Published in final edited form as:

Curr Oral Health Rep. 2018 March ; 5(1): 7–12.

Periodontal Treatment in Cancer Patients: An Interdisciplinary Approach

A.M. Decker¹, L.S. Taichman², N.J. D'Silva^{1,3}, and R.S. Taichman¹

¹Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA

²Department of Family Medicine, University of Michigan School of Medicine

³Department of Pathology, University of Michigan, Ann Arbor, MI, USA

Abstract

Purpose of Review—Dental care is an essential component in the comprehensive treatment for the cancer patient. As such, a review of the literature was completed to determine the relationships between periodontal and dental care in the cancer patient and provide strategic suggestions.

Recent Findings—Periodontal treatment must be personalized depending on the patient's current oral health status, systemic status, and progress in treatment. Oral mucositis, periodontal status, and osteonecrosis of the jaw (ONJ) remain periodontal concerns in the cancer patient. Contributing factors of ONJ include root amputation (OR= 6.64), extraction of a single tooth (OR=3.7), severe tooth mobility (OR = 3.60), and unclosed wound (OR = 2.51).

Summary—Preventive maintenance, oral hygiene instruction, use of fluoride and chlorhexidine are all important therapeutic strategies. If extractions are required in patients who have received bone modifying drug infusions, flap management and primary wound closure is needed to reduce the risk of complications.

Keywords

Periodontics; Patient Care Management; Neoplasms

Introduction

The increased accessibility to new technology (i.e. diagnostics, deep genomic sequencing, etc.), has contributed to a significant improvement in our knowledge base of cancer biology and cancer therapeutics. With the advent of targeted cancer therapy, advances in chemotherapeutics and radiation therapy, there have been significant advances in the field of

Correspondence: Russell S. Taichman D.M.D., D.M.Sc., Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, 1011 North University Ave., Ann Arbor, MI 48109-1078, Tel.: +1-734-763-8216, rtaich@umich.edu.

Compliance with Ethics Guidelines

Conflict of Interest

All authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

cancer treatment. Although many advances have been made, the primary modalities of treatment remain surgical resection, radiation therapy, and chemotherapeutics. Throughout these treatment modalities, it is important for periodontists and dental teams to have knowledge of the effects of cancer treatments. Knowledge of these cancer treatment strategies, will allow dental providers to provide these patients with the highest standard of care before, during, and after the patient's cancer treatment/management. Thus, the aim of this review is to provide dental practitioners with a updated review of the periodontal and restorative treatments in patients with cancer prior to, during, and after their oncology treatments.

Periodontal therapy of cancer patients at the time of diagnosis

Cancer therapy has a number of associated comorbidities (e.g. neutropenia, anemia, impaired wound healing) that can complicate periodontal maintenance and treatment. As such, it is advisable to devise and complete the treatment plan prior to cancer therapy. In a recent study, Tsuji et al. (2015)[1] completed a prospective study of dental intervention for patients with hematopoietic malignancy, reporting that patients who completed the partial pre-cancer therapy protocol had significantly lower incidence of systemic (15.8% vs. 37.4%) and dental complications (2.9% vs. 34.0%) compared to patients who did not complete any pre-cancer dental therapy. These complications were correlated with a higher degree of myelosuppression. Furthermore, Toljanic et al. (1999)[2] completed a prospective study for minimal treatment completed prior to intensive chemotherapy for cancer, that reported 10% (2 patients in the study population) of subjects had febrile episodes due to dental sources. More recently, Schuurhuis et al. (2011)[3] reported 3% of their total study population developed dental complications with minimal treatment completed prior to onset of cancer therapy. The variability in reports is likely due to the generic bias of research protocols, pre-existing dental conditions, dental care, and cancer therapy.

