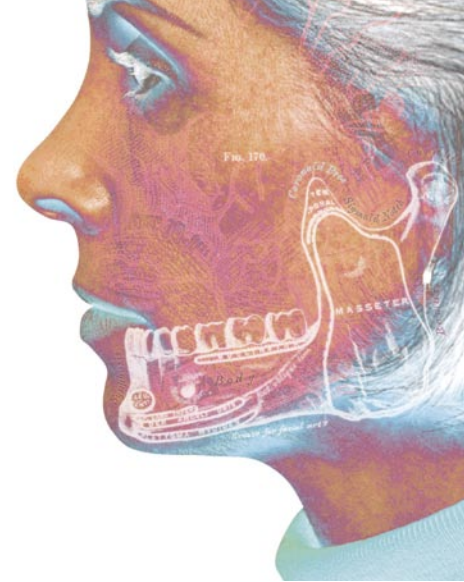


Dental Management of Chemoradiation Patients

Evelyn M. Chung, DDS, and Eric C. Sung, DDS



ABSTRACT

The utilization of combined chemoradiation therapy has recently increased in the treatment of head and neck cancers. This patient population is significantly more prone to various oral complications during and after medical therapy. Oral complications and long-term effects include mucositis, xerostomia, alterations in taste, vascular compromise, mucosal thinning and increased risk of rampant caries and periodontal disease. The most serious oral complication that can arise is osteoradionecrosis. Managing patients properly prior to medical treatment can help decrease these potential complications during and after treatment.

This purpose of this article is to review the different radiation and chemotherapy regimens used to treat patients with head and neck cancers, as well as protocols in the dental management of these patients before, during, and after medical treatment.



Surgery and/or radiotherapy, RT, are used routinely in the management of neoplasms of the head and neck region and treatment can be curative if tumors are diagnosed early (stage I and II).¹ RT is defined as the therapeutic use of ionizing radiation. Ionizing radiation disrupts and ultimately causes cellular death in replicating cells. RT can be delivered by an external source (external beam), or as a sealed radioactive material delivered close to the tumor site (brachytherapy). Either approach is effective in destroying most tumors, but the amount of radiation is limited by the tolerance of the normal surrounding tissues.

External beam RT is delivered in a series of treatments called fractions over a period of approximately five to seven weeks. Total dose is ultimately determined by the type and staging of the tumor. Modifications of conventional fractionation consist of hyperfractionation, accelerated fractionation and, more recently, the use of inten-

Authors / Evelyn M. Chung, DDS, is a clinical associate professor and co-director, Hospital Dentistry, Division of Advanced Prosthodontics, Biomaterials and Hospital Dentistry, clinical director, General Practice Residency Program. Eric C. Sung, DDS, is a clinical professor and chair, Hospital Dentistry, Division of Advanced Prosthodontics, Biomaterials and Hospital Dentistry, residency program director, General Practice Residency Program.

sity-modulated radiotherapy, IMRT. Hyperfractionation consists of increasing the total dose by increasing the total number of fractions and the number of fractions per day, but decreasing the dose per fraction. Although this method may improve tolerance to the late effects of radiation, it may increase the severity of the acute effects of radiation (oral mucositis). Accelerated fractionation decreases the total treatment time without changing the total dose by decreasing the dose per fraction and increasing the number of fractions per day. This method is employed to decrease treatment time and to increase tumor growth control by maintaining a lethal dose rate equivalent to the accelerated repopulation of tumor cells. However, like hyperfractionation, acute reactions can be severe and are usually dose-limiting. Intensity-modulated radiation therapy is an advanced mode of high-precision radiotherapy that utilizes computer-controlled X-ray accelerators to deliver precise radiation doses to a malignant tumor or specific areas within the tumor.

Brachytherapy consists of interstitial (direct insertion into tissue), intracavitary (placement within a cavity) or surface applications (molds). The advantage to this procedure is that it allows a high dose of radiation to be delivered directly or very close to the tumor site while sparing normal surrounding tissues. The disadvantage to this approach is underdosing portions of the tumor volume.

