1	Benefits of maxillectomy with internal dissection of masticator space
2	by transmandibular approach in the surgical management of
3	malignant tumor of the upper gingiva and hard palate: a clinical
4	review of 10 cases
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20	Keywords: oral malignant tumor; maxillectomy; masticator space; transmandibular
21	approach.
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23	Short title: Maxillectomy by transmandibular approach
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Abstract. The purpose of our study was to review patients with tumors that extended 2728to the posterior portion of the upper gingiva and hard palate, and to evaluate the 29postoperative outcomes. Ten consecutive patients with tumors in the upper gingiva and hard palate, who underwent maxillectomy with internal dissection of the masticator 30 space by the transmandibular approach were retrospectively reviewed. Among the 10 31 32patients, the pathological diagnoses were 7 squamous cell carcinomas, adenoid cystic 33 carcinoma, malignant melanoma, and osteosarcoma, respectively. Loco-regional control was achieved in 8 of 9 patients (88.9%). Two patients had residual moderate trismus. 3435 Cosmetic issues were not noted in any patients. En bloc resection of the maxilla with 36 the internal portion of the masticator space and neck through the parapharyngeal space by the transmandibular approach is useful and satisfactory for the excision of a tumor 37 38with involvement of the posterior portion of the upper gingiva and hard palate.

40 Introduction

Oral cancer represents about 1-3% of all human cancers, and is the 6th most frequent 41 cancer in the world.^{1,2} Oral cancer continues to show a poor prognosis and remains a 42lethal disease for more than 50% of cases diagnosed annually.³ The upper gingiva and 43hard palate, subsites of the oral cavity, represents 10% of all oral cancers.⁴ Oral cancers 44 of the upper gingiva and hard palate often have similar clinical presentations and 45management because of their adjacent anatomies; however, the relative rarity of these 46 cancers compared to other primary sites has resulted in only small case series lacking 47survival or other outcome analyses.⁵⁻¹¹ Several reports have revealed that patients with a 48tumor that extended to the retromaxillary region, oropharyngeal soft palate or 49infratemporal fossa had poor survival outcomes.^{8,12,13} One of the reasons for the poor 5051prognosis of these cases is thought to be recurrence in the parapharyngeal space or the masticator space.^{8,12-14} Some lymph vessels of the maxilla are known to pass through 52the parapharyngeal space and flow out into the upper jugular lymph nodes. Therefore, 53we previously suggested the necessity of en bloc resection of the maxilla and neck 54through the parapharyngeal space by the transmandibular approach in patients with a 55tumor that extended to the retromaxillary region.^{12,13} Moreover, the masticator 56compartment of the infratemporal fossa is an obvious source of local recurrence in 57maxillary malignant tumors with posterior extension to the infratemporal fossa.^{8,14,15} 58Anatomically, the masticator space is delineated by the superficial layer of the deep 59cervical fascia. At the base of the mandible, the superficial layer of the deep cervical 60 fascia splits into two layers.^{16,17} The outer layer encloses the masseter muscle, extends 61 62over the zygomatic arch and attaches to the temporalis muscle and the lateral orbital 63 wall. The inner layer extends deep into the medial pterygoid muscle and attaches to the skull base medial to the foramen ovale (Fig. 1A). These two layers fuse along the 64

anterior and posterior borders of the mandibular ramus, enveloping the space. This 65 66 space includes the mandibular nerve and its branches, internal maxillary artery and its branches, adipose tissue and masticatory muscles (Fig. 1B). Oral cancer adjacent to the 67 masticator space can deeply invade the masticator space components simply because of 68 anatomic vicinity, and is staged as T4b.¹⁸ At this site, surgical resection by a 69 conventional approach is often difficult, resulting in unsatisfactory survival.¹⁸ In 70 particular, a tumor with involvement of the posterior portion of the upper gingiva and 71hard palate sometimes relapses at the infratemporal fossa in the internal portion of the 72masticator space.^{8,12,13,15} In such cases, some authors have proposed that the 73transmandibular approach was an effective technique for maxillectomy with internal 74dissection of the masticator space.^{12,13,14,19} 75

The purpose of our study was to review our patients who underwent a maxillectomy with internal dissection of the masticator space by the transmandibular approach and to evaluate the postoperative outcomes.

79

80 Patients and methods

81 Patients

From 2004 to 2012, 10 consecutive patients with involvement of the posterior portion of the upper gingiva and hard palate (Fig. 2), who underwent maxillectomy with internal dissection of the masticator space by the transmandibular approach were retrospectively reviewed (Table 1). Staging was performed using clinical data recorded at the time of initial assessment of each patient according to the TNM classification system of the American Joint Committee on Cancer (AJCC), sixth edition.

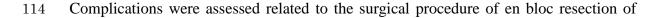
88 Surgical procedure of en bloc resection of the maxilla with the internal 89 portion of the masticator space and neck through the parapharyngeal

90 space by the transmandibular approach

The technique of en bloc resection of the maxilla and neck through the parapharyngeal 91 space has been previously described.^{12,13,14} The surgical technique for en bloc resection 92 starts with an incision in the lower lip and mandibular split after dissection of the neck 93 94(Fig. 3A and B), followed by resection of the medial pterygoid and temporalis muscles from the mandible (Fig. 3C). The inferior alveolar neurovascular bundle is cut off after 95ligating at the mandibular foramen (Fig. 3D), followed by resection of the lateral 96 97 pterygoid muscle from the condyle, and the mandibular ramus is pulled upwards and 98 backwards (Fig. 3E). The styloid process is cut off at the base, and the stylohyoid, styloglossus, and stylopharyngeal muscles are resected. The external carotid artery is 99 ligated and cut off beyond the lingual artery branch, and the dissection is extended 100 101 along the internal carotid artery into the posterior part of the parapharyngeal space while palpating the pharyngeal constrictor muscle. Maxillectomy is then performed in the 102103 usual manner. The upper cheek flap is raised over the maxilla through the upper 104gingivobuccal incision. This allows exposure to the orbital rim. After a standard 105osteotomy for maxillectomy, the soft tissue of the infratemporal fossa along with the 106 pterygoid muscles is left attached to the pterygoid plates (Fig. 3F). This is followed by 107 osteotomy in the upper part of the pterygoid process, and the maxilla and the internal portion of the masticator space and neck are resected en bloc through the pterygoid 108109 muscle and parapharyngeal space (Fig. 4). Finally, a large flap, usually a free radial 110forearm or rectus abdominis flap, is transplanted to the parapharyngeal and buccal space 111 to minimize cosmetic issues and difficulties with swallowing.

