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METHODOLOGY

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Compartmental surgery for squamous cell carcinoma of the buccal mucosa: description of a new surgical technique

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Abstract

Background Oral squamous cell carcinoma (OSCC) is the sixth most common cancer globally. Patient survival varies depending on tumour stage and oral cavity subsites. Buccal mucosa neoplasia is rare and burdened by worse prognosis than other oral subsites, showing a high rate of loco-regional relapses within six months after treatment. According to NCCN guidelines, the gold standard treatment is radical surgery. In the oral cavity, the buccal mucosa subsite lacks anatomical barriers opposing neoplastic growth. At this level, the tumour cells could hypothetically spread along the fibres of the platysma muscle or the lymphatic networks of the peri-facial vessels without encountering any resistance. Due to the aggressive locoregional spread, radical surgery is mandatory to improve patient survival.

Methods This technical note describes the cheek compartmental surgical approach step by step. For intermediate-advanced stage cancer, the surgery should include the resection of the tumour with adequate free margins, the dissection of neck lymph nodes and the lymphatic network with the structures between the tumour (T) and the neck (N), the so-called "T-N tract". The buccal mucosa compartment may be defined as a three-dimensional space between the oral cavity mucosa, the vessel plane, and the lymph nodes of the neck (levels I-IV). These structures, connected by the platysma muscle and the facial vessels, may be considered the T-N tract of the mucosal cheek compartment.

Results By removing all the possible pathways of tumour spread via compartmental surgery (*en-bloc* resection of the tumour with T-N tract and lymphatic network and lymph nodes) for buccal mucosa cancers, one could provide better locoregional control of disease in intermediate-advanced stages.

Conclusion This surgical technique may enable a more accurate control of the surgical margins, especially the deep margins.

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Keywords Buccal mucosa squamous cell carcinoma, Buccal mucosa, Mucosal cheek, Compartmental surgery, Oral squamous cell carcinoma

Background

Oral squamous cell carcinoma (OSCC) is the most frequent head and neck carcinoma [1, 2], with the tongue and the floor of the mouth being the most commonly-involved subsites. Buccal mucosa squamous cell carcinoma (BMSCC) is rare in western countries, accounting for approximately 5–10% of all oral cancers in North America and Europe [3–6].

Oral cavity subsite cancers show different survival outcomes and prognoses due to different biological behaviors. BMSCC is a highly aggressive form of oral cavity cancer, with a high tendency to recur locoregionally and an overall survival of 30–70% reported at 5 years [4]. Surgery represents the gold standard treatment according to the NCCN guidelines [7]. Surgery must be performed with radical intent, through adequate resection margins (R0) and the removal of the whole spreading cancer in order to prevent a locoregional recurrence. However, the definition of a wholly-removed tumour remains a matter of debate, including in BMSCC surgery [8]. Compared to other oral cancers, the buccal mucosa carcinomas seem the most challenging to remove entirely [9–11]. In the buccal mucosa of the cheek, tumour spread could occur via lymphatic networks, along the fibers of the platysma muscle or the facial vessels or also deep in the masticatory space; no anatomical barriers exist to contain the neoplastic cell growth, so that spread or infiltration of the cancer could occur with greater ease when compared to other oral anatomical regions. Standard surgery is generally performed by means of transoral and cervical approaches without removing all the structures contained in the space between the tumour (T) and the neck (N). In our hypothesis, this characteristic may be responsible for the high rates of locoregional relapses. Recently, the authors discussed the compartmental approach in advanced tongue cancer, to ensure the *en-bloc* resection of the tumour together with the neck lymphatic networks and related lymph nodes and T-N tract [12]. Borrowing this compartmental concept, in this detailed illustrated report we describe our surgical proposal, which involves the removal of the cheek tumour *en-bloc* with the lymph nodes of the neck, thus including the structures that connect them: the platysma muscle and the facial vessels (cheek T-N tract), a possible route of diffusion and the localization of cancer cells.

We provide a step-by-step description of the compartmental surgical treatment of a squamous cell carcinoma of the mucosal cheek in continuity with neck dissection, ensuring the removal of all the structures located in the T-N tract that play a possible role in tumour spread.

Methods

Patient's summary

A 71-year-old male with a progressively enlarging left-sided neck adenopathy (levels I-II) was referred to our Department of Otorhinolaryngology and Head and Neck Surgery of the European Institute of Oncology, IRCCS, Milan. At the ENT visit, there was a 10 mm, ulcerated lesion of the left buccal mucosa and a 30 mm neck lymph node on the left (level 1b). We performed a core biopsy under local anesthesia and the histopathological report identified squamous cell carcinoma. Fluorodeoxyglucose-positron emission tomography (FDG-PET) and the head and neck computer tomography (CT) scan revealed a superficial lesion of the left buccal mucosa (maximum diameter: 10 mm, depth of infiltration (DOI): 6 mm), with two voluminous lymph nodes at the Ib level (maximum diameter: 33 × 23 mm and 24 × 17 mm); there were no distant metastases (Fig. 1). The final clinical stage was cT2 N2b M0 [13].