In the pre-treatment protocol for chemotherapeutics, periodontal treatment is beneficial if performed prior to high-dose chemotherapeutics [4–6]. Periodontal therapy includes physical disruption/debridement of bacteria/biofilm through scaling and root planing techniques and oral hygiene instruction. Oral hygiene instruction is often one of the most important and effective measures to prevent bacterial recolonization and maintenance of disease control. In conducting these procedures in immune compromised individuals, complete and differential blood counts may be appropriate to determine if antibiotics should be adjunctively prescribed or if platelet transfusions are required prior to invasive periodontal treatment.

In a recent systematic review by Hong et al., 2017[7], there are broadly three levels of dental treatment protocols prior to anti-neoplastic therapy and bone marrow transplants: complete, partial and minimal.

- i. *Complete treatment* involves the treatment of all dental pathologies prior to cancer treatment or bone marrow transplantation.

- a. Dental pathologies include all caries (enamel and dentin penetration) and extraction of teeth exhibiting probing pocket depths of ≥ 6 mm, dentition with over 50% bone loss, and partially erupted third molars.
- ii. *Partial treatment* involves a graded approach to dental pathologies present prior to cancer treatment or bone marrow transplantation with the following criteria:
 - a. Minor caries (caries lesions extending to or just beyond enamel) observed and not treated (Tsuji et al.,).
 - b. Periapical lesions only treated if size ≥ 5 mm or symptomatic.
 - c. Teeth extracted if probing pocket depth of ≥ 8 mm, teeth with more than 1mm of mobility and vertical depression (Miller's Class III mobility), and partially erupted third molars that exhibit purulence.
- iii. *Minimal treatment* includes symptomatic treatment or if there are limited time constraints prior to cancer therapy or bone marrow transplantation.

Personalization of these treatment protocols is ultimately required due to the inherent risk associated with more invasive dental procedures. Dental complications could induce a delay in cancer treatment, which could be detrimental to the long-term survival of patients depending on their systemic diagnosis or presentation.

Periodontal therapy of cancer patients currently undergoing treatment

Periodontal disease and/or periodontal infections may be exacerbated during cancer therapy and present a significant risk to neutropenic patients. Ulcerated periodontal pocket epithelium may serve as a portal of entry for the translocation of microorganisms into the blood stream. Additionally, inflamed/infected periodontal tissues may serve as a reservoir of endotoxin and pro-inflammatory mediators that have systemic effects[8]. Dental-related infections are a concern during cancer therapy (specifically anti-neoplastic chemotherapy). The prevalence of these infections was recently reported as 5.4% (standard error of 1.16, 95% confidence interval 3.14-7.7)[7]. Vozza et al. (2015)[9] reported the prevalence of periodontal disease in a population with malignant solid tumors submitted to chemotherapy was 35.2% at the time of their cancer diagnosis, and periodontal treatment was effective in reducing plaque index, bleeding on probing, pocket depth and maintaining attachment loss as these patients underwent chemotherapy. As such, care must be taken to properly assess and treat periodontal disease in patients with compromised immune systems following chemotherapy.

Gingivitis is assessed by gingival erythema and bleeding on probing in the absence of bone loss. Periodontitis is assessed by attachment loss, bleeding, gingival erythema, and etiological factors including presence of bacterial plaque and calculus. However, gingivitis may be affected by hematological status. For example, gingiva may appear pale in cases of anemia, while they might appear erythematous in the thrombocytopenic patient[10]. Further, gingiva may appear erythematous and enlarged in patients with acute myeloid leukemia[11].

During neutropenia, periodontal probing should be avoided, meaning that pre-treatment evaluation is of absolute importance to coordinate oral care[8]. Moderate to severe periodontitis in a patient who develops neutropenic fever should be considered a clinically defined infection, even if gingival signs and symptoms of inflammation are not observed[8]. Antimicrobial agents for anaerobic bacteria should be added to current antibiotic regimes in these situations (i.e. metronidazole). Culture of diseased periodontal pockets and culture of blood samples (in the case of bacteremia) will indicate origin of the infection and provide further infection management information[8].