112

Assessment of complications



the maxilla and neck through the parapharyngeal space, including trismus, osteotomy site infection, cosmetic issues, difficulty with swallowing, or paresis of the inferior alveolar and lingual nerves. Trismus is defined using a gradual classification: mouth opening >30 mm indicates normal or light trismus, mouth opening between 15 and 30 mm indicates moderate trismus and mouth opening <15 mm indicates severe trismus.²⁰ These complications were evaluated 6 months postoperatively.

121

122 **Results**

123 **Patient characteristics**

There were 7 men and 3 women, with a median age 61.5 (range, 37 to 82). Among the 12410 patients with tumors, the pathological diagnoses were squamous cell carcinoma 125126(SCC; n = 7), adenoid cystic carcinoma (ACC; n = 1), malignant melanoma (n = 1), and 127osteosarcoma (n = 1), respectively. All patients underwent neck dissection at the same 128time as resection of the primary tumor. Patients presenting with a clinically positive metastatic cervical lymph node underwent modified radical neck dissection (mRND 129130 type II, n = 7), whereas patients with a clinically negative metastatic cervical lymph 131node underwent supraomohyoid neck dissection (SOHND, n = 1) or selective neck 132dissection (SND, n = 2). Eight patients were reconstructed with free vascularized flaps (radial forearm flap, n = 6; rectus abdominis flap, n = 1) or pectoralis major 133134myocutaneous flap, and all flaps survived without complications at the donor site.

135

136 Treatment outcome and complications

All tumors were removed en bloc with sufficient safety margins except for one adenoid
cystic carcinoma in the maxilla with positive histologic margins. Pathologic
examination of the surgical specimens revealed metastatic lymph nodes in 7 cases.

140 Postoperative adjuvant radiotherapy of 60 Gy was given in 2 patients.

Mean and median overall survival were 56.5 and 42 months, respectively. Seven patients (70%) are alive without evidence of disease. Local control was achieved in 8 of 9 patients (88.9%). One patient developed local recurrence 10 months postoperatively. However, this patient underwent salvage resection and is alive without evidence of disease. One patient who developed regional recurrence died of disease after 10 months, but this regional recurrence was contralateral neck recurrence.

Complications related to the procedure are presented in Table 2. Trismus was a 147148 common complaint, which improved with time and physiotherapy in all but 2 patients who had residual mouth opening between 15 and 30 mm (moderate trismus, +). 149Osteotomy-related complications such as metal miniplate exposure, infection, or 150151nonunion were not noted in any patients. Cosmetic issues because of the incision in the lower lip were not noted in any patients (Fig. 5). Two patients had a slight difficulty 152with swallowing. The inferior alveolar and lingual nerves were assessed. The inferior 153154alveolar nerve was sacrificed in 8 patients, and other patients had temporary paresis of the nerve. Hypoanesthesia of the lingual nerve was not noted in any patients with 155156preservation of the lingual nerve.

157

158 **Discussion**

The overall or absolute 5-year survival for the upper gingiva and hard palate ranges from 24% to 80% and is difficult to interpret, as they are often grouped to include other sites and other pathological entities, such as salivary gland tumors.^{5,8} In general, there is a trend toward a worse survival outcome in advanced disease stages, as observed in other series. Some authors have reported that patients with advanced primary tumors of the upper gingiva and hard palate exhibited high rates of regional failure.⁶⁻¹¹ In most

cases, successful salvage was not achieved. These retrospective studies recommended 165166 that elective neck dissection be considered for patients with SCC of the upper gingiva and hard palate.^{7,9-11} In the current cases, elective neck dissection was performed in 3 167 168 patients who were clinically as node-negative and were found to be pathologically N0. 169In this study, the necessity of elective neck dissection was not noted because of the 170small number of cases. Some authors reported that a few patients with involvement of 171the posterior portion of the upper gingiva and hard palate died of metastases to the lateral retropharyngeal node, despite successful control of local and regional 172tumors.^{12,13,21,22} There are two main routes for lymphatic vessels from the maxilla to the 173174neck. The first runs from the maxillary gingiva to the submandibular nodes through the buccal lymphatic vessels or buccal nodes. The second runs from the soft palate to the 175upper jugular nodes through the parapharyngeal or retropharyngeal space. The lateral 176177retropharyngeal nodes are located in the lateral area of the retropharyngeal space. 178Previously, the authors reported that carcinoma with involvement of the posterior portion of the upper gingiva and hard palate sometimes metastasized to the lateral 179retropharyngeal lymph node through the parapharyngeal or retropharyngeal space.^{12,13,22} 180 181 Therefore, we proposed that en bloc resections of the maxilla and cervical lymph nodes 182through the parapharyngeal space should be performed in patients with posteriorly invasive maxillary cancer accompanied by lymph node metastases in the upper jugular 183region.^{12,13} In our current cases, only one of 10 cases showed neck failure; however, this 184 patient died of distant metastasis to the lung because of contralateral neck recurrence. 185We considered that the improvement of regional control in patients with posteriorly 186 invasive maxillary cancer benefited from en bloc resection of the maxilla and cervical 187 188 lymph nodes through the parapharyngeal space.