The patient underwent a tumour resection with a compartmental approach (BMCS) plus left comprehensive lateral neck dissection (I, IIa, IIb, III and IV levels) [13]. A Bichat flap was used to reconstruct the surgical defect in the oral cavity [14]. The final histopathological examination confirmed a G2 squamous cell carcinoma (maximum tumour diameter: 9 mm) with a depth of infiltration (DOI) of 8.05 mm. All the resection margins were disease-free (R0). There were 13 lymph nodes in the neck dissection, of which two were metastatic with extracapsular extension (ECE): one was in the Ib level with a diameter of 30 mm and the second one in the T-N tract with a diameter of 36 mm (Fig. 2). The final tumour stage was pT2 N3b cM0, G2 [13]. A nasogastric feeding tube (NGT) was placed intraoperatively, and subsequently removed upon initiation of oral feedings (six days after surgery). There were no major complications during the postoperative period, and the patient resumed oral feeding on the sixth postoperative day. We noted a mild impairment of the marginalis mandibulae nerve due to an iatrogenic trauma that occurred during the dissection of the voluminous adenopathy of the Ib neck level. The patient underwent adjuvant radiotherapy in accordance with the disease stage and biological risk factors (DOI, ECE). Chemotherapy was proposed but excluded due to patient's age and comorbidities. After twenty-eight months, the patient is still alive with no evidence of disease (NED).

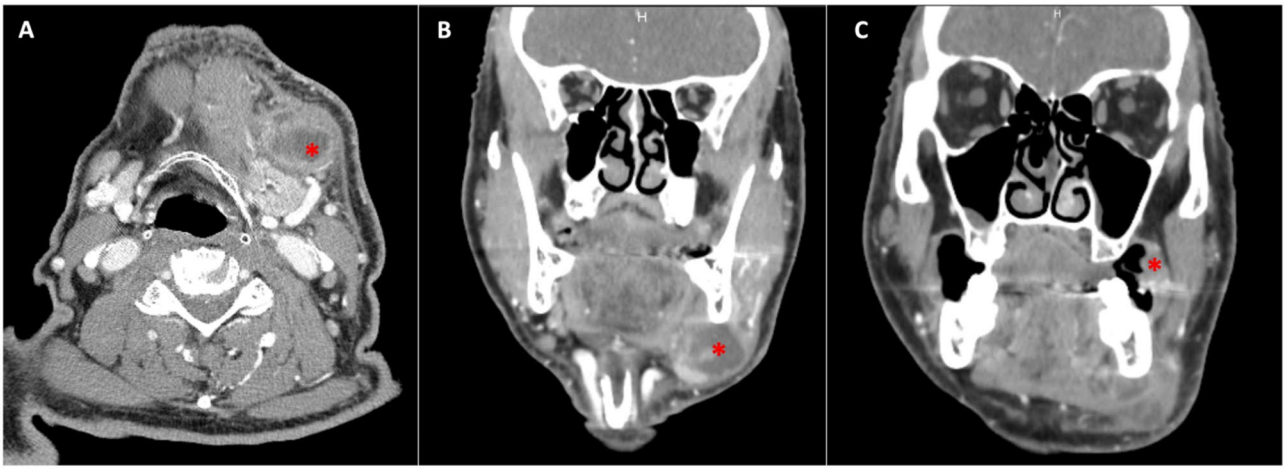

Fig. 1 Pre-operative contrast-enhanced CT scan. **A**) Axial CT image with the adenopathy at the Ib level (*); **B**) Coronal CT image with the adenopathy at the Ib level (*); **C**) Coronal CT image with the superficial lesion of the left buccal mucosa (*)

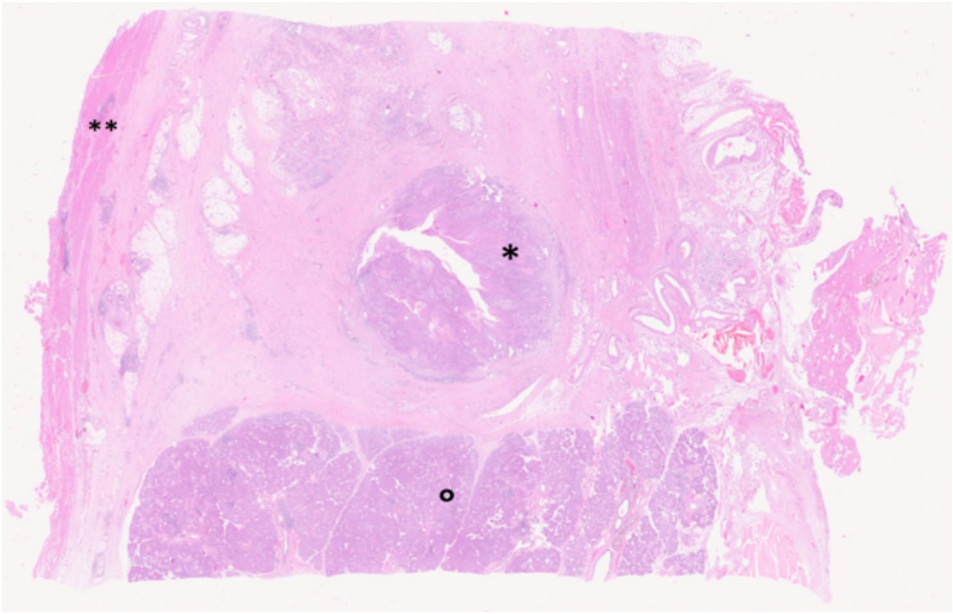

Fig. 2 The formalin-fixed paraffin-embedded (FFPE) block (stained with hematoxylin and eosin) of the T-N tract shows the presence of one pathological lymph node (*) close to the submandibular salivary gland (°) and the muscles fibers of platysma (**)

Compartmental anatomy and T-N tract of the buccal mucosa (cheek)