Side Effects of Radiation Therapy

During RT, acute effects (Table 1) on the oral mucosa include erythema, edema, ulceration and ultimately, desquamation (mucositis). The edema can often lead to cheek biting and the inability to wear a dental prosthesis. Mucositis is usually most severe in the soft palate (Figure 1) followed by, in descending order, the mucosa of the hypopharynx, floor of the mouth, buccal mucosa, base

Table 1

Effects of Radiation Therapy

| Acute effects of RT | Long-term effects of RT |
|--|---|
| <ol style="list-style-type: none"> 1. Erythema, swelling, pain 2. Desquamation and ultimately ulcerations (radiation-induced mucositis) 3. Inability to wear dental prostheses 4. Increased risk for fungal infections 5. Loss or alteration of taste 6. Trismus 7. Reduction in salivary output as well as changes in viscosity, pH and constituents | <ol style="list-style-type: none"> 1. Epithelial atrophy 2. Loss of keratinization 3. Telangiectasis of mucosa 4. Xerostomia 5. Increased risk for fungal infections 6. Delayed healing 7. Decreased bone remodeling ability 8. Possible increased risk for ORN 9. Decreased pulpal response 10. Possible inability to wear dental prostheses |

of the tongue, and the dorsum of the tongue. Tissue areas that have rapidly dividing cells are usually affected the most. Severity and location of the mucositis are dependent on the field and dose of radiation, but can vary from patient to patient. If the pain is severe, RT may need to be stopped until the patient is sufficiently recovered to continue with treatment. Treatment for the side effects during this time is supportive and symptomatic. Once the radiation treatment has been completed, the mucositis resolves in about two to four weeks.

Late effects (Table 1) include reduction in salivary flow, compromised buffering capacity of the saliva, temporary or permanent partial or complete loss of taste (hypoguesia or ageusia), and a decrease in keratinization of the mucosa. Decreased vascularity and increased fibrosis at the submucosal level may result in trismus, dysphagia, and at high doses may result in osteoradionecrosis, particularly in the mandible. Pulpal tissues also become hypocellular, atrophied and sometimes fibrotic.² Decreased salivary volume, buffering capacity and immunologic functions of saliva, predispose to changes in the oral flora and result in increased risk of dental caries. The

changes in saliva quantity and quality are usually permanent, especially in the range of radiation dose used for treatment of most head and neck cancers. Loss or changes in taste is usually most severe during and immediately following RT, and may return to normal gradually over a period of several years. Loss of keratinization in the oral mucosa leads to thin, friable tissue with prominent telangiectasias prone to ulcerations from minimal trauma (Figure 2). The most severe complication of head and neck RT is osteoradionecrosis, ORN, in which irradiated bone is exposed due to trauma or infection and fails to heal over a period of three months or longer in duration. ORN is seen most commonly in the mandible because the bone is dense thus absorbing more radiation and its unique blood supply as compared to the maxilla. If the total dose of radiation to the mandible exceeds 6500 cGy and the field consists of more than 75 percent of the mandible, there is an increased chance of ORN.³ Changes in the bone that predispose to ORN include: obliteration of fine vasculature, progressive fibrosis, loss of normal marrow cellular elements, and fatty degeneration of the bone marrow. As a result, bone is less able



Figure 1. Erythema and mucositis of the soft palate resulting from radiation therapy.



Figure 2. Thin tissues and telangiectasis present in areas of high-dose irradiation.



Figure 3a. Clinical view of osteoradionecrosis (ORN) arising in the furcation of a mandibular first molar.

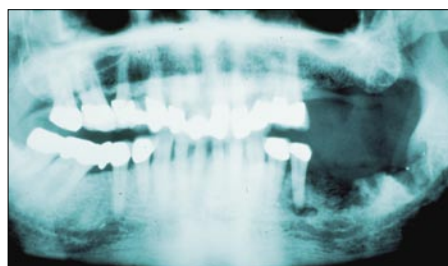


Figure 3b. Panoramic view of ORN in the left mandible.

to remodel and heal following trauma or infection. Clinical presentation of ORN may include pain, suppuration, exposed necrotic bone and pathologic fracture (Figures 3a and b).

Chemoradiation Therapy

Chemo RT is being used with increasing frequency, particularly for treatment of carcinomas of the nasopharynx, base of tongue, and tonsillar region. It is commonly employed and most effective when used concurrently with radiation therapy for advanced lesions (Stage III and IV), recurrent and/or metastatic squamous cell carcinomas, especially those with lymph node involvement when surgery and RT may not be sufficient to control the cancer.⁴ Expectations of CT include increasing the cure rate by either improved locoregional tumor control, elimination of micrometastases or tissue preservation

during surgery.