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Some investigators reported that there seemed to be a worse prognosis when the

infratemporal fossa was involved compared with when there was no infratemporal fossa 190 involvement.^{8,12,13,15} McMahon et al.¹⁵ reported that the masticator compartment of the 191192infratemporal fossa was an obvious source of recurrence. The contents of this space are 193 mainly the mandibular nerve and its branches, internal maxillary artery and its branches, adipose tissue, and masticatory muscles such as the medial and lateral pterygoids, 194 195masseter, and temporalis. The masticator pace is infiltrated by the direct spread of cancer from the maxillary alveolus and palate posteriorly.^{8,15} The trismus that 196 commonly accompanies masticator space involvement often makes physical 197198 examination difficult, so CT and MR imaging are important for characterizing and mapping of the pathology.^{17,23,24} In our current cases, tumor involvement of the 199 masticator space was assessed by both CT and MRI. In general, the pattern of local 200201recurrence is largely predictable and explained by anatomical considerations. 202Specifically, the posterior and superior portions of the upper gingiva and hard palate, which are more difficult to access, are the most common portions of relapse.¹⁵ 203Maxillectomy is usually performed through a Weber-Fergusson incision. With this 204205approach, however, it is difficult to access the pterygoid process, masticator space including pterygoid muscles, or infratemporal fossa extensively.¹⁴⁻¹⁵ Tiwari²⁵Tiwari²⁴ 206 207 reported the use of a transmandibular approach for total maxillectomy for en bloc 208resection of the pterygoid process with infratemporal muscles in addition to the 209 maxillectomy specimen. We have adopted this surgical approach for patients with involvement of the posterior portion of the upper gingiva and hard palate.^{12,13} In this 210211series, local recurrence was not observed in any of the 10 cases.

Hence, we considered that en bloc resection of the maxilla and neck using the mandibular swing approach in tumors extending from the posterior portion of the upper gingiva and hard palate to the masticator space could be useful and satisfactory for

215loco-regional control. On the other hand, trismus is the most common complication of 216the procedure. We previously reported that trismus became minimal by resection of the 217pterygoid muscles at the same time as parapharyngeal dissection using the mandibular swing approach. Chatni et al.¹⁴ reported that postoperative trismus was due to 218periarticular fibrosis at the temporomandibular joint, and this complication could be 219minimized to a certain extent by performing a coronoidectomy. In our series, however, 3 220221patients had residual moderate trismus, one patient was reconstructed with a pectoralis major myocutaneous flap, and other 2 patients did not undergo reconstruction. 222223Therefore, we concluded that reconstruction using free vascularized flaps such as a radial forearm flap and rectus abdominis flap should be performed whenever possible. 224Nair et al.¹⁹ reported that postoperative trismus was associated with the postoperative 225226radiotherapy. However, our 3 patients with residual moderate trismus did not received 227 postoperative radiotherapy. In our series, we could not clarify the effect of postoperative 228radiotherapy on trismus. Naturally, the complication of trismus should be managed by 229aggressive postoperative physiotherapy.

Although the Weber-Fergusson incision has been the classic approach for surgical 230management of maxillary tumors, this incision leads to poor cosmesis due to ectropion 231232and upper lip scarring. For en bloc resection of the maxilla with the internal portion of the masticator space and neck through the parapharyngeal space, the mandibulotomy is 233crucial procedure. The lower lip incision used for a mandibulotomy formed the upper 234part of the Macfee incision without additional incisions.¹⁶ In the lip split and 235mandibulotomy, moreover, effective methods that improve functional and aesthetic 236outcomes have been reported.^{16,2619,25} In our series, cosmetic issues because of the 237238incision in the lower lip were not noted in any patients. We therefore concluded that lip 239split mandibulotomy for access to the maxilla without additional upper lip incision 240 could result in good cosmesis.

In conclusion, en bloc resection of the maxilla with the internal portion of the masticator space and neck through the parapharyngeal space by the transmandibular approach is useful and satisfactory for excision of a tumor with involvement of the posterior portion of the upper gingiva and hard palate. This approach allowed good surgical access to the masticator space or parapharyngeal space, and resulted in the improvement of loco-regional control.

247

248 **Competing interests**

None declared.

250

- 251 Funding
- 252 None.
- 253

254 Ethics approval

255 This study was approved by the ethics committees of the Nagasaki University Hospital.

256

257 **Patient consent**

258 Consent obtained.

259

260 Statement to confirm

261 All authors have viewed and agreed to the submission

263 Figure legends

264

265Fig. 1. Anatomy of the masticator space. (A) Coronal line diagram shows the superficial 266 layer of the deep cervical fascia splitting into two layers at the base of the mandible. The 267outer layer encloses the masseter muscle, extends over the zygomatic arch and attaches 268to the temporalis muscle and the lateral orbital wall (1). The inner layer extends deep to 269the medial pterygoid muscle and attaches to the skull base medial to the foramen ovale 270(2). (B) Axial line diagram shows the outer and inner layers fusing along the anterior 271and posterior borders of the mandibular ramus and enveloping the space. The masticator 272space includes the mandibular nerve and its branches, internal maxillary artery and its 273branches, adipose tissue and masticatory muscles. Note the close relation of the 274masticator space with the prestyloid parapharyngeal space (black dots) medially. MP, 275medial pterygoid muscle; M, masseter muscle; LP, lateral pterygoid muscle; T, 276temporalis muscle; FO, foramen ovale, P, parotid gland; ECAR, external carotid artery; 277ICAR, internal carotid artery; JUG, jugular vein; STY, styloid process.

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Fig. 2. Computed tomography shows a tumor extending to the posterior portion of the upper gingiva and hard palate, pterygoid plates, and masticator space.

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Fig. 3. Intraoperative photographs. (A) Lower lip split and mandibulotomy after dissection of the neck. Site of mandibulotomy anterior to the mental foramen. (B) Subperiosteal dissection of the lingual aspect of the mandible. (C) The mandible was swung laterally, offering wide exposure of palatal, labial, and infratemporal surfaces of the maxilla. The medial pteryngoid muscle was detached from the mandible. (D) The mandible was swung further, cutting the inferior alveolar neurovascular bundle at the

288	mandibular foramen (hemostatic forceps pointing). (E) After resection of the lateral
289	pterygoid muscle from the condyle, the mandibular ramus was pulled upwards and
290	backwards. (F) Further mandible swing gave good exposure of the internal portion of
291	the masticator space, and was followed by osteotomy of the upper part of the pterygoid
292	process (white arrow).

Fig. 4. Final surgical specimen shows en bloc resection of the maxilla with the internal portion of the masticator space and neck through the parapharyngeal space.