Anatomically, the cheek comprises six layers: the mucosa, the submucosa, the buccinator muscle, the vessels plane with the lymph nodes and lymphatic pathways, the subcutis and the skin (Fig. 3) [15]. The lymphatic system of the buccal mucosa drains primarily into the submandibular space by collectors that pierce through the buccinator muscle toward the facial artery and vein [16–18]. The buccal mucosa compartment could be considered as a three-dimensional space: medially, it is composed of the buccal mucosa, laterally it consists of the vessels plane with buccal lymph nodes and the buccinator muscle, superiorly it comprises Stenons'duct and inferiorly it comprises the cranial fibres of the platysma muscle. The T-N tract is the set of structures between the tumour (T) and the lymph nodes of the neck (N) and composed of the platysma muscle, the facial vessels and the subplatysmal lymphatic network. The tumour spread pathways in the T-N tract are the vessels and lymphatic plane connected by the cranial portion of platysma muscle fibres to the cervical lymph nodes. To investigate the role of the platysma muscle in tumour spread as a component of the T-N tract, we performed immunohistochemical analysis with D2-40 antibodies (podoplanin), which specifically detect lymphatic endothelial vessels in formalin-fixed

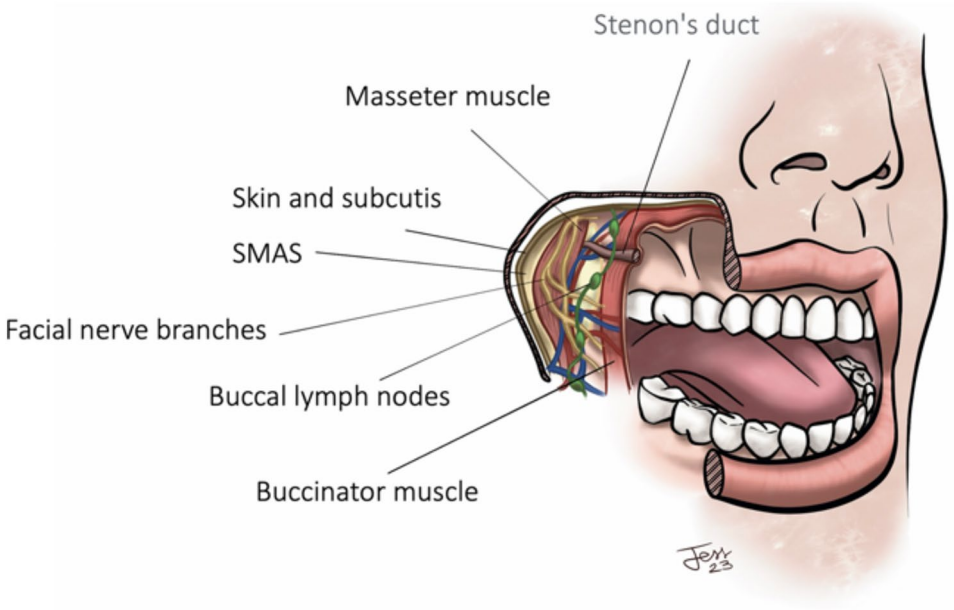

Fig. 3 The layers of the compartmental anatomy of the buccal mucosa

specimens [19]. As shown in Fig. 4, lymphatic vessels were found in the platysma muscle. The presence of lymphatic vessels in the platysma muscle according to our hypothesis could play a fundamental role in the tumour spread pathways represented by the T-N tract of the buccal mucosa.

Oncological indications

Compartmental buccal mucosa surgery can be proposed for all the cases of squamous cell carcinoma of the mucosal cheek: (1) if clinical N+, any T; (2) if clinical T2 with estimated radiological DOI > 5 mm, any N [13].

Due to the capability to ensure clear and safe margins, this approach could be recommended especially in case of infra-notch T4b buccal cancers (involvement of the masseter muscle, the ascending ramus of the mandible as well the lower portion of the medial pterygoid) [20]. This stage of disease is suitable for surgical treatment as reported by a Mair et al. [20].

Operative technique: buccal mucosa compartmental surgery (BMCS)

The cervical phase

A supra-platysmal flap is harvested removing the superior and cranial parts of the platysma muscle (Fig. 5A). In detail, the upper skin flap was harvested at the level of the posterior third of the platysma (also called pars modiolaris), including the third lateral part of the pars labialis, which crosses the body of the mandible and then continues under the depressor anguli oris (DAO) muscle to insert directly into the dermis of the lower lip and the orbicularis oris (OOr) muscle [21, 22].

Then, depending on the lymph node status (evidence of muscle and/or vascular infiltration) a neck dissection is performed from level I to IV. In the case of this patient, a comprehensive neck dissection (levels I-IV) was performed (Fig. 5B) [7, 13]. Once levels II, III and IV were completed, the management of level Ib required meticulous dissection to prevent injury to the marginalis mandibulae nerve (MMN). The incision of the deep cervical fascia covering the submandibular gland was made 2 cm below the border of the mandibular corpus. The MMN is found and carefully protected during level Ib dissection, with the surrounding soft tissue removing any lymph nodes in this area.

As reported by Hwang et al., the mandibular branch of the facial nerve was consistently found on the posterior side of the platysma [23]. The lowest branch of the MMN, which is usually the main branch, passes below the gonial angle and slowly passes from deep within the deep fascia to more superficial. Where the MMN crosses the margin of the mandible, it lies superficial within the deep fascia, just below the pars labialis of the platysma, and passes immediately superficial to the facial vein and artery. It passes immediately posterior to the mandibular ligament (within 2 mm) to continue its course cranial to this ligament, sending terminal branches to the platysma, DLI, depressor anguli oris (DAO) and mentalis. Once level Ib is completed, the MMN is followed retrogradely to the main inferior branch of the facial nerve, which is covered by the tail of the superficial lobe of the parotid gland. The meticulous retrograde dissection of the MMN from level Ib required incision of the deep fascia under the platysma