Chemotherapeutic agents such as 5-fluorouracil (5-FU) and the platinum compounds (cisplatin) enhance radiosensitization by disrupting DNA synthesis. 5-fluorouracil prevents angiogenesis thus inhibiting the formation and further growth of neoplasms. Cisplatin prevents DNA replication thus disrupting tumor cell growth. It is one of the most actively used chemotherapeutic regimens for the treatment of head and neck squamous cell carcinomas and has been recognized in some studies to possibly prolong the survival in patients with recurrent and/or metastatic head and neck cancer.⁵⁻⁷

In a study published by the Department of Veterans Affairs Laryngeal Cancer Study Group, induction chemotherapy, CT, plus RT compared with just surgery and RT in patients with advanced laryngeal cancer provided the

same two-year survival rate for both treatment groups.¹ Based on this study, chemo RT is used more in the overall management of oral neoplasms. Other studies performed evaluating the efficacy of chemo RT following surgical resection of head and neck cancers suggest that this modality of treatment may have a beneficial effect on locoregional control of tumors in patients that have multinodal involvement, rupture of the tumor through the lymph node capsule and/or microscopic involvement of the resected margins.^{8,9}

Side Effects of Chemoradiation Therapy

When a patient undergoes concomitant chemo RT, the acute oral complications are significantly more severe than those associated with radiation alone.¹⁰ Oral mucositis is considerably more severe and results in premature termination or disruption of treatment in 25 percent of the patients. Most patients require gastric tubes in order to make it through treatment, and the oral mucositis may last up to six months following therapy compared to two to four weeks with radiation alone. The main systemic side effects of CT consist of myelosuppression, hemorrhaging, nausea and vomiting, peripheral neuropathy, tinnitus, nephrotoxicity, hepatotoxicity and in some cases, cardiotoxicity.¹¹

With emerging trends of chemo RT as a prime multimodal approach in the management of oral cancer, increased attention should be given to the oral complications and their appropriate management. As mentioned previously, acute and late adverse effects are more severe in this treatment population than in patients treated by RT alone.^{7,12} Adverse effects are heightened with concomitant chemo RT, since chemotherapy potentiates the effects of RT. These effects include oral mucositis, severe trismus, dysgeusia, dysphagia, salivary dysfunction, impaired lymphatic drainage,

infection, detrimental changes in the mucosa and periodontium, increased risk of dental caries, increased risk of osteoradionecrosis, even in the maxilla, and nutritional complications.^{7,12} The role of dental professionals at all points of treatment is essential in the management of this patient population since the immediate and long-term effects of treatment such as ORN, rampant caries, and periodontal disease fall within the realm of dentistry.

Pretreatment Evaluation and Management

These patients should be seen by a dental professional with training or experience in treating these type of patients prior to undergoing any chemoradiation or radiation therapy (Table 2). A thorough medical and dental history and detailed clinical and radiographic examination should be obtained. The dose, type and fields of RT and the long-term prognosis of the patient are essential factors to help determine whether or not carious and/or periodontally involved teeth should be treated conservatively or be extracted. Knowing the fields of radiation is necessary since the larger the area radiated, the greater the morbidity. For example, if the major salivary glands are within the fields, mean salivary output can be significantly reduced 86 percent to 93 percent.¹³ If severe xerostomia following RT is anticipated, custom-fitted fluoride trays should be fabricated. The fluoride trays should be soft, well-fitting, and comfortable without any sharp edges. Patients apply a topical fluoride gel daily with these custom trays, and in compliant patients postirradiation dental caries can be prevented.¹⁴ Casein calcium phosphate may also be used for remineralization of enamel.¹⁵ Patients suffering from xerostomia should also be encouraged to keep the oral mucosa moist either by water, noncariogenic liquids or saliva substitutes. Pilocarpine has been proposed by some as a means of increasing salivary output, but the

Table 2

Summary of Dental Management of Chemo RT Patients

Pretreatment considerations

1. Comprehensive medical history and exam, full-mouth radiographs
2. Consultation with oncology team to delineate fields of RT and the use of concomitant CT
3. Full-mouth prophylaxis or scaling and root planing
4. Extractions of teeth with questionable and poor prognosis due to caries, periodontal disease, failing endodontic therapies, or patient compliance
5. Restoration of dental caries
6. Evaluation of any removable prostheses for proper fit and any needed adjustments
7. Fabrication of custom-fitted fluoride trays
8. Emphasis on meticulous oral hygiene to the patient