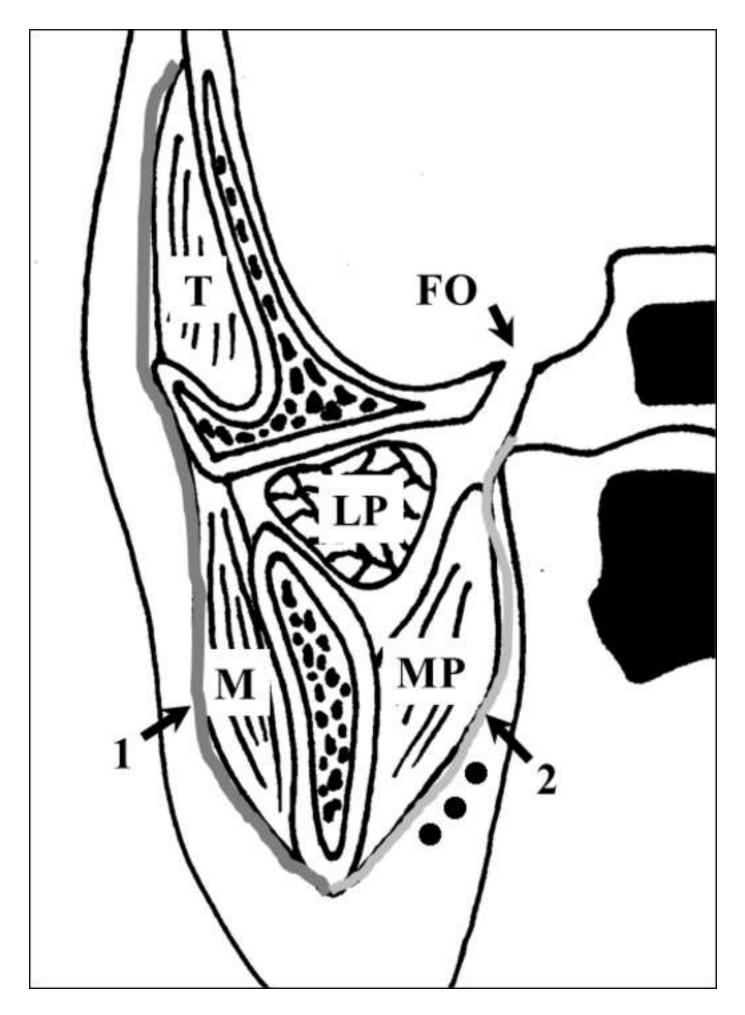
Fig. 5. Postoperative appearance of a patient showing good cosmesis.