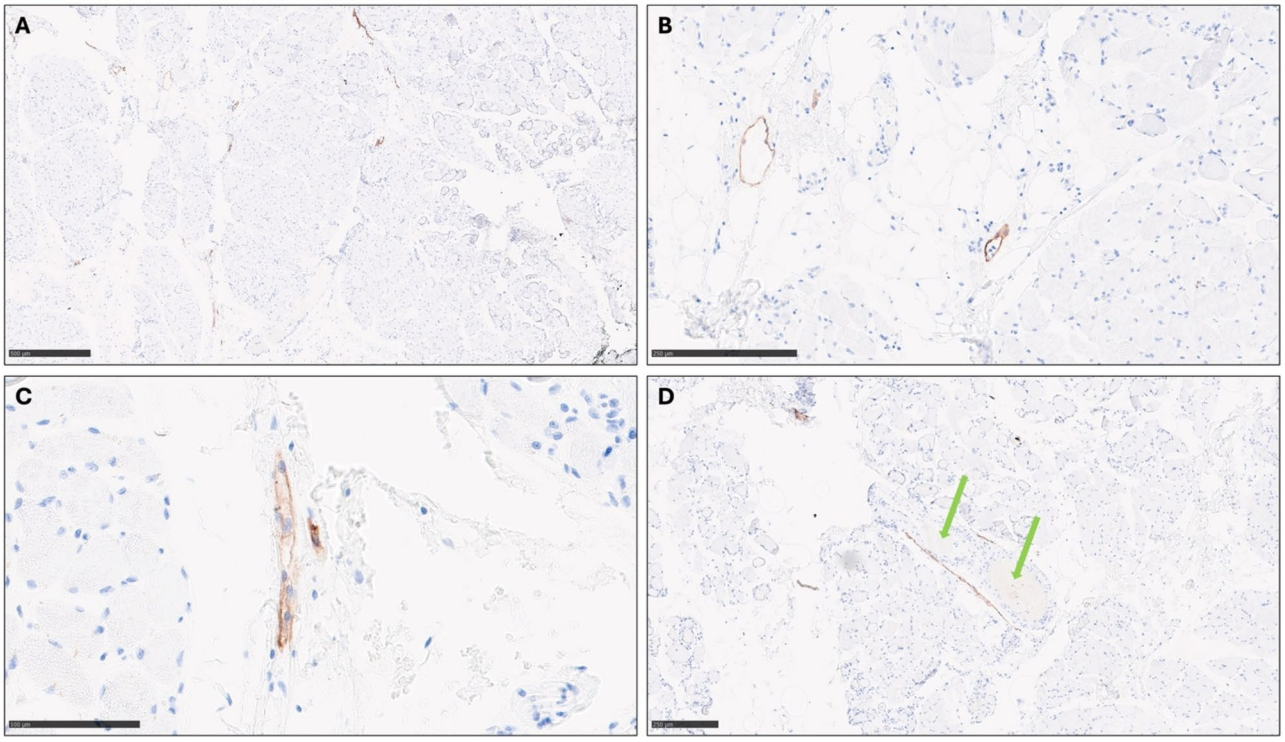

Fig. 4 Microscopic view of the platysma muscle. The immunohistochemical staining enhances the lymphatic vessels (visualized as brown colored cells). **A**) Formalin-fixed tissue stained with podoplanin (D2-40 antibodies) permits the identification of the lymphatic vessels in the muscle (500 micron scale bar); **B**) Formalin-fixed tissue stained with podoplanin (D2-40 antibodies), using a 250 micron scale bar – perpendicular view; **C**) Formalin-fixed tissue stained with podoplanin (D2-40 antibodies) using a 100 micron scale bar – longitudinal view; **D**) Formalin-fixed tissue stained with podoplanin (D2-40 antibodies) enhances a blood vessel (green arrows) surrounded by lymphatic channels (brown) (250 micron scale bar)