Perioperative management

1. Palliative treatment as needed
2. Use of mouthrinses for hygiene, lubrication, and/or pain management
3. Prescribe anti-fungal medication, antibiotics, and/or oral analgesics if necessary
4. Emphasis on meticulous oral hygiene to the patient

Postoperative management

1. Frequent dental recall examinations (every three months)
2. Restorations of dental decay
3. Consultation with radiation oncologist prior to oral surgical procedures
 - Low risk of ORN <5500 cGy
 - Moderate risk of ORN 5500-6500 cGy
 - High risk of ORN >6500 cGy
4. Use of oral lubricants to treat xerostomia
5. Prescribe anti-fungal medication and/or antibiotics, if necessary
6. Emphasis on meticulous oral hygiene to the patient as well as daily application of fluoride gel in custom carriers

results have been mixed.^{16,17}

At radiation doses below 5500 cGy, compromised teeth in the fields of radiation may not need to be extracted prior to RT. Generally, at doses below this level, postradiation extractions may be performed without any unfavorable complications, even in the mandible. However, at doses higher than 5500 cGy, the mandible may be predisposed to ORN and extractions of teeth in the field should be considered prior to RT.

Questionable teeth include those with class II or III furcation involvements, periodontal disease, gross caries or periapical pathology (Table 3).

Preradiation extractions should be performed in conjunction with radical alveolectomy and primary closure of the surgical site with minimum tension of the tissue flaps. Postextraction healing time usually requires seven to 10 days. A follow-up visit should be scheduled to ensure the wound sites have healed suf-

Table 3

Criteria for Preradiation Extractions

DENTAL DISEASE FACTORS

Condition of the residual dentition

- Advanced caries
- Periapical infection
- Periodontal bone loss
- Furcation involvement

Dental compliance of the patient

An aggressive policy of extraction is recommended in patients with poor dental compliance.

Maxillary teeth vs. mandibular teeth

Mandibular teeth are scrutinized more closely than maxillary teeth, since maxillary teeth in the field can be extracted postradiation with minimal risk of osteoradionecrosis.

ficiently without dehiscence of the flaps prior to initiation of RT or chemo RT. There are times that treatment needs to be initiated urgently. In such cases, it may not be possible to properly treat compromised teeth. Risks and possible complications of leaving these teeth untreated should be addressed by the oncology team.

Information about the type of CT regimen, such as the agents being used and the number of cycles of CT should also be obtained. The dose and type of CT is useful because it may reflect the amount of myelosuppression and severity of stomatitis to be anticipated. The schedule of the CT is also important because it may affect the timing and the type of dental treatment that should be rendered for the patient. Following each cycle, a patient's ability to recover from the effects of CT may become weaker due to the cumulative toxicities to the bone marrow, kidney, and nervous system.¹⁸ In a chemo RT patient, if the dose to the tumor area exceeds 5500 cGy, the patient may become susceptible to ORN. Currently, no studies have been reported that have definitively linked CRT with an increased incidence of ORN. However, emerging clinical

trends point to such an increase.¹⁹

Regardless whether the patient is having RT alone or chemo RT, priority should be to rule out all potential sources of dental infection prior to the start of cancer treatment (Table 2). Urgent treatment should be rendered first with less urgent dental needs addressed after the therapy is completed. Most importantly, during the patient's nadir, or when the patient is the most myelosuppressed and pancytopenic, all dental treatment should be avoided. Treatment prior to chemo RT should include dental prophylaxis, scaling and root planing, definitive restorations, endodontic therapy and/or extractions in order to ensure that the patient is at a low risk for an oral source of sepsis. Subacute odontogenic infections should be treated more aggressively in this patient population since myelosuppression will occur and dormant disease or infection could subsequently become active, resulting in sepsis. Teeth that have only fair or guarded long-term prognosis following chemo RT may need to be extracted. Some clinicians recommend that all mandibular teeth in the field be extracted in patients treated with chemo RT, since these teeth will be

even more difficult to maintain, and it is likely that patient compliance with routine dental care will further decrease following treatment.²⁰

If the patient wears a dental prosthesis, the prosthesis should be assessed. Adjustments should be made at this time to ensure proper fit and function since denture irritation may lead to ORN, sepsis or uncontrolled bleeding. If the prosthesis is so ill-fitting that adjustments cannot be made, it should be left out of patient's mouth, especially during periods of myelosuppression and/or in the presence of mucositis or stomatitis.