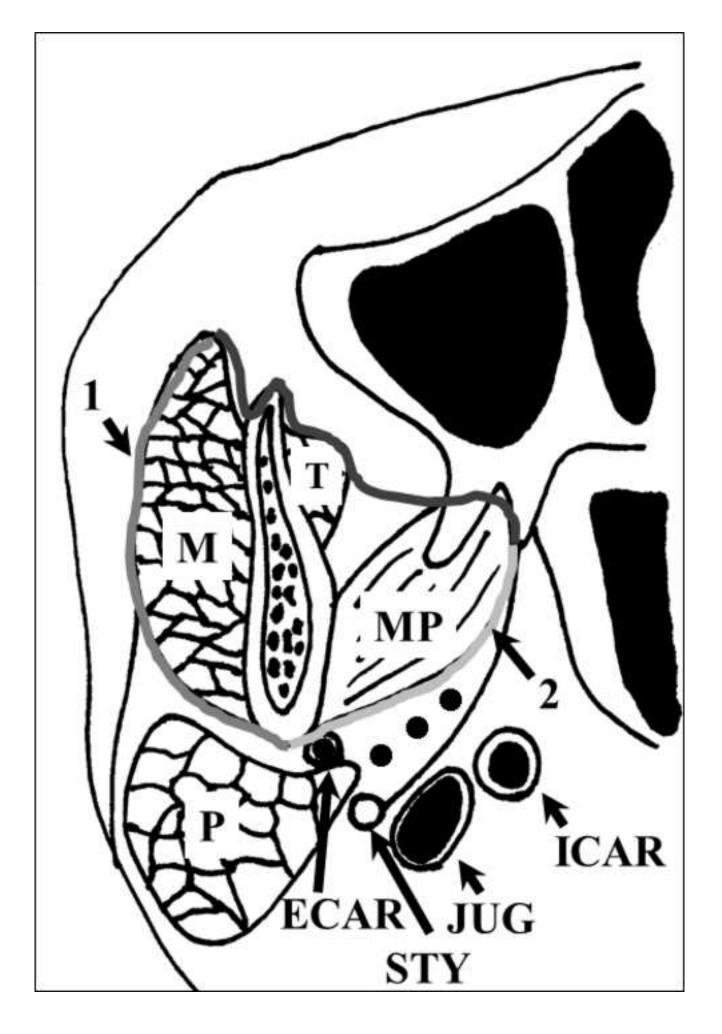
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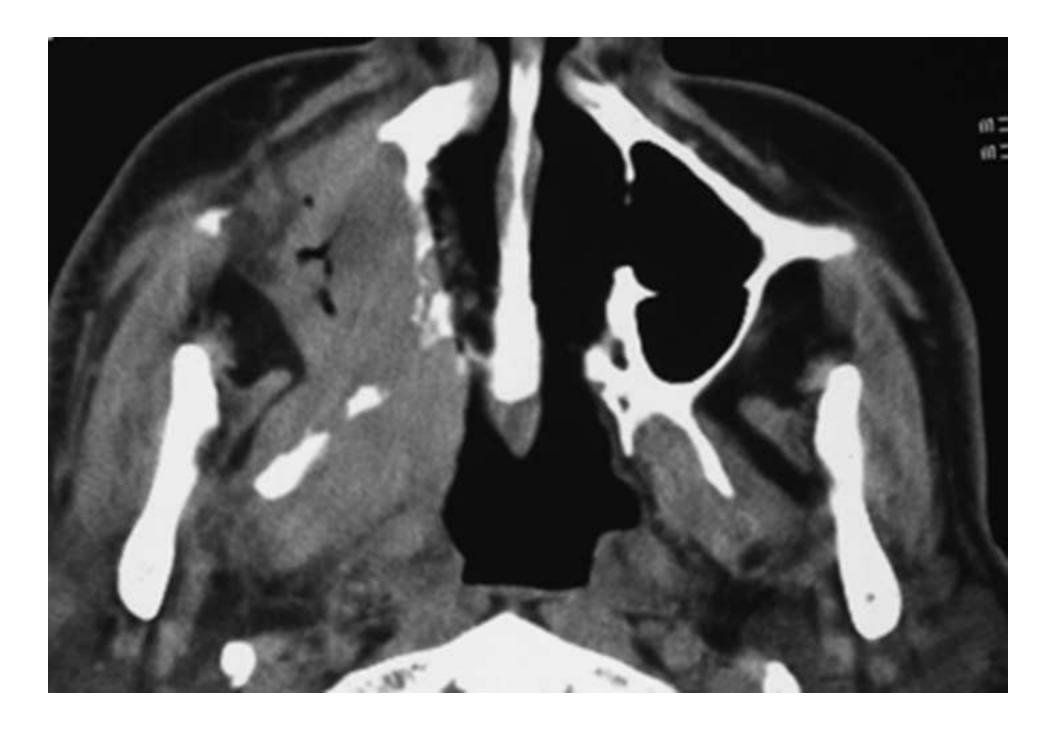
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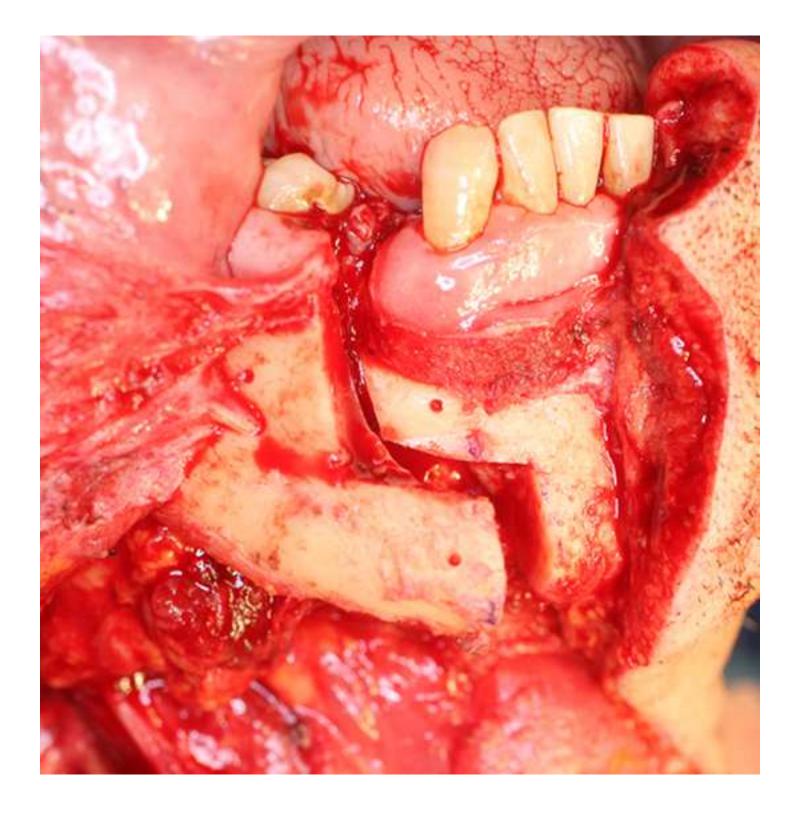
