

# Utilization of a Chimeric Medial Femoral Condyle Free Flap for Mandibular Osteoradionecrosis

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**Background:** Primary options for oromandibular reconstruction with osteocutaneous free flaps are the vascularized fibula and iliac crest. Complications of mandible reconstruction are not uncommon and include osteomyelitis, malunion, and osteoradionecrosis (ORN) after radiation therapy. The medial femoral condyle (MFC) free flap is an established salvage option for carpal reconstruction in hand surgery, frequently used for scaphoid nonunion and avascular necrosis. We hypothesize that the MFC flap can be utilized to restore blood supply and reverse the negative effects of radiotherapy in patients who require mandibular reconstruction due to ORN.

**Methods:** A retrospective chart review was conducted at Beaumont Health System, Royal Oak, for patients who underwent MFC free flap reconstruction for mandibular ORN between the years 2012 and 2018. Demographic data, operative details, complications, medical comorbidities, and patient outcomes were retrospectively gathered.

**Results:** A total of four patients were isolated. Four patients developed ORN after resection of squamous cell carcinoma and adjuvant radiotherapy. No patients experienced donor site deficits. Revisions after MFC reconstruction were dependent on individual aesthetics and involvement of neighboring tissue. All four patients continue to be followed with no current issues to the osseous component of the MFC flap.

**Conclusion:** Utilization of the MFC periosteal flap is a viable option in selected patients to salvage nonunion/resorption of mandible reconstruction and ORN of the mandible. Our experience found that the MFC is able to provide pain resolution and healing of intraoral soft tissue defects, and may halt the progression of ORN of the mandible. (*Plast Reconstr Surg Glob Open* 2022;10:e4489; doi: 10.1097/GOX.0000000000004489; Published online 24 August 2022.)

## INTRODUCTION

The incidence of osteoradionecrosis (ORN) has great variability in literature. As a result, the absolute incidence and prevalence of ORN of the jaws after radiation therapy for the treatment of head and neck cancer are difficult to precisely identify.<sup>1</sup> Clinical evidence of ORN related to radiotherapy was first reported by Regaud.<sup>2</sup> The overall incidence of ORN has been estimated to be around 6.28% after 1968.<sup>3</sup> The year 1968 was arbitrarily chosen

by Clayman<sup>1</sup> since essentially all radiation oncology units had embraced megavoltage therapy, updating all the published incidence studies of ORN.

The definition of ORN remains controversial. It is challenging to compare epidemiology and treatment efficacy. Marx<sup>4</sup> defines ORN as “an area greater than 1 cm of exposed bone in a field of irradiation that had failed to show any evidence of healing for at least 6 months.” He also clarified that in ORN, there is no interstitial infection but rather superficial contamination. For the purpose of this current study, we define ORN as a slow-healing radiation-induced ischemic necrosis of bone with associated soft tissue necrosis of variable extent occurring in the absence of local primary tumor necrosis, recurrence, or metastatic disease.<sup>5</sup>

The understanding of the pathophysiology of ORN has been a controversial subject since its first appearance in the early 1920s. Meyer<sup>6</sup> proposed his radiation, trauma, and infection theory suggesting that injury provided the opening for invasion of oral microbiological

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flora into the underlying irradiated bone. Other authors agreed and referred to ORN as secondary infection after devitalized bone injury and radiation-induced osteomyelitis.<sup>7</sup> Meyer's theory lasted for a decade and became the foundation for the widespread use of antibiotics with surgery to treat ORN. Marx<sup>4</sup> discovered that micro-organisms play a minor role in the pathophysiology of ORN of the jaws.

Furthermore, the following points seem to be agreed upon by the majority of authors<sup>8</sup>:

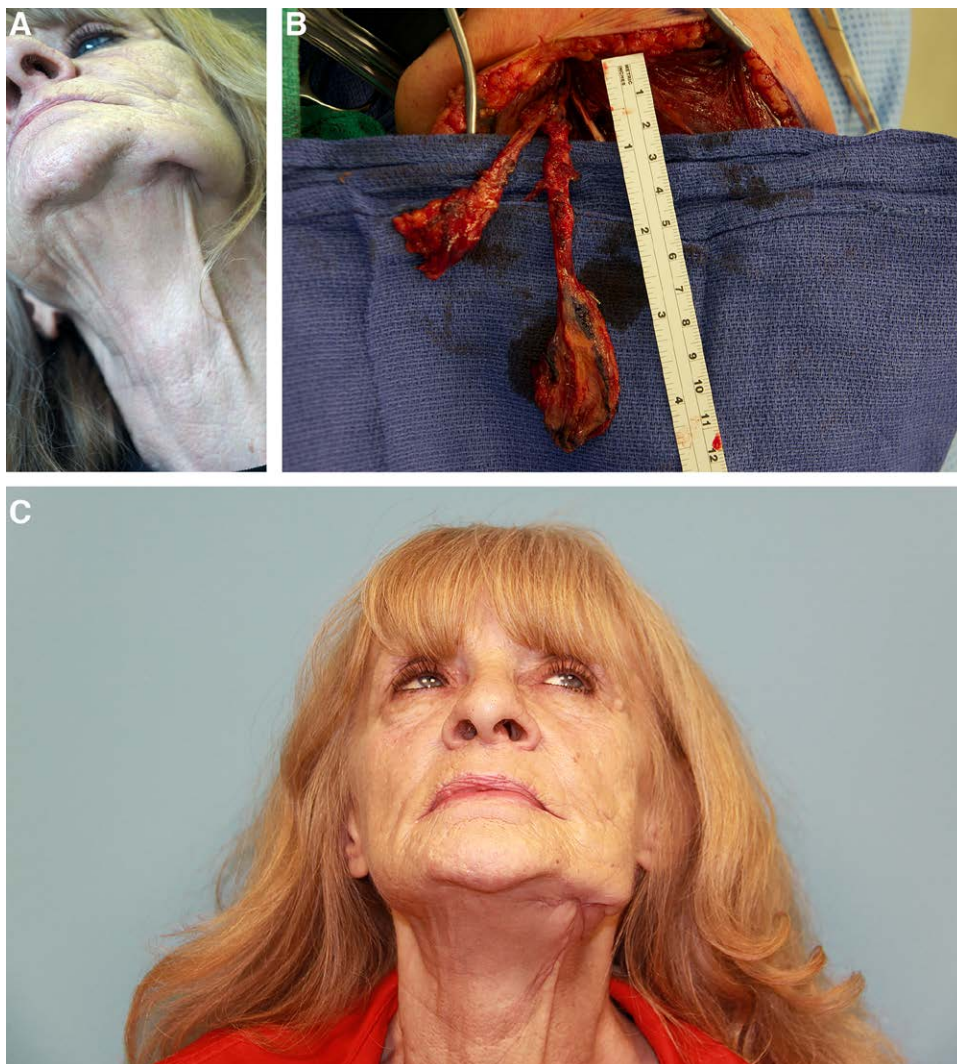
1. The affected site should have been previously irradiated.
2. There should be an absence of recurrent tumors on the affected site.
3. Mucosal breakdown or failure to heal should occur, resulting in bone exposure.

### Takeaways

**Question:** What are the indications for the utilization of the medial femoral condyle (MFC) free flap for osteoradionecrosis of the mandible?

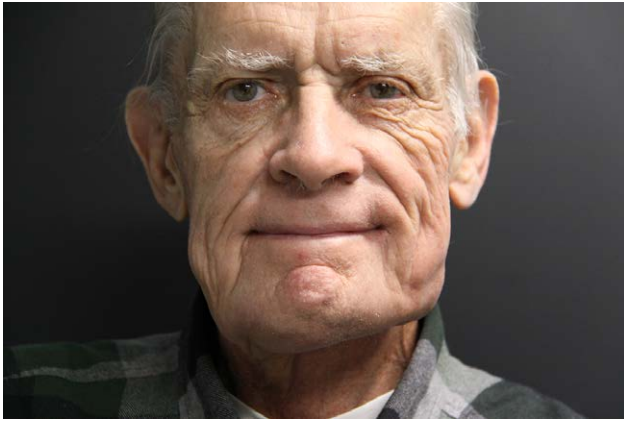
**Findings:** Our study found that the MFC free flap is relatively easy to raise with minimal morbidity. The flaps were able to provide bone healing, pain elimination, and healing of intraoral soft tissue defects.

**Meaning:** The MFC is a viable option in selected patients to salvage nonunion/resorption of mandible reconstruction and osteoradionecrosis of the mandible. Our experience suggested that an early application of the medial femoral condyle flap to the affected mandible may reverse or halt the progression of ORN of the mandible.



**Fig. 1.** Case 1. A, Preoperative image of patient with development of chronic sinus tract on left submandibular region, chronic left mandibular pain, and atrophic change of the mandible. B, Intraoperative image demonstrates reconstruction with MFC flap to enhance mandibular remodeling. The periosteal flap was secured to the native mandible with multiple screws. C, Twenty-four-month postoperative follow-up image demonstrates adequate healing resolution of the patient's symptoms.





**Fig. 2.** Case 2. Preoperative image of a patient who developed chronic pain and a pathological fracture after he was treated with chemoradiation for SCC of the base of the tongue and hypopharynx.

4. The overlying bone should be “dead,” usually due to hypoxic necrosis.
5. Cellulitis, fistulation, or pathological fracture need not be present to be considered ORN.

In hand surgery, the medial femoral condyle (MFC) free flap has emerged as a salvage option for carpal reconstruction, frequently used for scaphoid nonunion or avascular necrosis.<sup>9-11</sup> We hypothesize that the periosteal free flaps can restore blood supply and provide essential cells to reverse the negative effects of radiotherapy on the mandible.