Patients should be instructed on the importance of maintaining proper and meticulous oral hygiene during and after medical treatment. Maintaining good oral hygiene during chemo RT helps to decrease the severity of mucositis as well as reduce the probability for sepsis due to oral infections.²¹

Perioperative Management

During this period, most dental treatment consists of palliative care. Typical symptoms are oral discomfort and pain secondary to mucositis. Topical anesthetics such as viscous lidocaine, or dyclonine hydrochloride may help to soothe the oral cavity and permit swallowing. In more severe cases, patients may require systemic analgesics. Many chemo RT patients require gastric tubes due to the severity of mucositis.

Patients who have metal restorations in their teeth that are in the fields of radiation may suffer from radiation backscatter. The soft tissue areas immediately adjacent to these teeth will have increased radiation exposure resulting in a more severe mucosal reaction. This phenomenon can be alleviated by fabricating a plastic mouthguard that physically displaces the soft tissue away from the metal restoration. The mouthguard should be at least 1 millimeter in thickness and should have smooth edges to

prevent further mucosal irritation.

Xerostomia becomes apparent mid-way through treatment. Water, noncarciogenic liquids or salivary substitutes should be used to keep the oral mucosa moist at all times. Oral lubricants can also be used at this stage.

Whether the patient is undergoing RT or chemo RT, preventive oral care and meticulous hygiene must be strongly encouraged during and after treatment. Mouthwashes such as chlorhexidine gluconate can be used to help reduce the oral flora populations which may decrease severity of the oral mucositis. Patients should also brush carefully after every meal with a soft or extra soft toothbrush to prevent bleeding and trauma to delicate soft tissues.

With chemo RT, patients will present with varying amounts of myelosuppression and decreased platelet counts. If platelet counts are low, the patient may be at moderate (platelet count 20,000 to 60,000) or high risk (platelet count <20,000) for prolonged or spontaneous bleeding after minimal trauma. In such cases, the patient should use gauze or soft sponges to clean the teeth in lieu of a toothbrush to reduce the risk of trauma to the gingiva. If the patient is at high risk of spontaneous bleeding, flossing should not be done until the patient's platelet counts have recovered sufficiently.

If an odontogenic or periodontal infection should arise, consultation with the oncologist is advisable and options for treatment discussed. Should definitive treatment be necessary, it should be done as atraumatically as possible and patients should be placed on antibiotics following treatment for at least a week due to the patient's myelosuppression. In part due to myelosuppression and decreased salivary output, these patients can also be at an increased risk for local and systemic fungal infections.²²

With all these changes occurring in the patient's mouth as well as other side effects from their medical treat-



Figure 4. Generalized oral candidiasis.



Figure 5. Rampant radiation caries.

ment, patients often experience loss of appetite, dehydration, and subsequent weight loss. Enriched dietary supplements are useful in these situations, but can also contain high levels of sugar leading to increased caries activity. Therefore, it should again be stressed that patients brush or clean their teeth after every meal.

Post-treatment Management

Immediately following RT or chemo RT, palliative treatment may still be required since mucositis can take several weeks to heal. Once sufficient healing has occurred, the patient should be placed on a very strict and regular regimen of oral care and maintenance. A more frequent dental maintenance interval, approximately every three months, but ultimately dependent on patient compliance, is recommended. During visits, all areas of dentinal and cervical exposure, incisal tips, and any furcation-involved teeth for incipient carious lesions since these are the most vulnerable areas must be examined.²³ The most practical and effective method of keeping oral tissues moist is the intermittent use of water and other noncarciogenic liquids throughout the day in a portable spray bottle. Because of xerostomia, these patients are also at increased risk for fungal infections (Figure 4). The most common locations are the corners of the mouth (angular cheilitis), and

mucosal areas covered with removable prostheses. Patients may experience a burning or painful sensation, or be completely asymptomatic. Treatment is with anti-fungal powders or ointments. Clotrimazole troches, nystatin pastilles and suspensions are not recommended due to the high sugar content of these formulations which could increase the risk of dental caries of this already susceptible patient population.

