

Reconstruction of a mandibular segmental defect with a customized 3-dimensional-printed titanium prosthesis in a cat with a mandibular osteosarcoma

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CASE DESCRIPTION

A 12-year-old neutered male domestic shorthair cat had been treated for a mass arising from the lingual aspect of the caudal right mandibular body. Cytoreductive surgery of the mass had been performed twice over a 2-year period, but the mass recurred following both surgeries. The mass was diagnosed as an osteosarcoma, and the cat was referred for further evaluation and treatment.

CLINICAL FINDINGS

Clinical findings were unremarkable, except for a 2-cm-diameter mass arising from the lingual aspect of the right mandible and mild anemia and lymphopenia. Pre- and postcontrast CT scans of the head, neck, and thorax were performed, revealing that the osteosarcoma was confined to the caudal right mandibular body, with no evidence of lymph node or pulmonary metastasis.

TREATMENT AND OUTCOME

The stereolithographic files of the CT scan of the head were sent for computer-aided design and manufacture of a customized 3-D-printed titanium prosthesis. Segmental mandibulectomy was performed, and the mandibular defect was reconstructed in a single stage with the 3-D-printed titanium prosthesis. The cat had 1 minor postoperative complication but had no signs of eating difficulties at any point after surgery. The cat was alive and disease free 14 months postoperatively.

CLINICAL RELEVANCE

Reconstruction of the mandible of a cat following mandibulectomy was possible with computer-aided design and manufacture of a customized 3-D-printed titanium prosthesis. Cats have a high rate of complications following mandibulectomy, and these initial findings suggested that mandibular reconstruction may reduce the risk of these complications and result in a better functional outcome. (*J Am Vet Med Assoc* 2017;250:900–908)

A 12-year-old neutered male domestic shorthair cat weighing 4.6 kg (10.1 lb) was referred with a 2-year history of a mandibular mass. Cytoreductive surgery had initially been performed, and histologic examination of the resected tissue had revealed findings consistent with inflammation and no evidence of neoplasia. Local recurrence of the mass had been detected 11 months after the initial surgery. The mass had continued to grow and displace the tongue outside the oral cavity; however, the cat had continued to eat without difficulty.

A second cytoreductive surgery had been performed 3 months after the recurrence had been detected (14 months after the initial surgery). The mandibular mass had appeared more infiltrative during the second surgery and had been confirmed as a

fibroblastic osteosarcoma on histologic examination. Local recurrence of the mass had been noted again 7 months after the second surgery (21 months after the first surgery), primarily because of periodic signs of pain resulting from the ipsilateral maxillary molars and premolars contacting the recurrent mass. The cat was referred to VCA Canada Alta Vista Animal Hospital 3 months after the second recurrence of the mass was noted.

On physical examination at the referral hospital, the only abnormality identified in the cat was a 2-cm-diameter mass arising from the lingual aspect of the right mandible. The mandibular lymph nodes were non-palpable. A CBC revealed mild anemia (PCV, 27%; reference range, 29% to 48%) and lymphopenia (lymphocyte count, 1.05×10^9 cells/L; reference range, 1.20 to 8.00×10^9 cells/L). Results of serum biochemical analysis and urinalysis were within reference ranges. Mandibulectomy with reconstruction of the mandibular defect was discussed with the owner as an alternative to traditional mandibulectomy techniques without reconstruction because of the high compli-

ABBREVIATIONS

CAD-CAM	Computer-aided design and computer-aided manufacturing
TMJ	Temporomandibular joint

cation rate associated with mandibulectomy in cats.¹ The owner elected to proceed with segmental mandibulectomy with single-stage reconstruction of the mandibular defect.

In preparation for surgery, the cat was sedated with dexmedetomidine hydrochloride (5 µg/kg [2.3 µg/lb], IV) and butorphanol tartrate (0.2 mg/kg [0.09 mg/lb], IV). A precontrast CT scan was performed with 2-mm axial slices of the head and neck and 3-mm axial slices of the thorax. Iodixanol (2 mL/kg [0.9 mg/lb], IV) was administered, and a postcontrast CT scan of the head and neck was then performed with 2-mm axial slices. A well-circumscribed mass measuring 1.7 × 1.8 cm was identified on the lingual aspect of the caudal mandibular body (**Figure 1**). The mass appeared lytic, but bone lysis did not extend beyond the mass. The mass was also noted to extend across the midline of the intermandibular region. The mandibular, retropharyngeal, and parotid lymph nodes were symmetric with unremarkable size and structure. There was no evidence of pulmonary metastasis or intrathoracic abnormalities.