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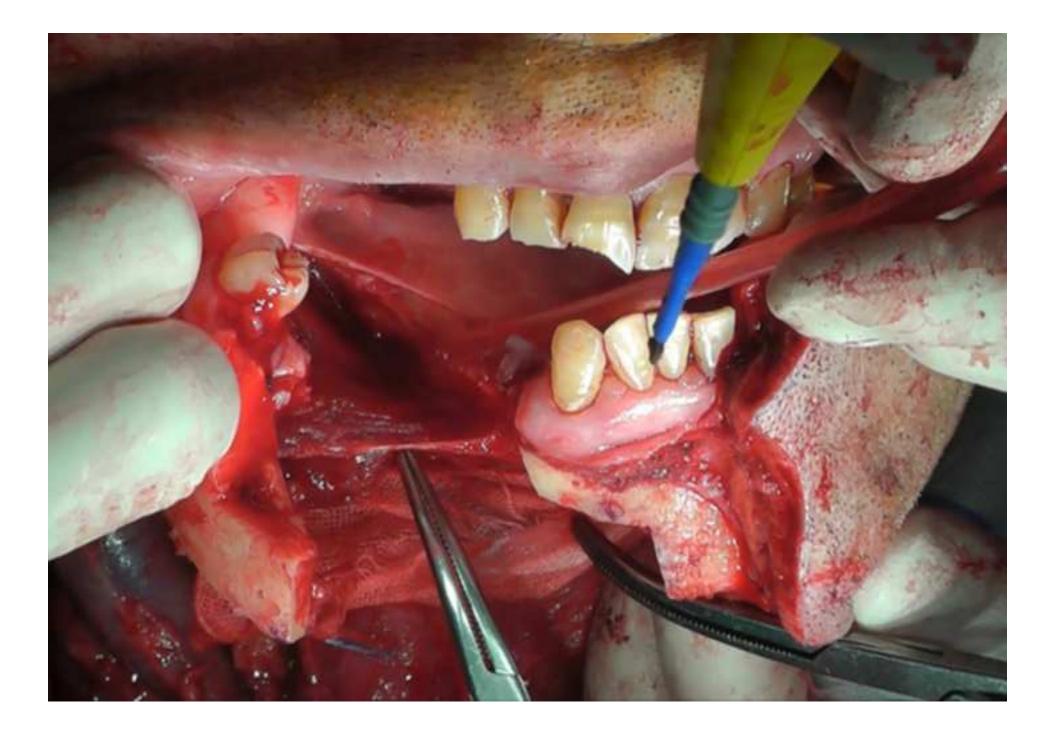
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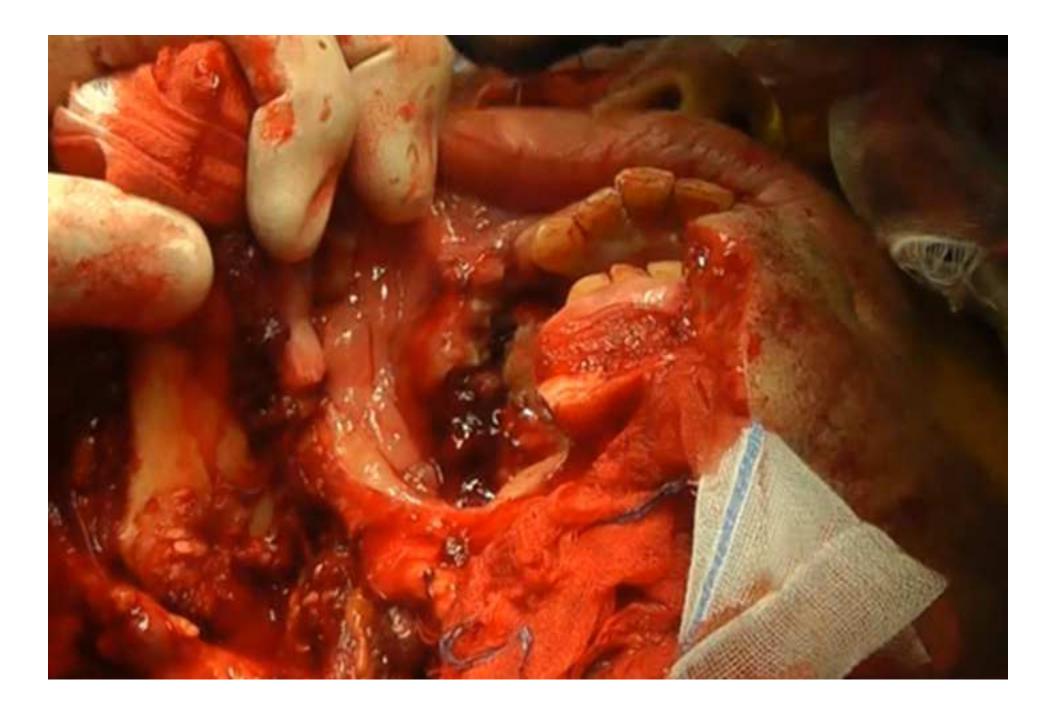


