) could achieve improved locoregional control and survival.^{37–39} Although all resection margins in the 7 present cases were negative, accurate osteotomy of the sphenoid bone is important to achieve en bloc resection with tumor-free margins (at least 3 mm) and prevent fatal damage to the clivus and brainstem. Cases with involvement of the anterior wall of the sphenoid sinus have been indicated for surgical resection in our hospital; however, the distance from the sphenoid ostium to the posterior wall of the sphenoid sinus was only 14 mm in an analysis of 224 CT images of the sphenoid sinus and surrounding structures from 122 Japanese adult patients.⁴⁰ The differences in values between the actual surgery and the preoperative surgical simulation at the inferior wall of the sphenoid sinus ranged from 0.8 mm to 8.3 mm (average of 3.5 mm); therefore, based on this study, the location in the actual surgery could be up to 8.3 mm anterior to the location in the preoperative surgical simulation. To perform accurate osteotomy of the inferior wall of the sphenoid sinus (which has a length of only 14 mm), surgeons should thus make the surgical resection lines in the posterior third of the sphenoid sinus.

There were limitations to the present study. It was a retrospective study, and it was performed at a single institution with a small number of patients. The results need to be corroborated in a larger study population. The simulation program is still for research purposes only and needs to be improved for general usage. However, it runs on commercially available laptop computers and the data can be transferred to surgical navigation systems. We consider that image-guided surgery will become increasingly popular in the near future, and we hope that the technology introduced in this article will help improve the surgical practice of skull base surgery.

In conclusion, we have found that virtual simulation of en bloc resection of advanced sinonasal sinus carcinoma by an anterolateral craniofacial approach provides a highly effective means of surgical planning, and it has become an indispensable means of continuous refinement of surgical strategies and surgical skills in our department. We believe that preoperative surgical simulation and postoperative feedback can contribute to training for surgeons and surgical support in patients undergoing skull base surgery for sinonasal carcinoma.

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