### METHODS

After institutional review board approval was obtained in accordance with the Declaration of Helsinki, clinical records were retrospectively reviewed for a single surgeon’s experience on all patients who underwent the MFC free flap for reconstruction in ORN of the mandible from 2013 to 2020. Patient characteristics, operative details, surgical outcomes, and complications were assessed.

#### Surgical Technique

##### Flap Harvest

The flap is harvested under tourniquet control in standard fashion using an incision in the distal third of the thigh. If a skin paddle is required, the incision is curved anteriorly to capture perforators. Subfascial dissection is performed to enter the interval between the vastus medialis and the sartorius and self-retaining retractors are used. Retrograde dissection is performed to get the descending genicular vessels to the source vessel. The periosteum is divided with cautery on its periphery, and osteoma is used to harvest the outer cortex of the femur.

##### Flap Inset

The flap is inset according to the requirements of the defect. A 5-mm self-drilling screw is used to fixate the periosteum to small isolated bone gaps. If additional support is needed, a 2.0 locking reconstruction plate can be used to span the defect. If there is a mucosal defect, the skin paddle is sutured with 3-0 Vicryl to the peripheral mucosa. If fat is harvested with the flap, this can be placed into the medullary defect of the recipient bone.



**Fig. 3.** Case 2. Chimeric MFC flap once surgical dissection from the donor site was complete.

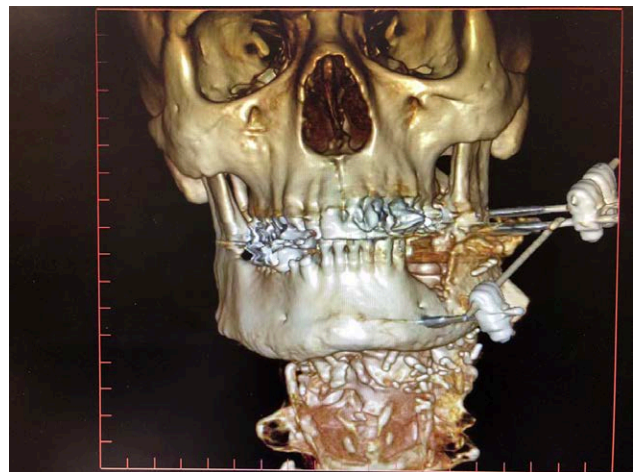
### RESULTS

#### Case 1

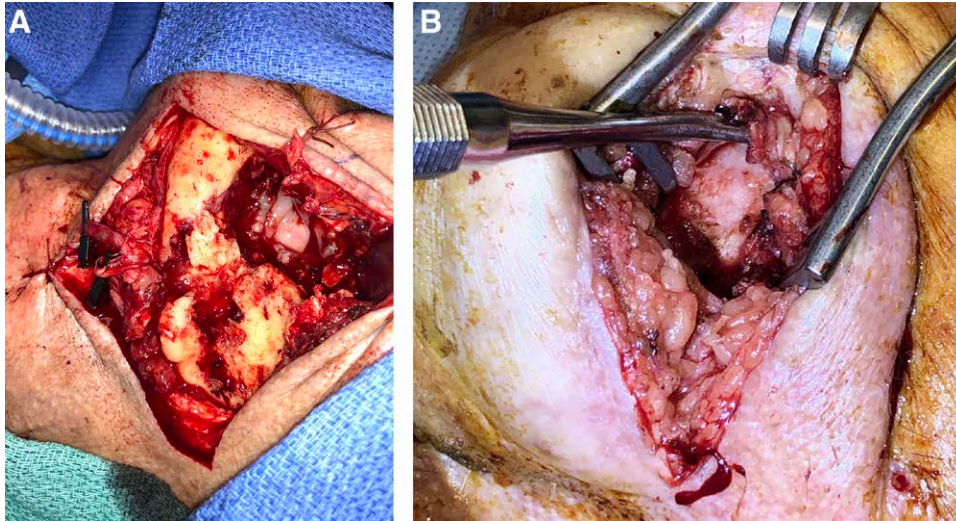
A 69-year-old woman with history of intraoral squamous cell carcinoma (SCC) diagnosed in 2012 underwent mucosal resection and received adjuvant radiation therapy 8 years before. At the initial visit, the patient had developed a chronic sinus tract on the left submandibular region, chronic left mandible pain, and atrophic change of the left angle of the mandible (Fig. 1A). She underwent mandible reconstruction with an MFC periosteal flap to enhance mandible remodeling. The periosteal flap was secured to the native mandible with multiple screws (Fig. 1B, C). The patient did well after surgery and reported that she was not only pain free but also pleased with her surgical outcome (Fig. 1D, E).

#### Case 2

An 81-year-old man with a history of SCC at the base of the tongue and hypopharynx, initially diagnosed in 2012 and treated with chemoradiation, developed chronic pain and a pathological fracture of the left mandible. He



**Fig. 4.** Case 2. three-dimensional CT scan demonstrates adequate placement of the external fixator to the left mandibular region.



