Therapeutic Radiation and Oral Health

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Cancers of the head and neck, which include squamous cell carcinoma of the oral cavity, larynx (voice box), pharynx, and nose/nasal passages account for approximately 4 percent of all malignancies in the United States. Cancers of the salivary glands, eyes, and skin are not squamous cell cancers so these are categorized differently.

The 5-year survival rate from squamous cell carcinoma of head and neck (SCCHN) is increasing, per the American Cancer Society. Treatment modalities for SCCHN have improved significantly, which include surgery, chemotherapeutic agents, anti-angiogenesis agents, photodynamic therapy, laser therapy, radiation therapy, biologic therapy (e.g., cetuximab epidermal growth factor receptor inhibitor), or combination of these. The prevention and screening of known risk factors (smoking, alcohol), promotion of good oral health, and dietary behaviors have aided in the declining trend of SCCHN prevalence. Early diagnosis, positive HPV-16, and better treatment options have aided in decreasing related mortalities. However, some treatments result in short-term and long-term side effects and complications, some of which directly involve the oral cavity.

This discussion is limited to oral complications of radiation therapy and potential methods to reduce these complications. The main objective of the therapeutic radiation (RT) is to achieve the cellular death by DNA damage or reactive oxygen species formation in the cancer cells. In the process, the normal structures surrounding the cancer cells in the path of radiation are also affected.

External beam ionizing radiotherapy is the most common form of RT for SCCHN. Other types of therapeutic radiation include intensity modulated radiation therapy (IMRT), which directs the radiation beams to the targeted cells/organs, which lessens the damage to the surrounding tissue. Depending on the type and location of cancer, the dosage and field of radiation varies. Patients generally undergo RT for three to seven weeks, with sessions five days a week. Depending on the type and nature of the pathology, the total dosage of radiation may range from 3000- 7000 cGy or more.

Dental professionals regularly perform head and neck exams and screen oral cancers. Early detection, diagnosis, and treatment of the SCCHN leads to better prognosis and survival rate. It is necessary that a dentist be part of the SCCHN treatment team, which may include RT and may have immediate and long-term side effects depending on cumulative dosage, fraction size, field, and type of radiation.

Pre-Radiation Assessment

Prior to the beginning of radiation, a comprehensive oral exam should be done, including full mouth radiographic series (FMX) and a panoramic radiograph. The aim of the dental exam is to find any potential sources of irritation, infection, and any pathology that would cause problems during or post-radiation therapy. Vitality of the suspected teeth should be checked and any extraction, if needed should ideally be done 10-14 days prior to the beginning of radiation to provide sufficient time for healing.

The following guidelines can be used in considering teeth for treatment or extraction:

- Irritation caused by any sharp edges of teeth, orthodontic brackets, defective restorations, or defective prosthesis must be corrected to prevent mucositis.
- Carious lesions and recurrent carious lesions should be restored.
- Deep pits and fissures should be sealed to reduce the probability of carious lesions in future.

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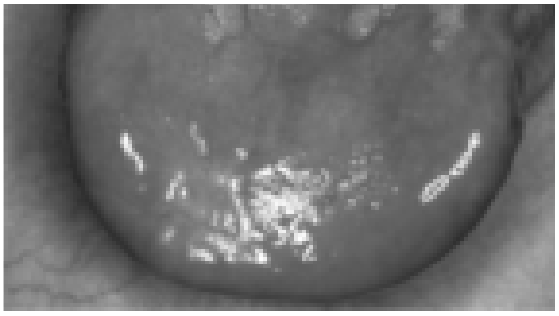

Radiation and Chemotherapy combined

• Any carious lesions that potentially threaten pulpal integrity should be treated with endodontic therapy or extracted.
• Any periapical lesions greater than the diameter of 3 mm in diameter radiographically should be considered for extraction, however, periapical lesions less than 3 mm diameter should be endodontically treated. If the prognosis of endodontics is poor, it is better to extract the teeth.

Coated tongue

• Patients with calculus build up and deep pockets should be treated with scaling and root planing.
• If pocket depths exist that are more than 6-7 mms, extraction of the involved teeth should be considered.
• Teeth with root furcation involvement (Class II) should also be considered for extraction as the teeth can become sources of infection.
• Non-strategic teeth (e.g., not in occlusion) and teeth prone to develop pericoronitis should be considered for extraction.
• Teeth with mobility greater than 2 should be considered for extraction.

A thorough prophylaxis is recommended (if patient has not had one in past 3 months) along with weekly application of fluoride varnish for 4 weeks or the use of silver diamine fluoride, if there is any evidence of incipient decay. Prescription-strength fluoride toothpaste should be prescribed, or a tray made for topical fluoride application along with the use of MI Paste Plus. Patients should be educated and nformed of the potential short- and long-term side effects of therapeutic radiation. A sialogogue (Pilocarpine 5-7.5 mg or Cevimeline 30 mg, TID-QID as titrated to maximum dose) should be prescribed. Caphosol® or Neutrosol® rinses QID can be used for remineralization and prevention of inflammation and infection of mucosa by the removal of dead tissue, microbiota, and food debris.