The stereolithographic files of the CT scan of the head were electronically sent to an external laboratory for CAD-CAM of a customized 3-D-printed titanium prosthesis, including rostral and caudal fixation plates (**Figure 2**). A prefabricated guide was also manufactured to assist in planning the site and direction of the mandibular osteotomies.

Segmental mandibulectomy and mandibular reconstruction with the 3-D-printed titanium prosthesis was performed 4 weeks following the staging and planning CT scan. This included 14 days for CAD-CAM of the prosthesis and a further 14 days for the prosthesis to be approved by US Customs and Border Protection and Canada Border Services Agency and delivered.

In preparation for surgery, the cat was sedated by IV administration of hydromorphone (0.05 mg/kg [0.02 mg/lb]) and midazolam (0.1 mg/kg [0.05 mg/lb]). Anesthesia was induced with alfaxalone titrated to effect, cephazolin was administered (22 mg/kg [10 mg/lb], IV, q 2 h), endotracheal intubation was performed, and anesthesia was maintained with isoflurane in oxygen. Crystalloid fluid was administered IV at a rate of 10 mL/kg/h (4.5 mg/lb/h) throughout the surgical procedure. Intraoperative analgesia included continuous rate IV infusions of hydromorphone (0.025 mg/kg/h [0.011 mg/lb/h]) and ketamine hydrochloride (0.4 mg/kg/h [0.2 mg/lb/h]). In addition, a 14-F red rubber esophagostomy tube was inserted because supplemental tube feeding is recommended following mandibulectomy in cats¹ and it was possible that the cat would not be able to eat properly after surgery. Following placement of the esophagostomy tube, the right mandibular canine tooth was extracted because fixation of the rostral aspect of the mandibular prosthesis would have resulted in trauma to the root of the tooth.

The cat was then repositioned in left lateral recumbency, the skin over the right mandible was clipped and aseptically prepared, and the patient was draped for surgery. The pharynx was packed with gauze swabs to prevent aspiration of blood and fluid during surgery. A mouth gag was placed between the left mandibular and maxillary canine teeth to maintain the mouth in an open position. The gingival mucosa was incised along the axial and abaxial aspects of the right mandible from the canine tooth to the angle of the mandible. The mucosa was reflected with a periosteal elevator to expose the lateral and lingual aspects of the right mandibular body. The skin was incised along the ventral border of the body of the