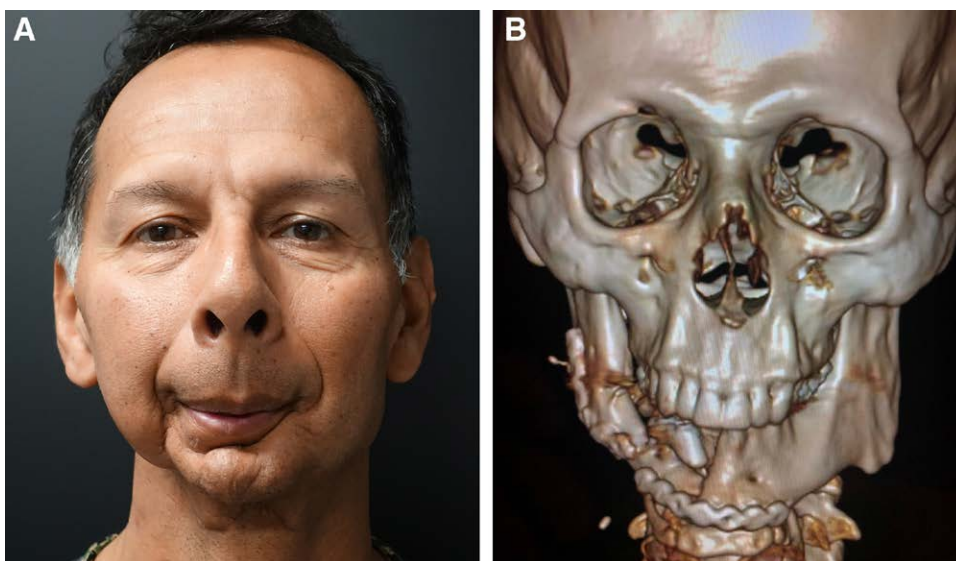
**Fig. 5.** Case 2. A, Three months after the initial surgical operation, the external fixator was removed and exploration of the surgical side was conducted. B, Complete healing and integration of the MFC flap to the mandible is seen.

reported that he had undergone multiple sessions of hyperbaric oxygen therapy (HBO). Due to persistent intraoral wound, chronic pain, and failed HBO treatment, surgical resection and reconstruction with a free tissue transfer were indicated. CT angiogram of both lower extremities demonstrated complete occlusion of bilateral peroneal arteries (Fig. 2). He refused to undergo scapula, radius, and iliac bone flaps due to his lifestyle as a golfer. An MFC free flap was conducted with rigid mandibular fracture fixation with an external fixator (Fig. 3). Postoperatively, the patient developed acute venous congestion (Fig. 4A). As a result, a revision of venous anastomosis was performed. Unfortunately, there was dehiscence between the MFC intraoral skin paddle and the native oral mucosa. The

patient then underwent the second free flap to resurface intraoral soft tissue with a radial forearm free flap anastomosed to the left transverse cervical vessels (Fig. 4B, D). Three months later, he underwent removal of the external fixator and exploration of the surgical site with a possibility of bone grafting. At his latest postoperative visit, it was noted that there was complete healing of the ORN with integration of the MFC to the mandible (Fig. 5).

### Case 3

A 61-year-old man with history of SCC of right gingiva and right retromolar trigone diagnosed in 2010 underwent right mandibulectomy, right selective neck dissection, and right mandible reconstruction with fibular