Beyond bacterial and fungal infections, gingival lesions may also be attributed to reactivated viral infections. The viral footprint appears clinically as round 1 to 2mm ulcerations coalescing together within the same area. Diagnosis of a viral infection can be confirmed by virus detection in exfoliated cells or by viral culture techniques[12].

Complications associated with periodontal therapy in cancer patients

Head and Neck targeted side-effects

Head and neck cancers, due to the sites and treatment of these diseases with radiotherapy and chemotherapy, directly impact oral structures, oral intake, weight loss, and dehydration. Acute symptoms include: mucositis, swallowing disorders, xerostomia, and dysgeusia[13]. Late effects include dysphasia, pain, xerostomia, mucosal sensitivity, taste alterations, trismus, osteoradionecrosis, and dental disease[13]. Frequently oral, enteral, and parenteral nutrition support is needed[14]. Oral mucositis may be highly influenced by the frequency of oral care in patients undergoing 20Gy radiation[15]. Oral mucositis at 50 Gy is positively correlated with the number of artificial teeth[16]. Xerostomia is a significant contributor to decline of oral health in these patients[13]. Thus, palliative oral treatment is important in treating these patients and continued support for oral hygiene is important to successfully achieve periodontal stability in these patients.

Osteonecrosis of the Jaw

Osteonecrosis of the jaw (ONJ) has been reported following tooth extraction in patients[17]. Hasegawa et al[17] completed a nonrandomized, multi-centered retrospective study including 1175 patients, to determine the significant risk factors for ONJ in patients taking oral bisphosphonates. Overall, the study reported a 1.7% frequency of post-extraction ONJ in patients taking oral bisphosphonates. The study determined that concurrent disease status (i.e. cancer, diabetes, etc.) was not significant. However, local treatment factors including: root amputation (OR= 6.64), extraction of a single tooth (OR=3.7), severe tooth mobility (OR = 3.60), and unclosed wound (OR = 2.51) significantly contributed risk to development of ONJ. The study also determined that a drug holiday didn't significantly prevent development of ONJ post-extraction, probably attributable to the fact that the half-life of oral bisphosphonates are on the time span of decades.

In addition to well-known use of oral bisphosphonates for osteoporosis, bisphosphonates are also used as bone-targeted therapies to decrease the risk of skeletal metastases in cancer patients. Common uses of bisphosphonates in cancer therapy include men with castration-

resistant prostate cancer and bone metastases, as well as treatment of bone metastases in women with breast cancer [18–20]. Previously, it was shown that monthly zoledronic acid infusions decreased the risk of skeletal-related events compared to placebo (38% vs 49%) in men with castrate resistant prostate cancer[21]. Moreover, Denosumab, a monoclonal antibody against RANK ligand, is also used in this context and further reduces the risk of skeletal-related events and increased time to the first bony complication by four months when compared to Zoledronic acid[22]. Vehmanen et al[23] completed a case series with 254 men with castrate-resistant prostate cancer and treated with Zolendronic acid, Denosumab, or both, who also received dental extractions by oral and maxillofacial surgeons. In total, 29 out of 254 men (11.4%) developed ONJ. Of the patients who developed ONJ, 2 received only Zolendronic acid, 9 received only Denosumab, and 18 received both Zolendronic acid and Denosumab. Seventeen of the 29 ONJ cases had chronic disability of the jaw or jaw necrosis that continued until death of the patient. Thus, treatment of patients taking infusions of bisphosphonates who require dental extractions must be regarded with extreme caution and complete tension-free closure of wound sites should be achieved to minimize risk of ONJ and further oral disability of these patients.

Osteoradionecrosis of the Jaws

Osteoradionecrosis (ORN) of the jaw is a well-known complication of radiation therapy to the head and neck with local risk factors that include tumor site, tumor stage, proximity of the tumor to bone, radiation field, dose of radiation, poor oral hygiene, and associated trauma (i.e. extractions before or after radiation therapy)[24]. It is defined as an area of exposed necrotic bone in an area previously irradiated that fails to heal over a period of 3-6 months[25].