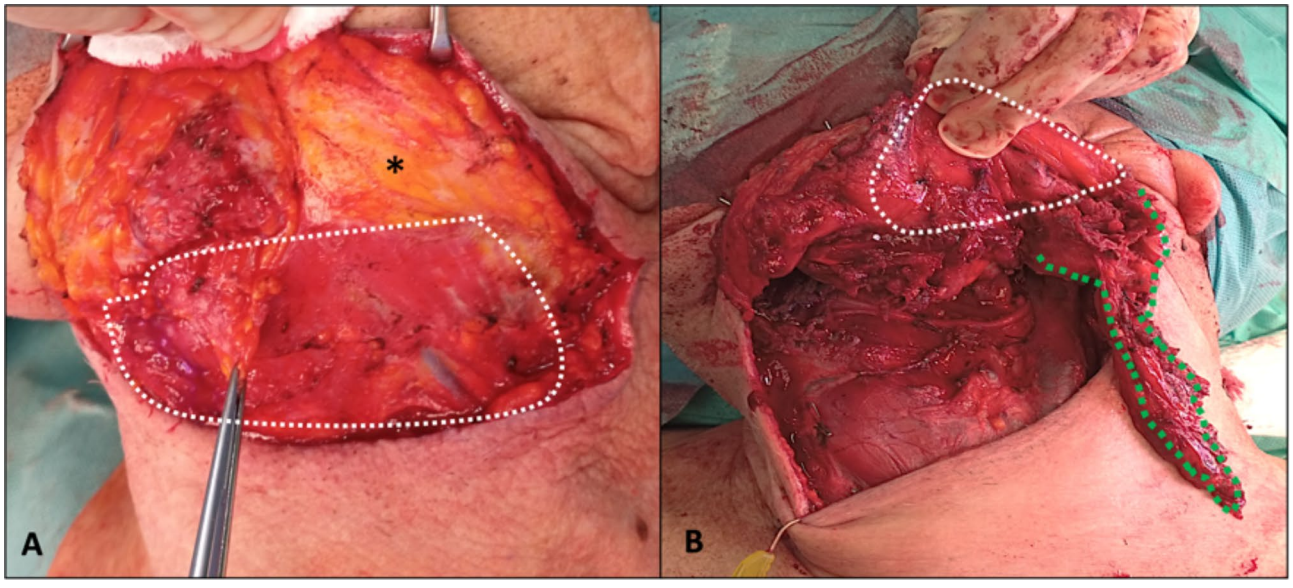

Fig. 5 The antero-lateral neck dissection (I, IIa, IIb, III and IV levels). **A**) The platysma muscle (white dashed line) is separated from the visor flap (*), composed of the skin and subcutis; **B**) The plastysma muscle (white dashed line) in connection with lymph nodes from I to IV level (green dashed line)

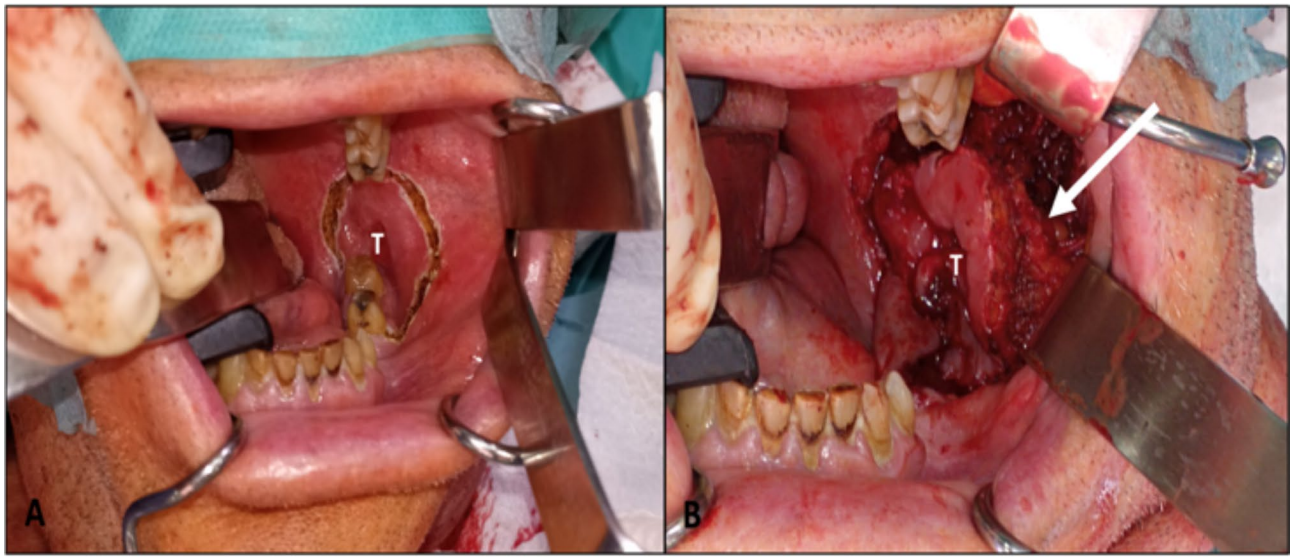

Fig. 6 The trans-oral excision of the tumour. **A**) The tumour (T) is removed with adequate margin of resection at least 1 cm; **B**) The deep margin of resection corresponds to the buccinator muscle (white arrow)

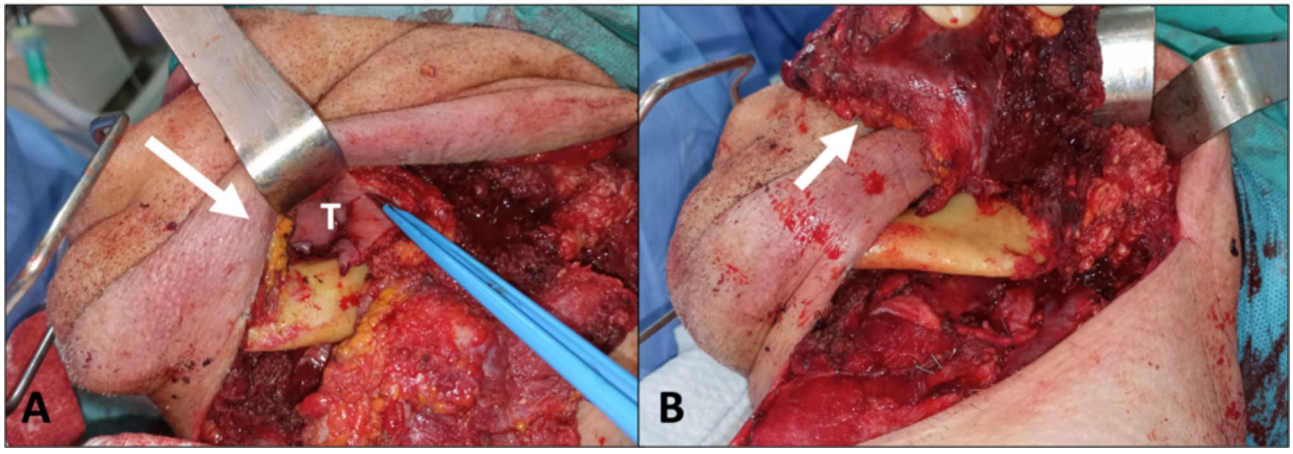

Fig. 7 The *en-bloc* resection. **A**) The tunnel connects the oral cavity where the tumour (T) is removed with lateral neck dissection elevating the superior visor flap (white narrow); **B**) Lifting of the specimen (white narrow) allows exposure of the body of the mandible

muscle, which protects the nerve until the origin of the MMN is found at the end of the parotid gland.