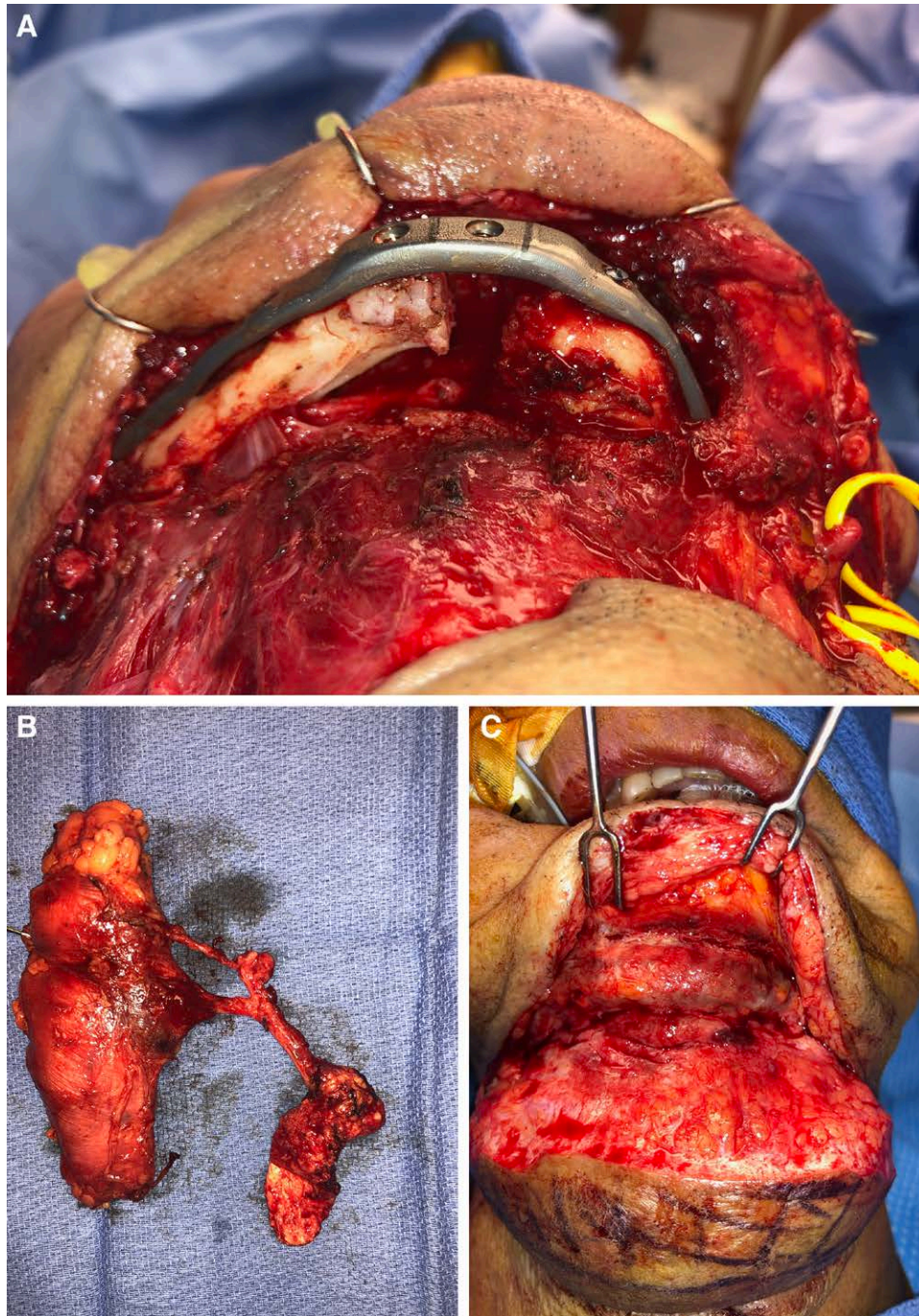


**Fig. 6.** Case 3. A, A 61-year-old man with a medical history of SCC of the right gingiva and retromolar trigone developed severe anatomical and physical defects as a result of previous surgical operations. B, three-dimensional CT scan reveals right-sided malocclusion and fibrous nonunion between the fibula flap and native mandible.



free flap elsewhere. The patient then underwent dental rehabilitation with dental implants 2 years later. He developed an infection that led to the removal of two of four implants, removal of reconstruction plates, and debridement of the mandible and nonvascularized iliac bone graft. He underwent another revision nonvascularized bone graft 2 years later without success. In addition, he underwent several HBO treatments. Another fibula-free flap was recommended by his initial surgical team (Fig. 6).

He presented to our institution for a second opinion. The patient underwent a removal of the hardware, reestablishment of dental occlusion, and mandibular reconstruction with an MFC chimeric free flap (Fig. 7). During a revision surgery and hardware removal, there was clinical evidence of union of the central mandible with the integration of the MFC periosteal flap (Fig. 7C). The patient subsequently underwent dental rehabilitation successfully (Fig. 8).



**Fig. 7.** Case 3. A, Perioperative imaging once the patient's prior hardware had been surgically removed. B, Perioperative image demonstrates the MFC chimeric free flap utilized for the mandibular reconstruction. C, Revision surgery found union of the central mandible with integration of the MFC periosteal flap.

#### Case 4

A 74-year-old woman with history of cancer in the base of her tongue diagnosed in 2005 underwent primary treatment with chemotherapy and radiotherapy. She developed left-sided ORN treated with segmental resection and fibula-free flap in 2012 after failed HBO treatment. She then developed a tooth infection on the right in 2017 and underwent tooth extraction, which caused persistent intraoral drainage and chronic pain (Fig. 9). After failed conservative therapy with oral rinses, antibiotics, and HBO treatment, she underwent a conservative mandible debridement and reconstruction with an MFC chimeric flap (Fig. 10). Suprapatellar fat was used to fill the dead space within the mandible (Fig. 11). Postoperatively, she reported a complete resolution of intraoral wound and jaw pain.