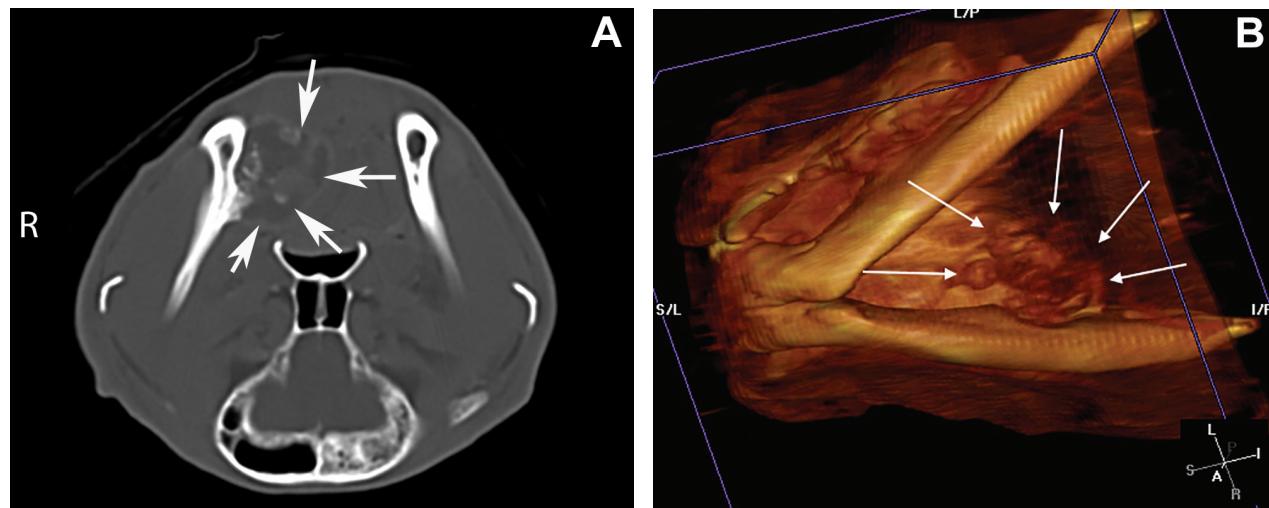
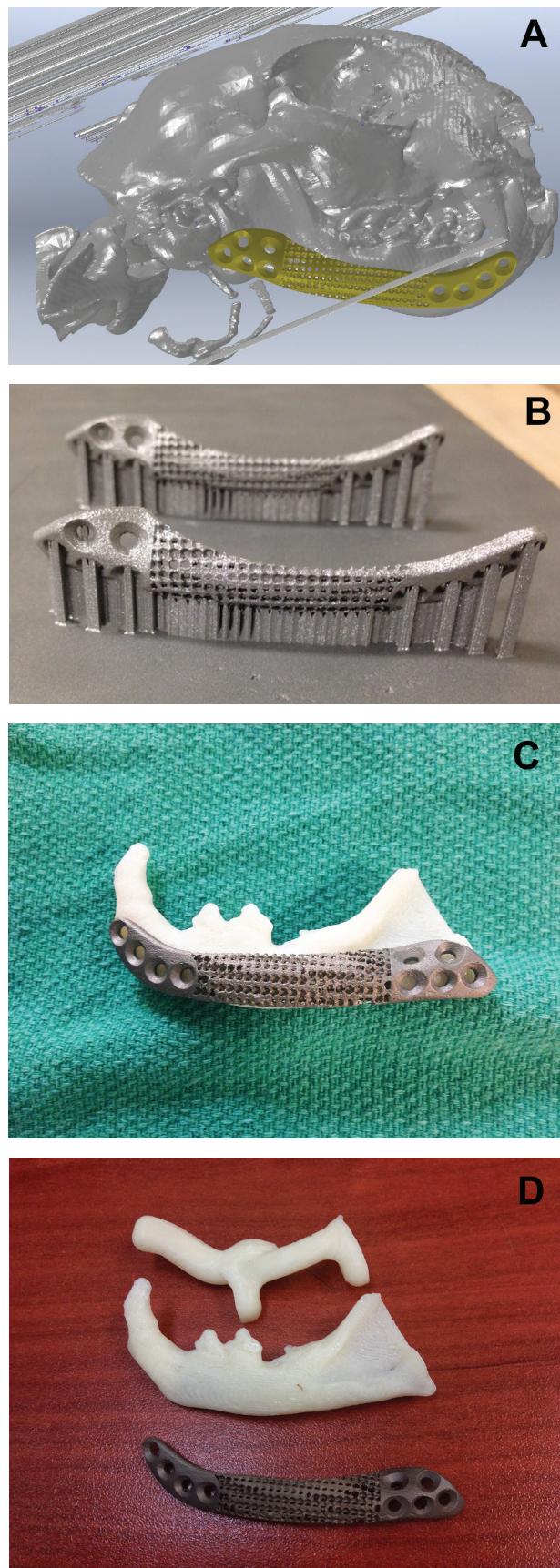


Figure 1—Postcontrast axial CT scan (A) and 3-D volume rendered reconstruction of the CT scan (B) of the head a 12-year-old neutered male domestic shorthair cat with a 2-year history of a mandibular mass. A contrast-enhanced, well-circumscribed mass (arrows) is visible arising from the lingual aspect of the caudal mandibular body. The mass is lytic, but there is no evidence of invasion into the mandible. I/R = Inferior/right. L/P = Left/posterior. S/L = Superior/left.



mandible. Through this incision, the digastricus muscle was elevated from the ventral aspect of the caudal portion of the right mandible and the masseter muscle was elevated from the lateral aspect of the body of the mandible. The prefabricated cutting guide was applied to the right third premolar, and rostral and caudal osteotomies were performed with a sagittal saw. The mandibular segment, which included the 20 X 22-mm mandibular mass and gross margins of 15 mm rostrally and 5 mm caudally, was removed.

The surgical site was lavaged with sterile saline (0.9% NaCl) solution. The oral mucosa and submucosa were closed in 2 layers with 3-0 polydioxanone in a continuous suture pattern. The surgical team applied new gloves and obtained new instruments, and the surgical site was again copiously lavaged with sterile isotonic saline solution to minimize the risk of contamination. The 3-D-printed titanium mandibular prosthesis was then inserted into the segmental mandibular defect through the ventral skin incision and secured to the remaining mandible with five 2.0-mm cortical titanium screws caudally and four 2.0-mm cortical titanium screws rostrally (**Figure 3**). The surgery site was lavaged with sterile saline solution. The ventral skin incision was closed in 3 layers, with the glossal and digastricus muscles closed with 3-0 polydioxanone in a simple continuous suture pattern, subcutaneous tissue closed with 3-0 poliglecaprone 25^a in a simple continuous suture pattern, and skin closed with 4-0 polypropylene^b in a cruciate pattern. Postoperative radiography revealed good positioning of the mandibular prosthesis and placement of the esophagostomy tube (**Figure 4**). No evidence of mandibular drift or malocclusion was detected clinically or radiographically.