In a recent case-control study by Owosho et al. (2017)[26] at Memorial Sloan Kettering Cancer Center, the authors determined the prevalence of ORN to be 4.3% during a median follow-up time of 52.5 months. Furthermore, the authors stated that patients treated for oropharyngeal cancer were prone to develop ORN earlier compared to patients with oral cavity cancer. In addition, these authors reported that poor periodontal status, history of alcohol use, and radiation dose were significant risk factors.

Despite our growing knowledge of this side effect in cancer patients, the treatment of ORN remains unreliable. A retrospective study by Chen et al (2016)[27], reported a prevalence of ORN of 6.2%. A total radiation dose to the primary site 75Gy, among others, was associated with ORN. However, after aggressive treatment using surgical intervention with/without hyperbaric oxygen, only 93.3% of the patients healed completely.

In a retrospective study that observed outcomes of hyperbaric oxygen therapy in 509 patients, Dieleman et al. (2017)[28] reported that the cause of ORN was most commonly extractions after radiation therapy (22%) or prosthetics (22%) followed by periodontal disease (11%) and tumor-related surgery (11%). Interestingly, treatment with hyperbaric oxygen is only significantly effective for lower stages of ORN, while higher stages of ORN still require segmental resection of the affected structure. Thus, it is important to for periodontists and physicians alike to identify those at risk and avoid unwanted complications.

Periodontal Status Affected by Aromatase Inhibitors

Aromatase inhibitors (AIs) are an adjunctive therapy, which mechanistically is used to interfere with estrogen production in postmenopausal women with hormone receptor positive early staged breast cancer. AIs are typically prescribed for long periods of time, approximately 5 and 10 years[29]. Systemic side effects of AI therapy in breast cancer patients include accelerated bone loss and osteoporotic fractures[30]. Interestingly, patients on AIs also had poorer oral hygiene, poorer health-related quality of life, lower salivary flow, and periodontal health[31]. Periodontal health including deeper periodontal probing depths, more clinical attachment loss and alveolar bone loss was reported over the 18-months of AI therapy[31]. As such, these patients may need to be placed on more frequent hygiene recall appointment status until periodontal stability can be successfully achieved long-term.

Summary and Management Considerations (Figure 1)

1. Pre-Treatment

Preventive periodontal and dental therapies are very important aspects in treating the cancer patient. Diagnosis, treatment, and establishment of regular maintenance protocols are essential in treatment of periodontal disease through neutropenic periods and prevent excessive oral bacterial shift changes in head and neck radiation changes. Further, extraction of untreatable teeth is also important to minimize risks of ONJ prior to onset of bisphosphonate infusions.

2. During Treatment

Periodontal maintenance should be continued in these patients in combination with good oral hygiene. Use of fluoride products to prevent dental caries in post head and neck radiation patients and if plaque accumulation continues, use of chlorhexidine mouth rinse (0.12%) once or twice daily can be prescribed. However, side effects of chlorhexidine (staining, calculus buildup, temporary changes in taste) should be emphasized. Regarding tooth restorations, use of composite resins, resin modified glass ionomer cements, and amalgam restorations are suggested compared to glass ionomer cements alone due to the requirement of frequent replacements from break down of margin integrity (Figure 1). Communication between health providers (i.e. dentist, periodontist, and oncologist) is crucial for the dental treatment of cancer patients. Communication materials can be crucial and are provided by NIDCR to facilitate this communication[32].

3. Post-Treatment

Periodontal maintenance should be continued in patients with careful evaluation of their periodontal and dental status. For patients experiencing xerostomia, fluoride trays can be fabricated for caries prevention. In addition, periodontal maintenance should be performed regularly to maintain oral hygiene and prevention of further attachment loss. These preventive steps are of utmost importance in patients who are at risk for ONJ and for whom extractions/implant placement are not ideal treatment options (Figure 1).