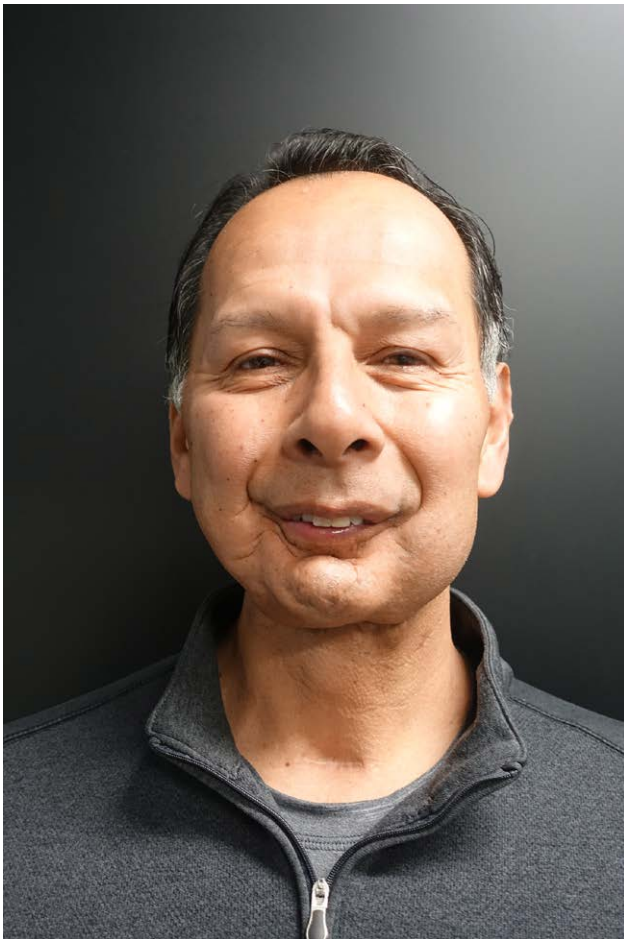
### DISCUSSION

Several surgeons have applied the MFC to craniofacial, head, and neck reconstruction.<sup>12</sup> This is attributable to several factors, including structural support from the

cortico-cancellous bone, a vascularized bone graft to assist revascularization of the transplant site, and osteogenic capacity of the cambium layer of the periosteum.<sup>13,14</sup> At a fracture site, the type of matrix synthesized by osteochondral cells is determined by oxygen concentration, with endochondral ossification and intramembranous ossification occurring at high oxygen concentration.<sup>15</sup> Furthermore, when the periosteum is removed, endochondral ossification occurs.<sup>16</sup> In animal models, bone allografts with vascularized periosteal flaps became revascularized, and intramembranous ossification protected against nonunion while providing torsional strength. Histologic analysis of the allografts revealed remodeling, making them indistinguishable from the host.<sup>17</sup> Although preexisting osteoblasts are involved to a limited extent, the undifferentiated progenitor cells from the autologous graft and the marrow and periosteum of the recipient site are stimulated by the fracture environment to differentiate into a bridge of osteochondral tissue before ossification.<sup>18</sup> Within the models of vascularized grafts, angiogenic factors are abundantly expressed in the periosteum allowing for revascularization centripetally.<sup>19</sup> Directly beneath the periosteum is the cambium layer, which supplies mesenchymal, differentiated osteogenic progenitor cells and osteoblasts to remodel and deposit new bone at the defect site.<sup>24</sup> Working in unison, the highly vascular periosteal layer lays down a rim of new bone followed by intramembranous ossification by the cambium layer.<sup>20,21</sup>

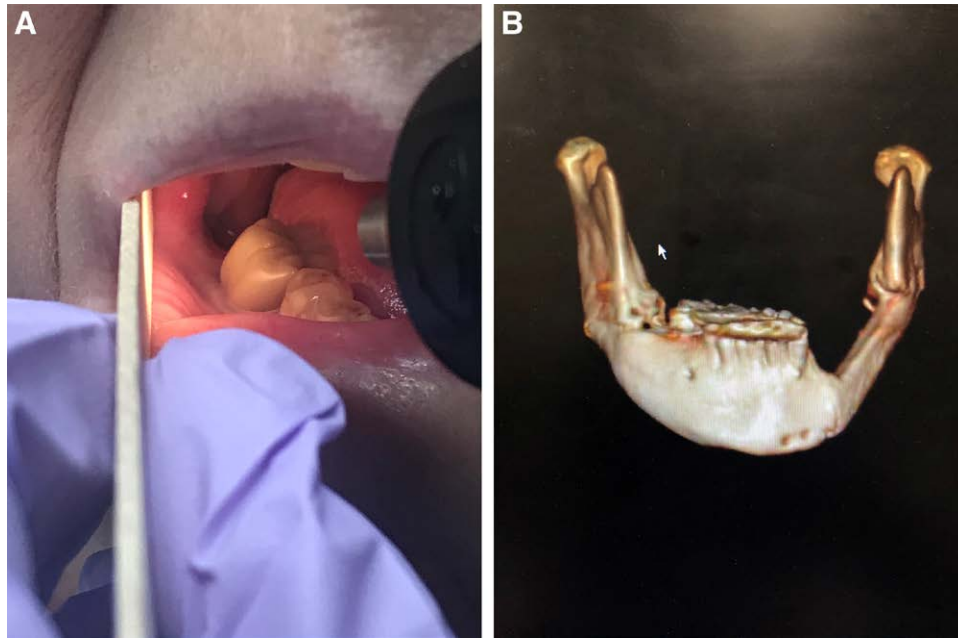
In 2004, Assael<sup>22</sup> hypothesized that ORN occurs by the same mechanism as other types of osteonecrosis (eg, bisphosphonate-related osteonecrosis) and results from decreased osteoclastic bone resorption. These authors are convinced that cellular radiogenic effects in bone occur earlier than the well-known vascular alterations. This hypothesis challenges the well-accepted “three-H concept” (hypoxia, hypocellularity, and hypovascularity) of Marx.<sup>7</sup> A theory proposes that ORN occurs by a radiation-induced fibroatrophic mechanism, including free-radical formation, endothelial dysfunction, inflammation, microvascular thrombosis, fibrosis and remodeling, and finally, bone and tissue necrosis.<sup>23</sup> The imbalance between synthesis and degradation in irradiated tissue is particularly dramatic in bone. The combination of the death of osteoblasts after irradiation, failure of osteoblasts to repopulate, and excessive proliferation of myofibroblasts results in a reduction in the bony matrix and its replacement with fibrous tissues.