Immediate postoperative management included continuation of IV administration of crystalloid fluid (1.4 mL/kg/h [0.6 mL/lb/h]) and continuous rate infusions of hydromorphone (0.0125 to 0.025 mg/kg/h [0.006 to 0.011 mg/lb/h]) and ketamine (0.2 to 0.4 mg/kg/h [0.09 to 0.18 mg/lb/h]), meloxicam (0.1 mg,

Figure 2—Image created (A) and photographs of various stages of prosthesis development (B through D) during computer-aided design of the mandibular prosthesis on the basis of stereolithographic files obtained from the CT scan represented in Figure 1. B—The initial result of computer-aided manufacture of the 3-D-printed mandibular titanium prosthesis with 2 versions of the prosthesis printed. C—The 3-D-printed mandibular titanium prosthesis following CAD-CAM, positioned in the planned location of the implant on a 3-D-printed model of a partial right mandible of the cat. D—The separate 3-D-printed components included, from top to bottom, the prefabricated osteotomy guide, partial mandible model, and customized titanium prosthesis. The prefabricated osteotomy guide was autoclavable and fitted intraoperatively to the third premolar (the canine tooth was intended as a second point of fixation of this guide but had been extracted for fixation of the prosthesis) to assist in positioning of the rostral and caudal osteotomy sites to ensure ideal placement of the mandibular prosthesis.

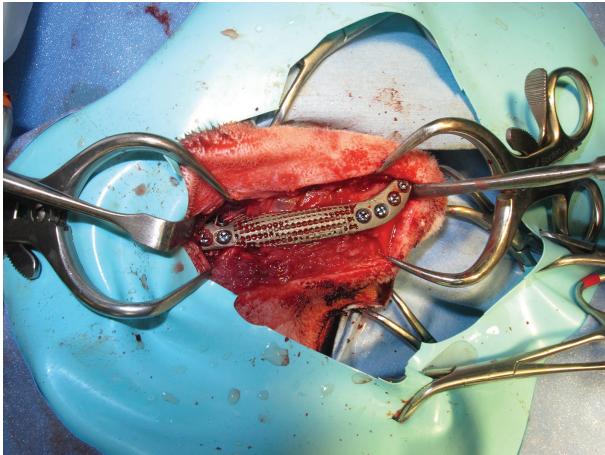


Figure 3—Intraoperative photograph of the customized 3-D-printed titanium prosthesis fixed in position with titanium screws in the cat in Figure 1. The prosthesis was used to reconstruct a segmental defect of the right mandibular body following segmental mandibulectomy for resection of a mandibular osteosarcoma.

q 24 h, SC), and cephalazolin (22 mg/kg, IV, q 6 h for 24 hours). The ketamine and hydromorphone continuous rate infusions were discontinued 11 and 25 hours after surgery, respectively.

The cat recovered well from surgery and was discharged from the hospital 1 day later with meloxicam (0.05 mg, PO, q 24 h for 14 days), buprenorphine (20 µg/kg [9.1 µg/lb], PO, q 12 h for 5 days), and amoxicillin-clavulanic acid (13.75 mg/kg [6.25 mg/lb], PO, q 12 h for 7 days). The cat did not eat in the hospital but started eating at home after being discharged. The cat was eating normally by 3 days after surgery. Supplemental tube feeding was not required, and the esophagostomy tube was removed 7 days after surgery.

Histologic evaluation of the mass revealed findings consistent with osteosarcoma, with 2 to 3 mitoses/hpf, mild necrosis, prominent and pleomorphic nucleoli, and invasion into adjacent tissue. The tumor had been completely excised.