Acknowledgments

Financial Support: Direct funding was provided by the NIH/NCI PO1-CA093900, the NIH/NCI Tumor Microenvironment Network U54-CA163124 and supplement, Department of Defense W81XWH-14-1-0403, and NIH/NIDCR DE027551 (NJD).

References

1. Tsuji K, Shibuya Y, Akashi M, Furudoi S, Yakushijin K, Kawamoto S, et al. Prospective study of dental intervention for hematopoietic malignancy. *Journal of dental research*. 2015; 94(2):289–96. These authors completed a prospective study of dental intervention for patients with hematopoietic malignancy, reporting that patients who completed the partial pre-cancer therapy protocol had significantly lower incidence of systemic (15.8% vs. 37.4%) and dental complications (2.9% vs. 34.0%) compared to patients who did not complete any pre-cancer dental therapy. [PubMed: 25503612]
2. Toljanic JA, Bedard JF, Larson RA, Fox JP. A prospective pilot study to evaluate a new dental assessment and treatment paradigm for patients scheduled to undergo intensive chemotherapy for cancer. *Cancer*. 1999; 85(8):1843–8. [PubMed: 10223580]
3. Schuurhuis JM, Stokman MA, Roodenburg JL, Reintsema H, Langendijk JA, Vissink A, et al. Efficacy of routine pre-radiation dental screening and dental follow-up in head and neck oncology patients on intermediate and late radiation effects. A retrospective evaluation. *Radiotherapy and Oncology*. 2011; 101(3):403–9. [PubMed: 22001103]
4. Borowski B, Benhamou E, Pico J, Laplanche A, Margainaud J, Hayat M. Prevention of oral mucositis in patients treated with high-dose chemotherapy and bone marrow transplantation: a randomised controlled trial comparing two protocols of dental care. *European Journal of Cancer Part B: Oral Oncology*. 1994; 30(2):93–7.
5. Peterson D. Pretreatment strategies for infection prevention in chemotherapy patients. NCI monographs: a publication of the National Cancer Institute. 1989; 9:61–71.
6. Greenberg MS, Cohen SG, McKittrick JC, Cassileth PA. The oral flora as a source of septicemia in patients with acute leukemia. *Oral Surgery, Oral Medicine, Oral Pathology*. 1982; 53(1):32–6.
7. Hong CH, Hu S, Haverman T, Stokman M, Napeñas JJ, Bos-den Braber J, et al. A systematic review of dental disease management in cancer patients. *Supportive Care in Cancer*. 2017:1–20.
8. Raber-Durlacher JE, Epstein JB, Raber J, van Dissel JT, van Winkelhoff A, Guiot HF, et al. Periodontal infection in cancer patients treated with high-dose chemotherapy. *Supportive care in cancer*. 2002; 10(6):466–73. [PubMed: 12353125]
9. Vozza I, Caldarazzo V, Polimeni A, Ottolenghi L. Periodontal disease and cancer patients undergoing chemotherapy. *International dental journal*. 2015; 65(1):45–8. These authors reported the prevalence of periodontal disease in a population with malignant solid tumors submitted to chemotherapy was 35.2% at the time of their cancer diagnosis, and periodontal treatment was effective in reducing plaque index, bleeding on probing, pocket depth and maintaining attachment loss as these patients underwent chemotherapy. [PubMed: 25181024]
10. Philipone, E., Yoon, AJ. *Oral Soft Tissue Manifestations of Hematologic Abnormalities and Diseases Oral Pathology in the Pediatric Patient*. Springer; 2017. p. 129-34.
11. Lowenberg B, Downing JR, Burnett A. Acute myeloid leukemia. *N Engl J Med*. 1999; 1999(341): 1051–62.
12. Epstein J, Page J, Anderson G, Spinelli J. The role of an immunoperoxidase technique in the diagnosis of oral herpes simplex virus infection in patients with leukemia. *Diagnostic cytopathology*. 1987; 3(3):206–9.
13. Bressan V, Stevanin S, Bianchi M, Aleo G, Bagnasco A, Sasso L. The effects of swallowing disorders, dysgeusia, oral mucositis and xerostomia on nutritional status, oral intake and weight loss in head and neck cancer patients: a systematic review. *Cancer treatment reviews*. 2016; 45:105–19. [PubMed: 27010487]
14. Dechaphunkul T, Martin L, Alberda C, Olson K, Baracos V, Gramlich L. Malnutrition assessment in patients with cancers of the head and neck: a call to action and consensus. *Critical reviews in oncology/hematology*. 2013; 88(2):459–76. [PubMed: 23830808]