Trauma stimulates the proliferation of osteoblasts, mainly from the periosteum, to repair the damage to the bone. Radiation of bone leads to endarteritis obliterans with thrombosis of small blood vessels, fibrosis of the periosteum and mucosa, and damage to osteocytes, osteoblasts, and fibroblasts. The damaged osteocytes and osteoblasts may survive until they attempt to divide when mitotic death occurs. An individual bone cell may undergo mitotic death at an interval of months or years after irradiation, or it may never divide unless stimulated by trauma. There is, therefore, a slow loss of bone cells

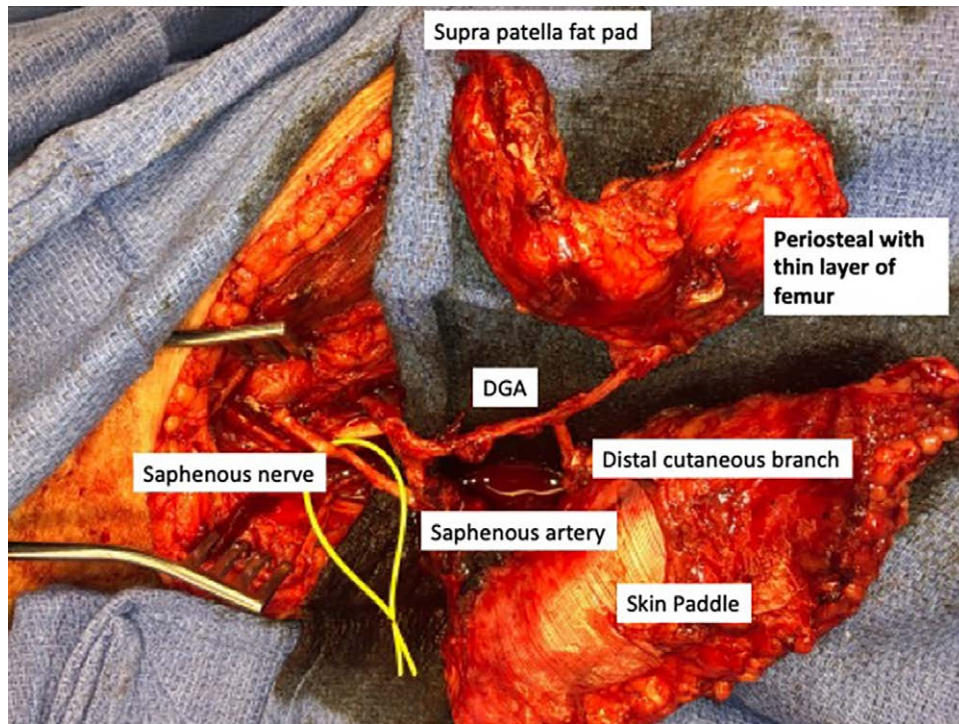


**Fig. 8.** Case 3. One-year follow-up of patient after he underwent removal of hardware, reestablishment of dental occlusion, and mandibular reconstruction with MFC chimeric free flap.