The oral phase

According to NCCN guidelines [7], the transoral resection is performed excising the neoplasia in "safe" margins of at least 1 cm from the around tumour, as also recently recommended by some authors (Fig. 6A) [24, 25]. The deep margins of resection include the buccinator muscle and the vessels plane. At this level, all the branches of the facial vein and artery are closed and cut. The resection of the primary tumour should include the neoplasia with the surrounding safe mucosa, the submucosa, the buccinator muscle with its facial branches and the vessels plane below (Fig. 6B). The subcutis and the skin of the cheek should be removed based on the tumour depth of infiltration.

The en-bloc resection

Once the transoral phase is completed and the neoplasia is removed with wide adequate margins (of at least 1 cm), by a pull-through approach: a surgical tunnel is created between the subcutaneous tissue and the platysma muscle. This tunnel is delimited superiorly by the superior visor flap (skin and subcutis). The inferior boundary is represented by the body of the mandible with the masseter muscle laterally (Fig. 7A). The body of the mandible is exposed after the surgical specimen (antero-lateral neck dissection, T-N tract and mucosa) is raised (Fig. 7B). The compartmental demolition of the cheek is completed with a pull-through and *en-bloc* with the neck dissection

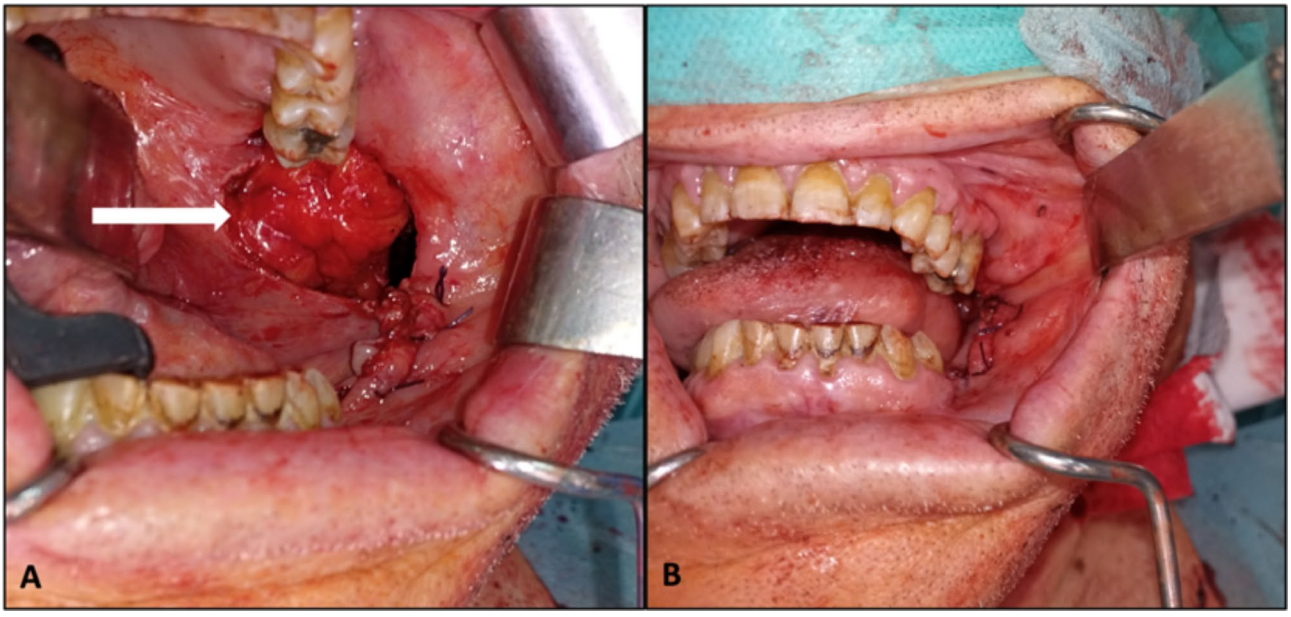

Fig. 8 The reconstructive phase. **A**) The Bichat flap is harvested (white narrow) to restore the surgical defect; **B**) The surgical cavity after the reconstruction phase