The cat was reassessed 13 days after surgery because of concern regarding the rostral aspect the oral incision. Oral examination revealed partial necrosis of the rostral mandibular mucosa, most likely secondary to contact from the ipsilateral maxillary canine tooth. The cat was anesthetized and endotracheally intubated as for the previous surgery. Ampicillin was administered (22 mg/kg, IV) at induction of anesthesia, and crystalloid fluid was administered IV at a rate of 10 mL/kg/h throughout the surgical procedure. Preoperative dental radiography revealed resorption of the left and right maxillary third premolars. The right maxillary canine tooth was extracted, and crown amputation of the left and right maxillary third premolars was performed. The necrotic and traumatized rostral mandibular mucosa was debrided and closed with 5-0 polyglycaprone 25^a in a simple interrupted suture pattern. The cat was discharged

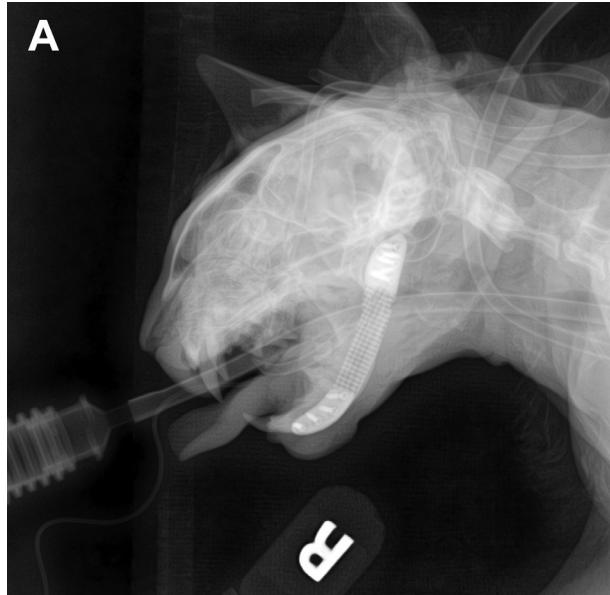


Figure 4—Lateral (A) and ventrodorsal (B) postoperative radiographic views showing good position of the prosthesis and reconstructed mandible of the cat in Figure 1.

from the hospital on the same day with meloxicam (0.05 mg, PO, q 24 h for 7 days), codeine (0.5 mg/kg, transdermal, q 12 h for 3 days), and amoxicillin-clavulanic acid (13.75 mg/kg, PO, q 12 h for 7 days).

Pre- and postcontrast CT of the head, neck, and thorax were performed 7 months after surgery, as previously described, and there was no evidence of local tumor recurrence, regional metastasis, or pulmonary metastasis. The mandibular prosthesis and screws were stable, with no evidence of failure or

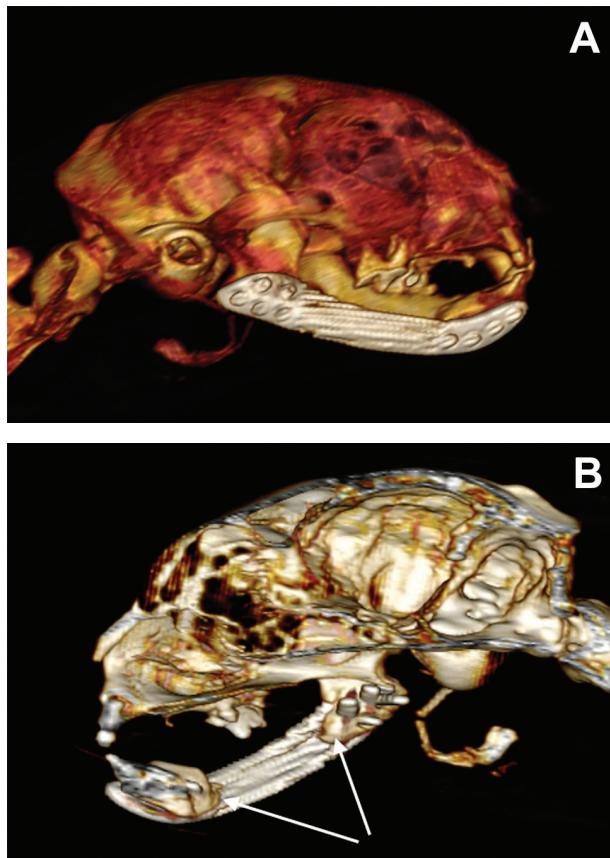


Figure 5—Lateral (A) and lingual (B) 3-D volume rendered reconstructions of the CT scan performed 7 months following mandibular reconstruction in the cat in Figure 1, showing an intact mandibular titanium prosthesis with no evidence of failure and possible osseous integration (arrows).

infection (**Figure 5**). Fourteen months after surgery, the cat was alive and disease free. No further complications were reported, and the cat continued to eat without difficulty or pain.