These patients require daily fluoride treatments for the rest of their lives. Use of 0.4 percent stannous or 1.1 percent neutral sodium fluoride gels is recommended. Because of the high risk of caries, incipient lesions may rapidly progress to larger decayed areas and may need to be treated either with more aggressive fluoride applications (increasing the frequency to twice a day and/or increasing the time of application from four to 15 minutes per treatment) or remineralization solutions.

Cervical caries in the early stages are best treated conservatively with either amalgam or composites. Fluoride releasing restorations probably do not have a significant impact on anti-caries activity since the greatest release of fluoride is usually in the first 24 hours and then drops off considerably.²⁴ Full coverage or partial coverage crowns should be provided only when the patient can demonstrate good oral hygiene, since caries can quickly progress around the

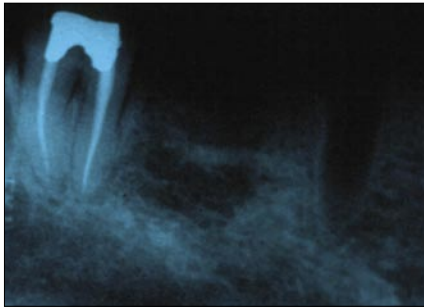


Figure 6a. Radiograph of endodontically treated molar adjacent to ORN.



Figure 6b. Clinical view of endodontically treated molar with crown amputation.

margins of these types of restorations eventually leading to carious amputation of the crown. Should full coverage be warranted, the margins should be placed subgingivally.

Patients with poor compliance may present with rampant caries (Figure 5). For these patients, there are few options. Aggressive caries control along with increased daily fluoride usage should be immediately implemented. Mandibular teeth that are deemed nonrestorable either due to severe caries, periodontal disease, or infection should only be extracted after consultation with the radiotherapist to determine whether or not these teeth were within the field of RT and if the total dose to bone was less than 5500 cGy. For maxillary or mandibular teeth out of the field or maxillary teeth in the field, extractions may be done with relatively low risk of developing ORN. If mandibular teeth in the field of radiation received 6500 cGy or greater, the risk of developing ORN following surgical procedures is substantial and does not consistently respond well to conservative treatment measures such as endodontic therapy (Figure 6a) and crown amputation (Figure 6b) and hyperbaric oxygen may be required.²⁵ Endodontic therapy and root contouring can be employed to reduce the depth of the periodontal pockets and/or expose furcation areas to maintain better hygiene. Should the

furcation area need to be opened using a bur, care should be taken to avoid exposing the interradicular bone. The remaining root tips in either scenario will eventually exfoliate over time while hopefully maintaining mucosal coverage of the underlying bone.

If soft tissue ulcerations occur in the areas of high dose radiation (>6500 cGy), the area should be monitored closely for healing and to rule out recurrence of tumor. Immediate biopsy is not advisable since any surgical procedure can subsequently lead to further bone exposure. In cases where a patient develops ORN, there are many approaches to treatment ranging from periodic conservative debridement and irrigation, to hyperbaric oxygen treatments, combined with surgical resection, sequestrectomy and reconstruction. Beumer reported that in patients who received greater than 6500 cGy or when 75 percent of the mandible was in the fields of RT, ORN did not respond favorably to conservative measures.³ Conservative measures include local debridement, irrigation with saline or chlorhexidine, analgesics and/or antibiotics for acute infections. In more severe cases of ORN, patients can develop fistulas and subsequently pathologic fractures of the mandible. These unfortunate patients may eventually require surgical resection of the involved bone leading to discontinuity defects. Vascularized bone

grafts provide an effective means of restoring the mandible.^{26,27} Because of the severity of ORN, prevention of oral infections through meticulous oral care and hygiene, and daily fluoride treatments is an absolute priority.

Conclusion

Head and neck cancers have traditionally been treated with surgery and/or radiation therapy, but concomitant use of chemotherapy is becoming quite common. However, these patients are faced with difficult dental maintenance issues following their cancer treatments. The dental team needs to actively participate in the delivery and maintenance of proper dental care to control oral complications that may arise due to medical treatments. This will ultimately help to improve a patient's quality of life. ■■■■

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To request a printed copy of this article, please contact / Evelyn M. Chung, DDS, University of California, Los Angeles, School of Dentistry, Box 951668, B3-087 CHS, Los Angeles, CA 90095.