15. Ogama N, Suzuki S, Umeshita K, Kobayashi T, Kaneko S, Kato S, et al. Appetite and adverse effects associated with radiation therapy in patients with head and neck cancer. *European Journal of Oncology Nursing*. 2010; 14(1):3–10. [PubMed: 19734089]
16. Ogama N, Suzuki S. Adverse effects and appetite suppression associated with particle beam therapy in patients with head and neck cancer. *Japan Journal of Nursing Science*. 2012; 9(1):28–37. [PubMed: 22583938]
17. Hasegawa T, Kawakita A, Ueda N, Funahara R, Tachibana A, Kobayashi M, et al. A multicenter retrospective study of the risk factors associated with medication-related osteonecrosis of the jaw after tooth extraction in patients receiving oral bisphosphonate therapy: can primary wound closure and a drug holiday really prevent MRONJ? *Osteoporosis International*. 2017:1–9. These authors completed a nonrandomized, multi-centered retrospective study including 1175 patients, to determine the significant risk factors for ONJ in patients taking oral bisphosphonates. Overall, the study reported a 1.7% frequency of post-extraction ONJ in patients taking oral bisphosphonates. The study determined that concurrent disease status (i.e. cancer, diabetes, etc.) was not significant. However, local treatment factors including: root amputation (OR= 6.64), extraction of a single tooth (OR=3.7), severe tooth mobility (OR = 3.60), and unclosed wound (OR = 2.51) significantly contributed risk to development of ONJ.
18. Van Poznak CH, Temin S, Yee GC, Janjan NA, Barlow WE, Biermann JS, et al. American Society of Clinical Oncology executive summary of the clinical practice guideline update on the role of bone-modifying agents in metastatic breast cancer. *Journal of Clinical Oncology*. 2011; 29(9): 1221–7. [PubMed: 21343561]
19. Rennert G, Pinchev M, Gronich N, Saliba W, Flugelman A, Lavi I, et al. Oral bisphosphonates and improved survival of breast cancer. *Clinical Cancer Research*. 2017; 23(7):1684–9. [PubMed: 27683176]
20. Vale CL, Burdett S, Rydzewska LH, Albiges L, Clarke NW, Fisher D, et al. Addition of docetaxel or bisphosphonates to standard of care in men with localised or metastatic, hormone-sensitive prostate cancer: a systematic review and meta-analyses of aggregate data. *The Lancet Oncology*. 2016; 17(2):243–56. [PubMed: 26718929]
21. Saad F, Gleason DM, Murray R, Tchekmedyian S, Venner P, Lacombe L, et al. Long-term efficacy of zoledronic acid for the prevention of skeletal complications in patients with metastatic hormone-refractory prostate cancer. *Journal of the National Cancer Institute*. 2004; 96(11):879–82. [PubMed: 15173273]
22. Fizazi K, Carducci M, Smith M, Damião R, Brown J, Karsh L, et al. Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double-blind study. *The Lancet*. 2011; 377(9768):813–22.
23. Vehmanen L, Suojanen J, Kontio R, Utriainen T, Blomqvist C. High frequency of osteonecrosis of the jaw among denosumab-treated prostate cancer patients. *Acta Oncologica*. 2017; 56(1):104–6. These authors completed a case series with 254 men with castrate-resistant prostate cancer and treated with Zoledronic acid, Denosumab, or both, who also received dental extractions by oral and maxillofacial surgeons. In total, 29 out of 254 men (11.4%) developed ONJ. Of the patients who developed ONJ, 2 received only Zoledronic acid, 9 received only Denosumab, and 18 received both Zoledronic acid and Denosumab. Seventeen of the 29 ONJ cases had chronic disability of the jaw or jaw necrosis that continued until death of the patient. [PubMed: 27921521]
24. Lee IJ, Koom WS, Lee CG, Kim YB, Yoo SW, Keum KC, et al. Risk factors and dose–effect relationship for mandibular osteoradionecrosis in oral and oropharyngeal cancer patients. *International Journal of Radiation Oncology* Biology* Physics*. 2009; 75(4):1084–91.
25. Marx RE. Osteoradionecrosis: a new concept of its pathophysiology. *Journal of Oral and Maxillofacial Surgery*. 1983; 41(5):283–8. [PubMed: 6572704]
26. Owosho AA, Tsai CJ, Lee RS, Freymiller H, Kadempour A, Varthis S, et al. The prevalence and risk factors associated with osteoradionecrosis of the jaw in oral and oropharyngeal cancer patients treated with intensity-modulated radiation therapy (IMRT): The Memorial Sloan Kettering Cancer Center experience. *Oral oncology*. 2017; 64:44–51. These authors completed a case-control study at Memorial Sloan Kettering Cancer Center. The authors determined the prevalence of ORN to be 4.3% during a median follow-up time of 52.5 months. Furthermore, the authors stated that patients treated for oropharyngeal cancer were prone to develop ORN earlier compared to patients with