Discussion

To the authors' knowledge, this is the first report of mandibular reconstruction in a cat. Mandibular reconstruction, primarily following resection of mandibular tumors, has been reported in both dogs and humans. In dogs, reported techniques include free cortical ulnar and rib autografts with autogenous cancellous bone graft following segmental mandibulectomy,^{2,3} rib allograft with recombinant human bone morphogenetic protein 2 following segmental mandibulectomy,⁴ and absorbable compression resistant matrix (containing collagen, hydroxyapatite, and tricalcium phosphate soaked in recombinant human bone morphogenetic protein 2) following segmental mandibulectomy^{5,6} and bilateral rostral mandibulectomy.⁷ Common techniques used in humans for reconstruction of segmental mandibular defects include vascularized free osteocutaneous grafts,⁸⁻¹⁰

particularly fibular osteocutaneous grafts, and distraction osteogenesis.¹¹

The increase in the availability of CT planning has resulted in advances in the management of mandibular defects in humans, including creation of 3-D models of the affected mandible for surgical planning (such as prebending and improved fitting of titanium plates, optimization of bone-to-bone contact, and shorter duration of surgery),^{9,12-19} creation of prefabricated intraoperative guides (for optimization of the length and number of fibular grafts, improved fitting of titanium plates, and improved postoperative cosmetic appearance and function),^{9,16,19-21} and development of CAD-CAM customized and patient-specific 3-D-printed reconstruction plates^{9,22} and prostheses.²³ Customized 3-D printing of mandibular prostheses provides several theoretical advantages over other techniques, such as the ability to design the prosthesis to match the geometry and weight of the original mandible to better withstand the bending, torsion, and shear forces associated with mastication as well as the incorporation of tissue engineering technology into the prosthesis to promote its osseous integration.²³ However, despite isolated Web-based reports of the use of customized 3-D-printed prostheses for the reconstruction of mandibular defects in humans, there are no peer-reviewed publications describing the use of a CAD-CAM customized 3-D-printed prosthesis for mandibular reconstruction in any other species.

The need to reconstruct mandibular defects in dogs is controversial. Segmental and hemimandibulectomies result in mandibular drift with consequent malocclusion.²⁴⁻²⁷ In dogs, mandibular drift infrequently results in functional problems.²⁴⁻³⁰ In 1 study,²⁴ the median time to returning to voluntary eating was 1.0, 2.0, and 2.5 days following unilateral rostral, bilateral rostral, and total mandibulectomy, respectively. In another study,²⁶ 5% of 81 dogs treated with mandibulectomy had eating difficulties after surgery. In contrast, in cats, mandibulectomy is associated with a high complication rate.¹ Regardless of the mandibulectomy procedure, only 5% of 40 cats had no short-term (< 4 weeks) adverse effects, with dysphagia or inappetence in 73% of cats, mandibular drift in 43% of cats, pain in 20% of cats, malocclusion resulting in palatine trauma in 10% of cats, and TMJ crepitus in 5% of cats.¹ Long-term (> 4 weeks) complications were also common, with dysphagia or inappetence, mandibular drift, and TMJ crepitus persisting in 42%, 37%, and 3% of 38 cats, respectively, whereas the incidence of palatine trauma secondary to malocclusion increased to 18%.¹ Furthermore, 12% of cats never returned to voluntary eating following mandibulectomy.¹ The cause of these eating difficulties is unknown and is likely to be multifactorial, but mandibular drift with the associated malocclusion and pain are possible contributors. If that is the situation, then reconstruction of a mandibular defect may decrease the risk of eating difficulties following man-

dibulectomy in cats. Although definitive conclusions cannot be made on the basis of a single case, the cat of the present report had no apparent eating difficulties following surgery, supporting the supposition that mandibular reconstruction may be beneficial in cats treated with mandibulectomy.

The cat of the present report was an ideal candidate as a preliminary case for mandibular reconstruction because of the type, location, and local characteristics of the tumor. Osteosarcoma is an uncommon bone tumor in cats and rarely described in the mandible, accounting for between 0% and 5% of all feline osteosarcoma cases³¹⁻³⁴ and 14% of mandibulectomy cases.¹ In a series of 6 cats with mandibular osteosarcoma treated with mandibulectomy, 1 cat developed local tumor recurrence and was euthanized and the remaining 5 cats survived for at least 2 years following mandibulectomy with no evidence of either local recurrence or regional or distant metastasis.¹ Appendicular osteosarcoma has a low metastatic rate in cats, ranging from 0% to 7%,³¹⁻³³ and mandibular osteosarcoma in dogs has a less aggressive biological behavior than osteosarcoma in appendicular and some axial sites.^{35,36}

The osteosarcoma in the cat of the present report was slowly recurrent with no evidence of metastasis over the 2-year period prior to referral, which suggested a tumor with low aggressive biological behavior and was consistent with published reports^{1,31-33} of osteosarcoma and mandibular osteosarcoma in cats. Furthermore, the tumor was restricted to the 1 location, with minimal evidence of bone invasion on CT scans, and distant to both the TMJ and mandibular symphysis. Hence, segmental resection was possible with adequate surgical margins while preserving the TMJ. Wider caudal margins would have been preferable, but the locations of the osteotomy sites were determined by the prefabricated cutting guide and revising the location of the caudal osteotomy would have resulted in less than ideal placement of the mandibular prosthesis and possible consequent malocclusion. Furthermore, the tumor appeared to be noninvasive on CT scan and the surgical margins required for excision of osteosarcoma are unknown.