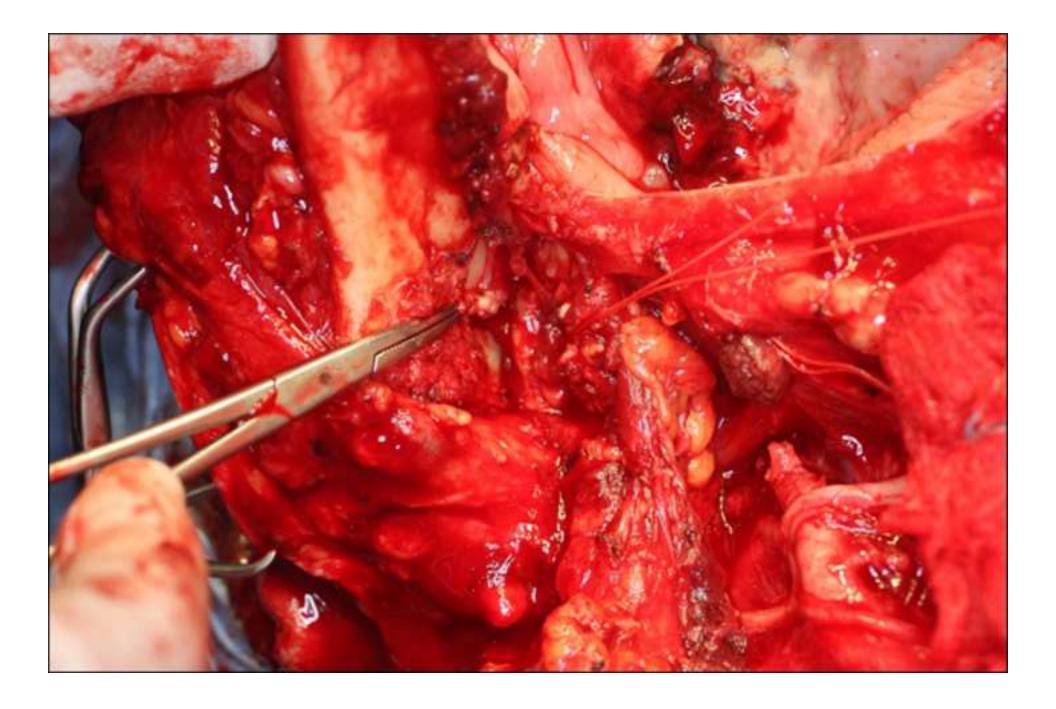


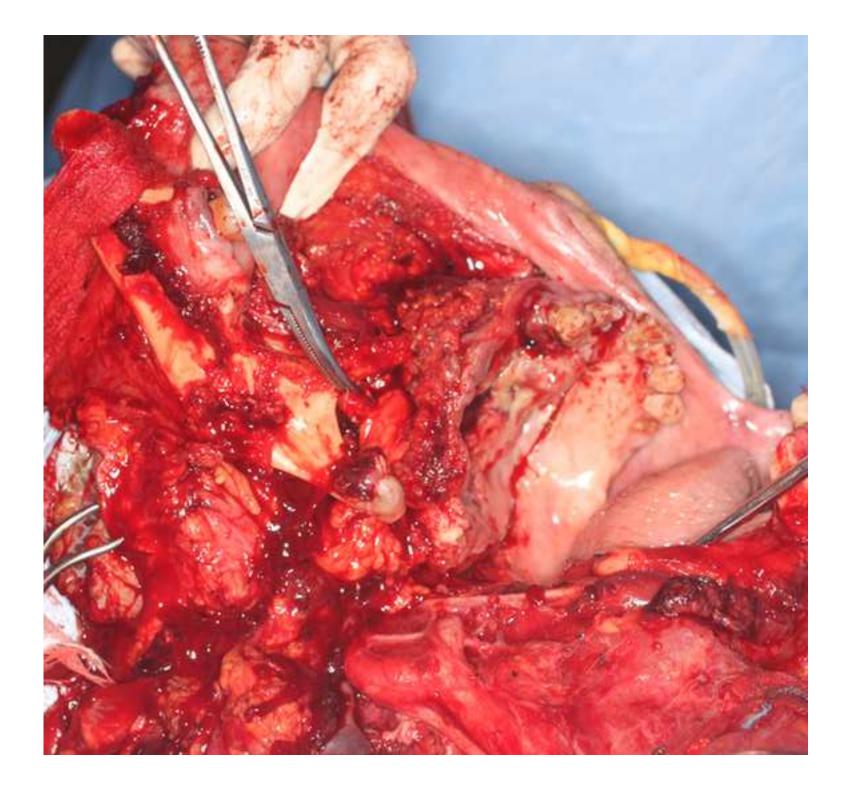


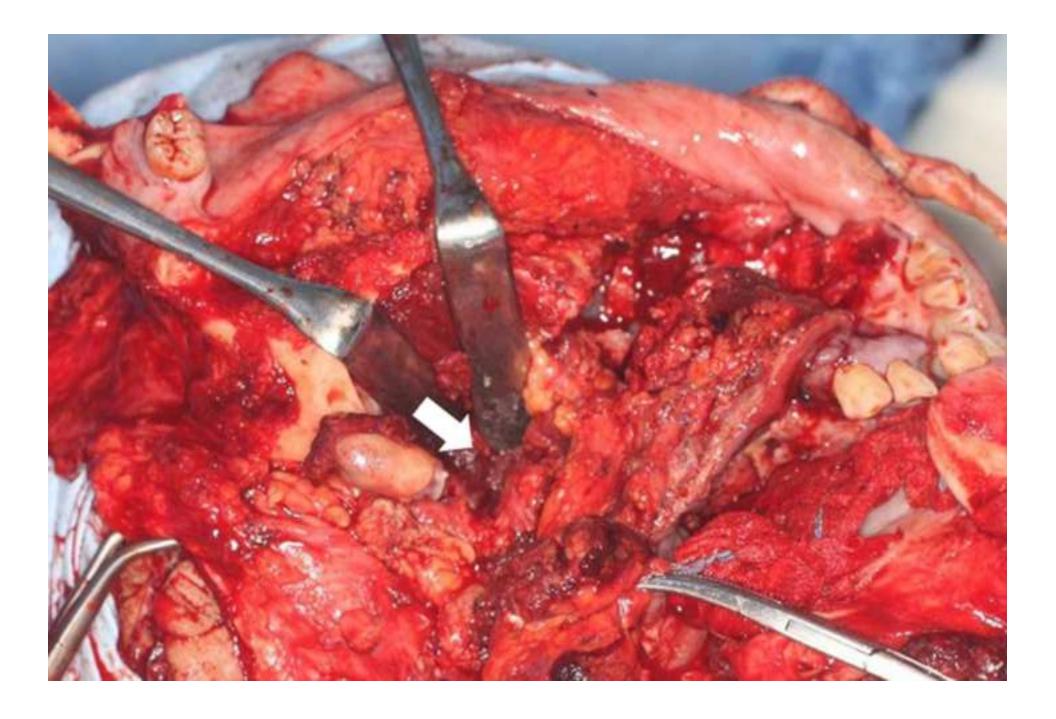


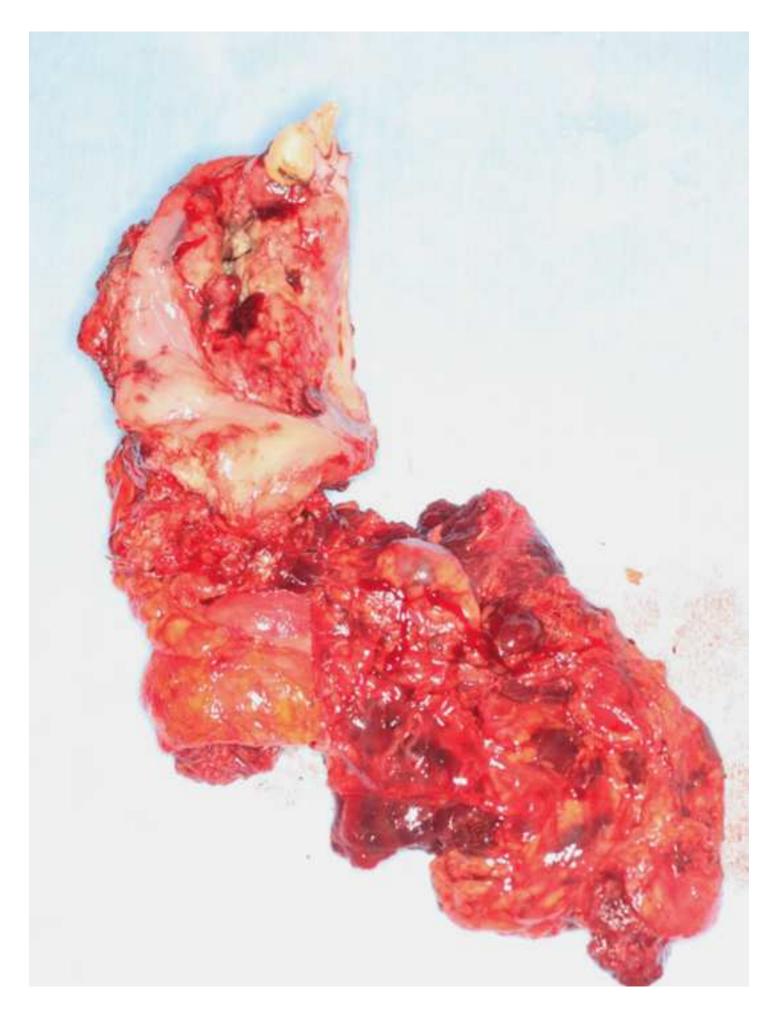












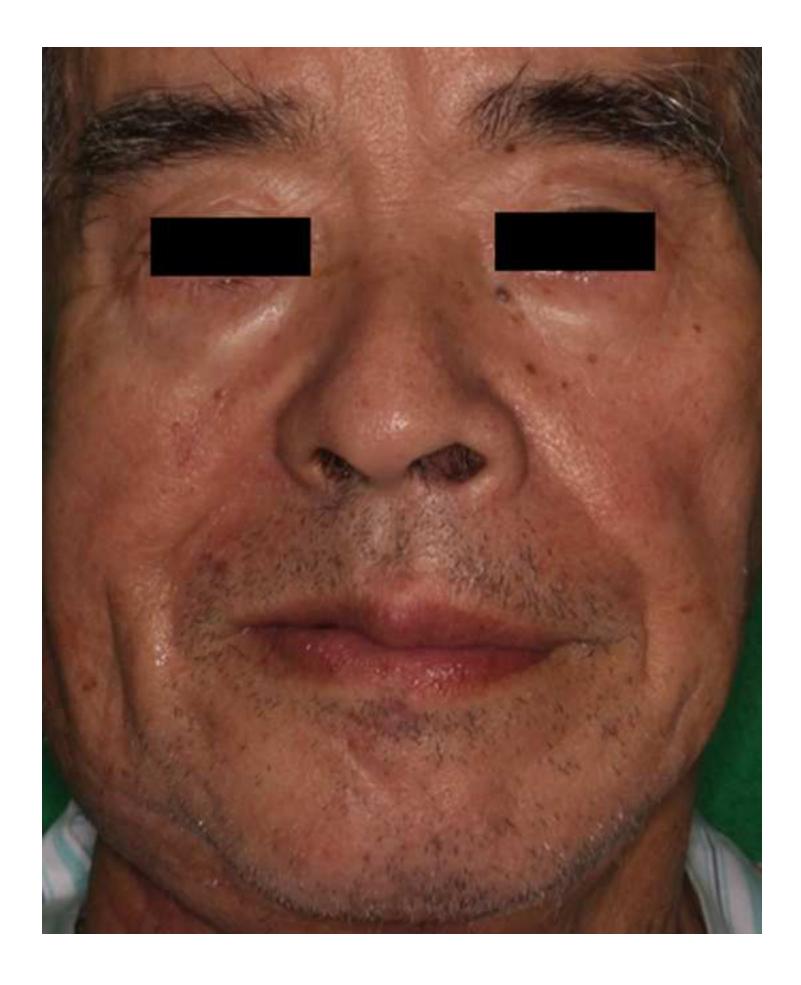


Table 1. Demographics and treatment summaries of 10 patients undergoing en bloc resection of the maxilla with the internal portion of masticator space and neck through the pararharyngeal space by transmandibular approach

Patient	Age /Gender	Site	Pathological diagnosis (TN stage)	Procedure ^a	Reconstruction	Survival
1	37/F	Hard palate	Adenoid cystic carcinoma (T4bN0)	Maxillectomy + SND	Radial forearm free flap	Alive 10 years with lung metastasis
2	52/M	Maxillary gingiva	Squamous cell carcinoma (T4bN1)	Maxillectomy + mRND	No reconstruction	Alive without evidence of disease after 9.5 years
3	52/M	Maxillary gingiva	Squamous cell carcinoma (T4bN1)	Maxillectomy + mRND	Radial forearm free flap	Alive without evidence of disease after 8.5 years
4	72/M	Maxillary gingiva	Squamous cell carcinoma (T4bN2c)	Maxillectomy + bilateral mRND	Radial forearm free flap	Died of pneumonia after 3 months
5	76/F	Maxillary gingiva	Squamous cell carcinoma (T4bN2b)	Maxillectomy + mRND→PORT	Radial forearm free flap	Alive without evidence of disease after 6.5 years
6	82/M	Maxillary gingiva	Squamous cell carcinoma (T4bN2b)	Maxillectomy + mRND→PORT	Radial forearm free flap	Alive without evidence of disease after 4.5 years
7	63/M	Hard palate	Malignant melanoma (T4bN1)	Maxillectomy + mRND	Rectus abdominis flap	Died of neck recurrence after 10 months