- oral cavity cancer. In addition, these authors reported that poor periodontal status, history of alcohol use, and radiation dose were significant risk factors. [PubMed: 28024723]
27. Chen JA, Wang CC, Wong YK, Wang CP, Jiang RS, Lin JC, et al. Osteoradionecrosis of mandible bone in patients with oral cancer—associated factors and treatment outcomes. *Head & neck*. 2016; 38(5):762–8. [PubMed: 25521838]
28. Dieleman F, Phan T, van den Hoogen F, Kaanders J, Merckx M. The efficacy of hyperbaric oxygen therapy related to the clinical stage of osteoradionecrosis of the mandible. *International journal of oral and maxillofacial surgery*. 2017; 46(4):428–33. These authors completed a retrospective study and reported that the cause of ORN was most commonly extractions after radiation therapy (22%) or prosthetics (22%) followed by periodontal disease (11%) and tumor-related surgery (11%). Interestingly, treatment with hyperbaric oxygen is only significantly effective for lower stages of ORN, while higher stages of ORN still require segmental resection of the affected structure. [PubMed: 28043745]
29. Burstein HJ, Prestrud AA, Seidenfeld J, Anderson H, Buchholz TA, Davidson NE, et al. American Society of Clinical Oncology clinical practice guideline: Update on adjuvant endocrine therapy for women with hormone receptor–positive breast cancer. *Journal of Clinical Oncology*. 2010; 28(23): 3784–96. [PubMed: 20625130]
30. Eastell R, Adams JE, Coleman RE, Howell A, Hannon RA, Cuzick J, et al. Effect of anastrozole on bone mineral density: 5-year results from the anastrozole, tamoxifen, alone or in combination trial 18233230. *Journal of Clinical Oncology*. 2008; 26(7):1051–7. [PubMed: 18309940]
31. Taichman LS, Van Poznak CH, Inglehart MR. Self-reported oral health and quality of life of postmenopausal breast cancer survivors on aromatase inhibitors and women without cancer diagnoses: a longitudinal analysis. *Supportive Care in Cancer*. 2016; 24(11):4815–24. [PubMed: 27455851]
32. NIDCR. Cancer Treatment and Oral Health. 2017. <https://www.nidcr.nih.gov/OralHealth/Topics/CancerTreatment/>

Figure 1.

These are key points to remember depending on the stage at which a patient presents to the periodontal clinic in his/her cancer treatment.