In contrast to the mandibular osteosarcoma in the cat of the present report, squamous cell carcinoma is the most common oral tumor³⁷⁻³⁹ in cats and is usually extensive and invasive.⁴⁰ As a result, total or subtotal mandibulectomy, occasionally with resection of some portions of the contralateral mandible, is often required for complete excision of oral squamous cell carcinoma.¹ Reconstruction of large mandibular defects with free osteocutaneous fibular grafts is a particular challenge in human medicine because of the complexity of harvesting and contouring the grafts and contouring titanium reconstruction plates.^{23,41-43} The autogenous mandibular reconstruction techniques used in dogs and humans have not been investigated in cats, but the ulna and fibula are likely too small to act as autogenous cortical bone grafts, particularly relative to the large size of mandibular

defects. An additional consideration in humans is that autogenous grafts are associated with harvest-site complications and long-term adverse effects, such as chronic pain and decrease in function.⁴⁴ A CAD-CAM customized and patient-specific 3-D-printed titanium prosthesis is an attractive option for mandibular reconstruction in cats because the mandibular prosthesis can be designed and manufactured regardless of the size of the mandibular defect. The prosthesis can also be optimized for conformity to the remaining mandible and designed to preserve ligamentous and muscular attachments (for maintenance of masticatory function) and promote osseous integration with host bone.

The biomechanics of the mandible in cats need to be studied to further optimize prosthesis design, and the design and manufacture of the mandibular condyle to reconstruct the TMJ following total mandibulectomy needs to be investigated. In humans, total alloplastic TMJ replacement is performed for treatment of ankylosis⁴⁵ and idiopathic-progressive condylar resorption⁴⁶ with satisfactory results; however, this involves replacement of both the temporal and mandibular components of the TMJ rather than just the mandibular condyle. Replacement of the mandibular condyle with preservation of the temporal component of the TMJ has not been described. Cats maintain good clinical function following condylectomy for various nonneoplastic diseases, such as articular and extra-articular ankylosis,⁴⁷⁻⁴⁹ despite postoperative evidence of mild malocclusion,⁴⁸ and so it is possible that a prosthetic mandibular condyle or total alloplastic TMJ replacement may not be required for mandibular reconstruction following total mandibulectomy. However, a cadaveric biomechanical study⁵⁰ revealed significant differences in occlusion following unilateral mandibular condylectomy in clinically normal cats, so studies of the biomechanical and clinical importance of the necessity of the mandibular condyle are required to optimize mandibular prosthesis design. Lastly, study of a clinical series of cats is required to determine the clinical outcome and short- and long-term complications associated with mandibular reconstructions by use of CAD-CAM customized 3-D-printed titanium prostheses.

The only complication noted for the cat of the present report was trauma to the rostral mandibular mucosa secondary to contact from the ipsilateral maxillary canine tooth. Minimal distance exists between the lateral surface of the rostral portion of the mandible and the lingual aspect of the maxillary canine tooth, and the thickness of the mandibular prosthesis (despite being < 2 mm) was likely sufficient to position the rostral mandibular mucosa laterally into the occlusal plane of the maxillary canine tooth and result in mucosal trauma. This resolved following extraction of the maxillary canine tooth. Although not a complication, the ipsilateral mandibular canine tooth required extraction at the time of mandibular resection and reconstruction because of unforeseen circumstances at the time the mandibular prosthesis

was designed. This tooth was extracted because fixation of the rostral aspect of the mandibular prosthesis would have caused trauma to the tooth root and may have resulted in pain, eating difficulties, and mechanical failure of the mandibular prosthesis.