8	77/M	Hard palate	Osteosarcoma (T4bN0)	Maxillectomy + SND	No reconstruction	Alive without evidence of disease after 2.5 years
9	78/M	Maxillary gingiva	Squamous cell carcinoma (T4bN1)	Maxillectomy + mRND	Pectoralis major myocutaneous flap	Alive without evidence of disease after 2.5 years
10	78/F	Maxillary gingiva	Squamous cell carcinoma (T4bN0)	Maxillectomy + SOHND	Radial forearm free flap	Alive without evidence of disease after 2 years

a mRND, modified radical neck dissection; SOHND, supraomohyoid neck dissection; SND, selective neck dissection; PORT, postoperative radiotherapy.

Table 2. Complications related to the procedure in 10 patients undergoing en bloc resection of the maxilla with the internal portion of masticator space and neck through the parapharyngeal space by transmandibular approach

Patient	nt Trismus ^a	Osteotomy-related	Osteotomy-related Cosmetic Difficulty with		Inferior alveolar nerve	Lingual name
Fatient		complication	issues	swallowing	interior arveolar herve	Lingual nerve
1	_	No	No	No	Sacrificed	Normal
2	+	No	No	No	Temporary paresis	Normal
3	-	No	No	No	Sacrificed	Normal
4	Unknown	Unknown	No	Unknown	Sacrificed	Normal
5	-	No	No	No	Sacrificed	Normal
6	-	No	No	No	Sacrificed	Normal
7	-	No	No	No	Sacrificed	Sacrificed
8	+	No	No	Slight	Sacrificed	Normal
9	+	No	No	Slight	Sacrificed	Normal
10	_	No	No	No	Temporary paresis	Normal

a –, mouth opening >30 mm indicates normal or light trismus; +, mouth opening between 15 and 30 mm indicates moderate trismus; ++, mouth opening <15 mm indicates severe trismus.