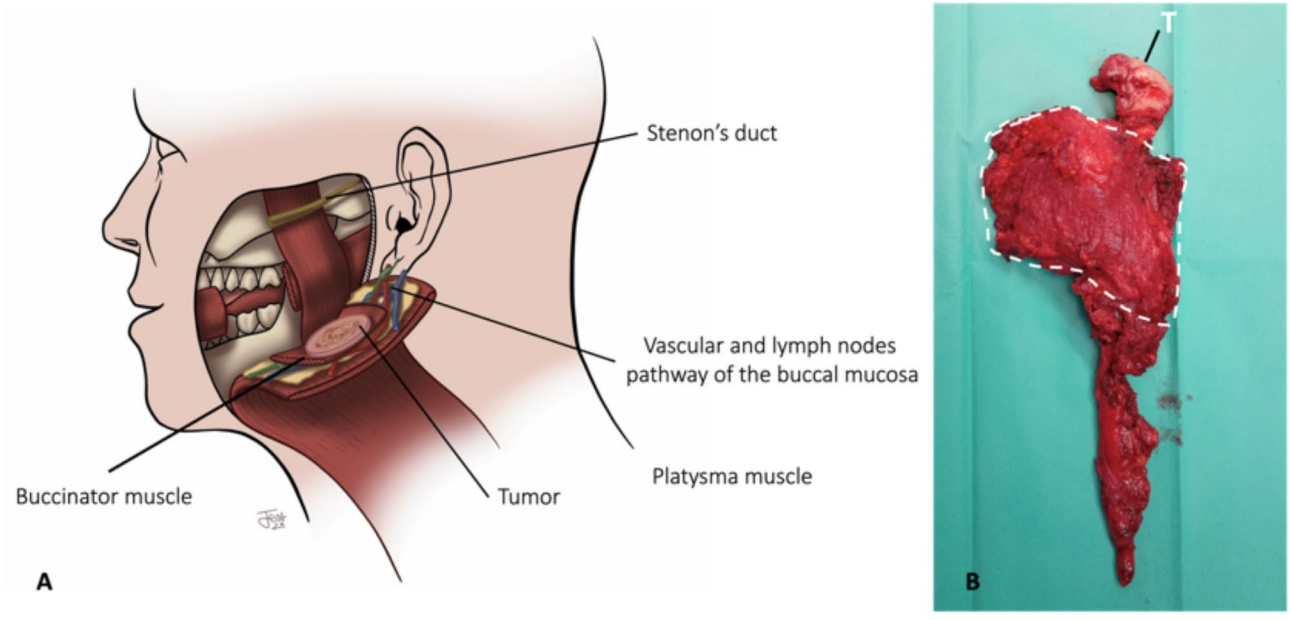

Fig. 9 **A**) The compartmental approach is obtained by a surgical tunnel that connects the oral cavity and the tumour with all the removed layers of the buccal mucosa and the T-N tract; **B**) The surgical specimen: the tumour (T) connected by the T-N tract (white dashed line) and the lateral neck lymph nodes (I, IIa, IIb, III and IV levels)

and the T-N tract, composed by facial vessels plan and lymph nodes with lymphatic pathways connected by the platysma muscle.

The reconstructive phase

A Bichat flap is raised in the case of a small surgical defect (Fig. 8) [14]. In the case of a larger defect or tumour extending to the skin, a free flap is required (i.e., forearm free flap, medial sural free flap, anterolateral thigh flap).

Finally, Fig. 9A schematizes the surgical technique highlighting the relationship between the tumour resection with all the removed layers of the buccal mucosa, and the T-N tract. Figure 9B shows the surgical specimen obtained from the compartmental approach.

Table 1 Case series treated by buccal mucosa compartmental surgery (BMCS)

Patients's number	1*	2	3
Gender	M	M	M
Age (years-old)	71	68	58
cTN (8th edition)	T2 N2b	T3 N2b	T3 N0
pTN (8th edition)	T2 N3b	T2 N0	T2 N0
Tumor diameter (mm)	9	16	17
DOI (mm)	8.05	6	5.5
Grading	G2	G2	G2
Buccinator muscle involvement	yes	yes	yes
T-N tract status	Involved by ECE adenopathy of 36 mm	Free from disease	Free from disease
Surgical margins status	R0	R0	R0
Type of reconstruction	Bichat flap	Bichat flap	RFFF
Adjuvant therapy	RT	None	none
Status at follow up	NED	NED	NED
Follow up (months)	28	54	17

Legend: DOI = deep of invasion; RT = radiotherapy, NED = no evidence of disease, RFFF = Radial forearm free flap; * = patient reported in this case report

Case series report

Table 1 summarized patients' data treated by buccal mucosa compartmental surgery (BMCS).

Discussion

Compared to other oral cavity subsites, the BMSCC shows a worse risk in terms of OS (HR, 2.0, 95% CI, 1.7–2.3) and DSS (HR, 4.7, 95% CI, 3.6-6.0) [26]. The five-year locoregional control, overall survival, and cause-specific survival rates were 36.3%, 34.3%, and 36.9%, respectively. The locoregional recurrence rate was 80% occurring at the level of the primary site [27, 28].

Considering these features, several studies have investigated peculiar risk factors and anatomical aspects that could distinguish the oncological behaviour of the buccal mucosa subsite from that of other subsites [8, 9, 12, 29].

As reported, critical and positive margins were more significatively frequent compared to other oral subsites [8, 11, 30]. Woolgar et al. showed that 87.1% of the involved margins in oral SCC and 100% in BMSCC are in the deep resection plane compared to the other oral cavity subsites [31]. Recently Adriaansens et al. revealed that adequate tumour-free margins (with a maximum of 5.0 mm from the tumour) were associated with a better local recurrence free survival (LRFS) of 100% compared to patients with < 1.0 mm ($p = 0.02$) [8]. The complex anatomy of the buccal mucosa may not allow easy access to the root margins. Excessive sample shrinkage may correlate with the risk of inadequate margins before and during formalin fixation as well as the prevention of facial nerve damage and the muscles and skin face to minimize the aesthetic sequelae [11, 30].

Hirai et al. revealed that buccinator muscle invasion was the most significant predictive risk factor for lymph node metastasis in BMSCC [24]. In our experience, the measurement of the distance of the buccinator muscle from the basal lamina and the DOIs revealed that the buccinator muscle location ranged from 1.18 to 1.9 mm deep (mean 1.5 mm), while the DOI ranged from 5.5 to 8.5 mm (mean 6.5 mm). Therefore, if the DOI is at least 1.5 mm, an involvement of the buccinator muscle may be presumable. Ota et al. proposed a clinical classification to evaluate the tumour infiltration of the buccinator muscle [10]. In the case of invasion in or through the muscle into the subcutaneous fat, the resection routinely included the facial skin. This approach led to a through-and-through defect in 34% of their patients and a high LRFS of 92.3% at 5-year survival, hampering complete tumour removal, especially in the deep resection plane [10].