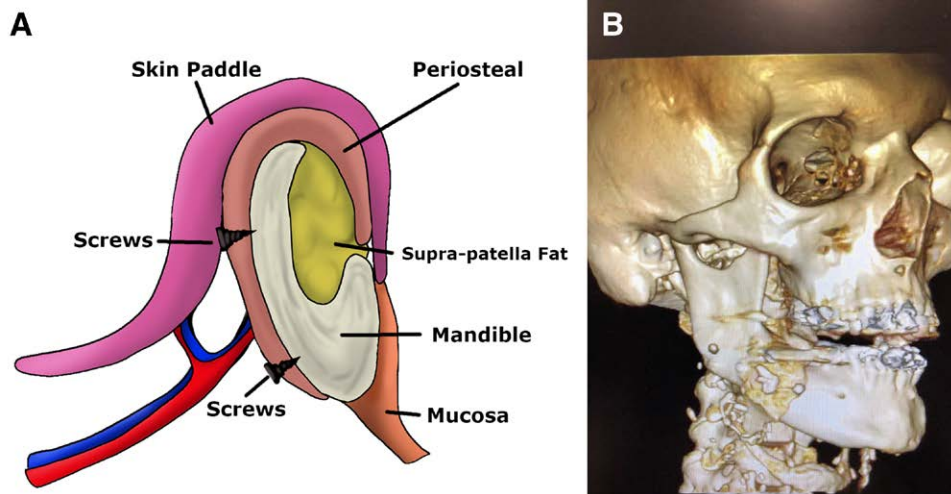
**Fig. 9.** Case 4. A, Preoperative clinic imaging finds right-sided location causing persistent pain and intraoral drainage for this 74-year-old woman with a medical history of SCC located at the base of the tongue. B, three-dimensional CT scan reveals location causing persistent intraoral drainage.



**Fig. 10.** Case 4. Perioperative imaging of the right mandible demonstrates conservative mandibular debridement and reconstruction with a chimeric MFC flap.

after radiotherapy with a consequent slowing down of the remodeling process, which leads to the risk of bone necrosis.<sup>9</sup> Osteoclasts arise from hematopoietic tissues, followed by vascular dissemination and the generation of resting preosteoclasts and osteoclasts in the bone itself.<sup>24</sup> Radiation damage to the marrow and blood vessels would

explain their absence. Equally important is the absence of the osteoblast, which is regarded as the significant influence in recruiting and activating the osteoclast. A third consideration was the likelihood that osteoclasts do not find irradiated necrotic bone a suitable substrate for phagocytosis.



**Fig. 11.** Case 4. A, Mandibular cross section demonstrates inset of the chimeric MFC flap. A suprapatella fat pad was used to fill the marrow of the mandible after debridement had been conducted. The periosteum was molded to wrap around the mandible, and the skin paddle was utilized as an intraoral lining with external skin coverage. B, three-dimensional CT scan demonstrates that the periosteum free flap was molded to match the contour of the mandible.

The treatment protocol for ORN of the mandible is controversial. The current algorithm of ORN management begins with conservative therapy consisting of hyperbaric oxygen, antioxidants, and pain control, reserving surgery for high-grade ORN with significant oral dysfunction.<sup>25</sup> Rogers et al<sup>26</sup> studied 71 patients with ORN of differing severity levels suggested that it may be appropriate to use nonsurgical management of osteonecrosis for as long as possible, delaying resection and reconstruction until the patient experiences a significant reduction in quality of life, and pain control becomes difficult. In 1983, Marx<sup>4</sup> demonstrated successful resolution of mandibular ORN in 58 patients using a staged protocol with HBO and surgery.

However, HBO has not been shown to prevent the development of ORN, and it does not reverse established ORN. However, several studies have shown some benefit in using HBO in managing stage I and II ORN.<sup>27,28</sup> Based on the available data from the Internet, the average cost of hyperbaric oxygen ranges between \$250 and \$450 per dive.<sup>29</sup> HBO treatment is undoubtedly an expensive treatment with uncertain outcomes. Conservative management is often insufficient, and longer time intervals between radiation or injury and ORN development led to higher flap failure with local wound complications.<sup>30,31</sup> Microvascular osteocutaneous free tissue transfer is considered the standard of care for stage III ORN management. It is generally accepted that particular care must be exercised in delineating the margins of resection when a primary bone flap is planned. However, all of our patients did not have a composite mandible resection. We used a periosteal flap to “wrap” the affected bone in all cases. In case 3, in addition to wrapping the bone with the periosteum, we used a small segment of femur 2 cm × 2 cm to bridge the gap between the previous fibula-free flap and native mandible. This approach

of wrapping the affected bone alone with a periosteal-free flap without a composite resection proved successful in our case series. The convenience of this flap over other reconstructive options is that it provides a way to regenerate bone for small osseous defects with less morbidity than a fibula, scapular, or osteocutaneous radial free flap.

Preliminary results from our small cohort suggested that in selected early (lytic lesion with intact mucosa) or late ORN cases, the early application of an MFC free flap to the affected part of the mandible may reduce overall cost, reduce total treatment times, and reverse the ORN process. An MFC flap is relatively easy to raise with minimal morbidity. There is no sacrifice of major end vessels.

## CONCLUSIONS

The MFC periosteal flap is a viable option in selected patients with ORN of the mandible. There is no universal agreement regarding the classification or staging of mandibular ORN. Many authors have attempted a classification of ORN, and the majority have relied on the history and clinical progression of the disease or its response to treatment.<sup>32-34</sup> Further studies are needed to come up with an objective, universal, and accepted classification of ORN using imaging studies. Once we identify the universally accepted classification, further studies can be conducted to clarify the indications for the MFC free flap in the management of ORN.

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