In cats and dogs, tooth roots and neurovascular structures comprise most of the bone volume in the mandibles and maxillas, and avoiding these structures is important during mandibular and maxillary fracture repair.⁵¹ This is a further challenge in the rostral portion of the mandible because the canine tooth root fills most of the mandible.⁵² The rationale for avoiding the tooth roots is the high likelihood of tooth death and consequent periapical periodontitis resulting in an infection and potential implant failure.^{53,54} Endodontic treatment of the canine tooth prior to fixation of the prosthesis would have been an alternative to tooth extraction.⁵¹ Future attempts at mandibular reconstruction with CAD-CAM customized 3-D-printed titanium prostheses should account for both of these anatomic features to avoid similar complications, by either prosthesis design or surgical planning.

Common complications in other prosthetic surgeries in small animals, primarily dogs treated with limb-sparing surgery^{55,56} or total joint replacement,⁵⁷⁻⁶⁰ include implant-associated infection and implant failure. Implant-associated infection is a major concern following mandibular reconstruction because the rich microflora of the oral cavity of cats^{61,62} can result in contamination of the surgical site and predispose to implant-associated infection. To minimize this risk, the surgical site should be thoroughly lavaged, the intra-oral incision should be closed following excision of the mandibular tumor, and a ventral extraoral approach should be used to secure the mandibular prosthesis with the use of new gloves and surgical instruments. Future considerations to minimize the risk of implant-associated infection include the use of tissue engineering technology to embed slow-release antimicrobial or silver nanoparticles into the prosthesis.⁶³⁻⁶⁸ Implant failure has been reported in humans following mandibular reconstruction with free fibular grafts because of failure to counteract the complex biomechanical forces (bending, torsional, and shearing) acting on the mandible as a result of the actions of individual masticatory muscles during chewing and the magnitude of forces generated during biting.^{42,43} As mentioned previously, biomechanical studies are required to further elucidate the direction and magnitude of these forces in clinically normal cats to provide information for the optimal design of CAD-CAM customized 3-D-printed mandibular prostheses to minimize the risk of implant-prosthesis failure.

The mandibular reconstruction in the cat of the present report involving a CAD-CAM patient-specific and customized 3-D-printed titanium prosthesis resulted in immediate return to voluntary eating, thus avoiding a common and debilitating complication of mandibulectomy without reconstruction in cats. Although research is required to optimize the design

and manufacture of mandibular prostheses and determine short- and long-term outcomes in a greater number of patients, the outcome for this cat suggested that mandibular reconstruction with CAD-CAM customized 3-D-printed titanium prostheses may be the preferred technique for the surgical management of cats with mandibular tumors.

Acknowledgments

The authors declare that they had no financial conflicts of interest.

Footnotes

- a. Monocryl, Ethicon, Johnson & Johnson, Cornelia, Ga.
- b. Prolene, Ethicon, Johnson & Johnson, Cornelia, Ga.

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From this month's AJVR

Randomized, controlled clinical trial of safety and plasma concentrations of diclofenac in healthy neonatal foals after repeated topical application of 1% diclofenac sodium cream

Susan E. Barnett et al

OBJECTIVE

To determine the plasma pharmacokinetics and safety of 1% diclofenac sodium cream applied topically to neonatal foals every 12 hours for 7 days.

ANIMALS

Twelve 2- to 14-day old healthy Arabian and Arabian-pony cross neonatal foals.

PROCEDURES

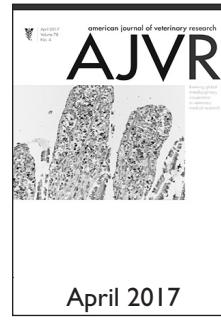
A 1.27-cm strip of cream containing 7.3 mg of diclofenac sodium ($n = 6$ foals) or an equivalent amount of placebo cream (6 foals) was applied topically to a 5-cm square of shaved skin over the anterolateral aspect of the left tarsometatarsal region every 12 hours for 7 days. Physical examination, CBC, serum biochemistry, urinalysis, gastric endoscopy, and ultrasonographic examination of the kidneys and right dorsal colon were performed before and after cream application. Venous blood samples were collected at predefined intervals following application of the diclofenac cream, and plasma diclofenac concentrations were determined by liquid chromatography–mass spectrometry.

RESULTS

No foal developed any adverse effects attributed to diclofenac application, and no significant differences in values of evaluated variables were identified between treatment groups. Plasma diclofenac concentrations peaked rapidly following application of the diclofenac cream, reaching a maximum of < 1 ng/mL within 2 hours, and declined rapidly after application ceased.

CONCLUSIONS AND CLINICAL RELEVANCE

Topical application of the 1% diclofenac sodium cream to foals as described appeared safe, and low plasma concentrations of diclofenac suggested minimal systemic absorption. Practitioners may consider use of this medication to treat focal areas of pain and inflammation in neonatal foals. (Am J Vet Res 2017;78:405–411)



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