The buccal mucosa lacks anatomical barriers to prevent tumour spread into the buccal fat pad, bone, and skin. Once the buccinator muscle is infiltrated, the contraction of the muscle itself could favour neoplastic dissemination to the subcutaneous fat, spreading the neoplastic cells more deeply around and in the platysma fibres [4, 32].

The T-N tract, the soft tissue located between the primary tumour (T) and the neck lymph nodes (N), could negatively influence patients' prognosis [12, 33, 34]. As previously investigated for tongue cancer, the involvement of the T-N tract by the disease showed a significant triple risk of distant metastases (hazard ratio [HR], 2.70; 95% CI, 1.01–7.19; $p = 0.05$) and double risk of death (HR, 2.09; 95% CI, 1.13–3.85; $p = 0.02$), worsening the disease-free survival (DSF) and especially the overall survival (OS) [12]. The T-N tract represents a relevant route of tumour spread to the neck lymph nodes. Therefore, cancer cells may be found in the T-N tract, as micrometastases or even bigger cancer nodules among vessels or nerves [33, 34]. As already reported, it is hypothesised that the T-N tract offers a possible pathway of "accelerated" tumour spread. It is known that patients who underwent compartmental tongue surgery (CTS) with *en-bloc* resection of the T-N tract had a better prognosis due to a significant reduction of probability for locoregional events [32, 34, 35].

There is no consensus regarding indications for lateral neck dissection based on the DOI of buccal mucosa carcinoma. Many studies confirm the risk of occult nodal metastases in 20% of cN0 patients [36–38]. Therefore, a prophylactic neck dissection may be considered for T2N0 carcinomas [37], while other authors recommended when buccinator muscle invasion is clinically detected, independently of the DOI [24]. Furthermore, Brindha et al. reported that the tumour volume was

positively correlated with locoregional control. In his series, T2 and T3 showed 25% and 33.3% of metastatic lymph nodes, respectively [38]. Concerning the lymph node ratio (LNR), considered as an important risk factor for loco-regional relapses, a significant impact on overall survival for patients with squamous cell carcinoma of the buccal mucosa ($p = 0.02$) and of other subsites such as the tongue ($p < 0.001$) was reported [39]. The LNR is calculated as the ratio of positive lymph nodes to dissected nodes and has been shown by various authors to be an independent prognostic factor in patients with OSCC and other malignancies [40–42]. Tomioka et al. confirmed that the buccinator and mandibular nodes were recognized as typically metastatic sites than other oral SCCs [43]. Therefore, the treatment of submandibular lymph nodes (level Ib) is mandatory for improving survival and a compartmental approach enables the surgeon to carry out an en-bloc resection of the primary lesion and the dissected tissue, including the adipose tissue surrounding the facial artery and vein with the lymphatic tissue from the cheek to the neck, including the buccinator and mandibular nodes [24]. Finally, as evidenced by peer-reviewed medical publications and our surgical technique, the prophylactic supra-omohyoid neck dissection could be considered at least for T2 tumours [37, 44]. Since patient survival is mainly correlated with disease recurrences, well-studied risk factors in OSCC (advanced T stage, lympho-vascular or perineural tumour invasion, the presence of cervical lymph node metastases ($N > 1$), extracapsular extension (ECE), the depth of infiltration (DOI), the incomplete resection margins (R1), the lymph node ratio (LNR)), should be considered and emphasised in cases of surgical treatment for BMSCC, considering the biological behavior of this tumour [39, 45].

This work describes how buccal mucosa compartmental surgery characterized by a wide *en-bloc* resection with adequate margins (R0) and the removal of all of the pathways of tumour spread, could ensure a good loco-regional control of disease. As described for tongue surgery, the goal of compartmental surgery is to remove the paths of least resistance and thus at risk of metastases, thereby improving local disease control as compared to the standard wide tumour resection [46]. With this approach, the deep margins were controlled by removing the buccinator muscle, ensuring an adequate resection according to the DOI, an important prognostic factor for locoregional disease control [10, 28]. Furthermore, the resection of the cranial fibres of the platysma muscle with lateral neck dissection allows the removal of the disease *en-bloc* along with all the possible pathways of tumour spread, not only the simple removal of the lymph nodes. Therefore, compartmental surgery may be recommended, if at least one clinically positive lymph node is presented - independently of the tumour dimension - and if there is a clinical T2 with an estimated radiological DOI > 5 mm, independently of lymph nodes status.

We are aware that this technique has a weakness represented by the high risk of damage to the marginalis mandibulae nerve (MMN). The MMN should be preserved in all cases; its surgical sacrifice is only indicated in the case of infiltration by cancer, for the sake of radical surgery. Furthermore, due to the rarity of this subtype of tumour, this approach needs to be validated in a comparison with the traditional wide resection, especially through a large cohort of cases in terms of oncological outcomes and aesthetic sequelae.

Conclusion

Further studies, such as retrospective, prospective and multicentric studies we are already working on, may allow us to better assess this surgical management in terms of feasibility, oncological effectiveness, limitations, and weaknesses for BMSCC.

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Author contributions
S. R. conceptualized the study. R.D.B. drafted the text and collected all data. F. C. and M. T. revised the manuscript. M. A., R. B. and G. G. supervised and validated the manuscript. F. M. and D. L. collected histopathological figures. N. F. supervised and reviewed the manuscript. All authors reviewed and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent for publication
Written informed consent was obtained from the patient for publication of this report and any accompanying images.

Competing interests
The authors declare no competing interests.

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