Frothy Saliva

During Radiation Treatment

Alteration of taste may begin early on in the treatment, with symptoms possible at 200-1000 cGy. With an increasing dosage of radiation, the mucosa of the oral cavity becomes hyperemic, edematous, and pseudomembranous and necrosis occurs at the basal layer, and it may become ulcerated. The dead tissue can become a feeding ground for bacteria and candida and the population can increase exponentially (e.g., streptococcus mutans and lactobacilli, 103 to > 106 CFU), which is accentuated by loss of protective antimicrobial functions of saliva. Due to loss of lubrication and diluting properties of saliva, which can start at 800-1000 cGy, speaking and swallowing becomes a difficult task. Levels of pain depend on the degree and extent of mucositis and ulceration, and can often lead to the patient needing pain medication and an alternative method of feeding (e.g., gastric tube). The discomfort, irritation, pain, and difficulty in chewing and swallowing can potentially lead to malnutrition (which can be detrimental to healing process) and substantial weight loss. Food may need to be ground and served at room temperature or refrigerated to ease swallowing. Feeding through gastric tube may be necessary for the nutritional demands. Frequent feedings are important and also maintaining the swallowing during radiation therapy is important.

Think, viscous, ropy saliva post-radiation

The lateral borders of the tongue, lips, soft palate, buccal mucosa, and floor of the mouth are most susceptible to mucositis. Sometimes, mucositis can become so severe that the treatment may be halted and may need to be treated with cryotherapy (ice chutes), application of topical anesthesia, and/or analgesics (including narcotics).

Secondary infections are common occurrences during RT and may include candidal, bacterial, and viral infections. In the case of persistent candidiasis, use of antifungals such as nystatin oral rinses, clotrimazole troches (only after RT), or systemic azoles (e.g., fluconazole) may be necessary. To minimize super infections during RT, the use of saline and baking soda rinses may help wash away bacteria, candida, and dead tissue. These rinses can also neutralize pH in the oral cavity, especially when oral hygiene is an issue, and the oral cavity becomes acidic. At a decline of 50-70% of the original salivary volume, a subjective sensation of dryness in the oral cavity is perceived (xerostomia). With continued

Severe decay post-radiation

and irreversible destruction of the acinar and serous salivary gland cells, the salivary characteristics change to thick, viscous, ropey, mucus with loss of immunological components.

Post Radiation

The short- and long-term side effects of RT depend on the field, cumulative dosage, and radiation fraction. When muscle tissue, the most resistant to radiation, is affected it causes limited opening of the mouth (trismus). Impairment of blood supply to the temporomandibular joint, masticatory muscles, and salivary glands can have significant effect on masticatory process.

Normal growth and development in children may be affected by RT with maxillofacial deformity, hypodontia, and developmental defects in the permanent teeth. Hyalinization of the blood vessels and fibrosis results in compromised perfusion to tissues. The qualitative and quantitative loss of saliva results in subjective sensation of dryness of the mouth (xerostomia), diminished clearance of carbohydrate substrate, increased cariogenic bacterial and candidal populations, decreased potential of remineralization, and increased demineralization to bacterial and dietary acids. The diminished pellicle formation on the tooth surface also makes the dentition vulnerable to tooth surface loss. Also due to the lack of saliva and its lubrication function, opposing tooth surfaces results in increased attrition and toothpaste abrasion. To overcome these problems, patients should decrease frequency and contact duration of acidic drinks. They should be advised not to brush immediately after acidic challenges with erosive potentials when the tooth surfaces lose micro-hardness and are prone to erosion and abrasion as buffering capability of saliva is decreased. Rinsing with a low (300ppm) fluoride containing rinse, baking soda rinse (1 tsp. baking soda in 8 oz. water), Caphosol or Neutrasol, water or milk, or chewing arginine product (e.g., Basicbites) may restore pH to normal level

Osteoradionecrosis

Due to disruption in "caries balance," primarily because of salivary hypofunction and consequent loss of protective factors of saliva, loss of minerals from teeth is rapid. The decrease in unstimulated (resting) saliva below 0.1ml/min (normal = 0.3ml/min) is principally due to reduction in flow from the submandibular and sublingual glands, which are supersaturated with calcium and phosphates. This lessens the reuptake of the minerals and reduces the remineralization potential. The altered enamel and dentinal structures due to radiation, not necessarily in the field of radiation, become vulnerable, and resistance to bacterial acidic challenges decreases. The qualitative and quantitative change in saliva and the resultant microenvironment in the oral cavity becomes conducive for formation of carious lesions.

Therefore, carious lesions are formed even at non-plaque retentive areas, e.g., cusp tips and incisor edges, where the fluid film is the least. Plaque retentive smooth surfaces and deep fissures are also prone to develop carious lesions. The threat of increased carious lesions and failures of restorations remains for life.

Overcoming risk factors for carious lesions is a lifelong challenge. In our experience, patients are not well-educated in advance about the preventable potential complications. Plaque removal with meticulous oral hygiene must be emphasized. Daily use of prescription-strength fluoride toothpaste (5000 ppm) or fluoride in a custom-made tray (without rinsing after use), and the application of Calcium and phosphates in supersaturated state (rinse or paste in phosphopetide) soluble glass remineralizing agents, are recommended. Sialogogues (Pilocarpine HCl 5 -7.5 mg tid/qid or Cevimeline 30 mg tid) should be titrated to the maximum dose that the patient can tolerate without side effect. Chewing gum, lozenges, or mucoadhesive tables with xylitol may be helpful for gustatory and mechanical stimulation and will increase production from remaining functional salivary glands. This increased salivary flow will clear carbohydrate substrate, dilute the acidity in the oral cavity, and reduce deleterious microbial populations, thereby, decreasing demineralization and increasing remineralization. Suggestion of salivary substitutes should be done with caution, and pH of the products should be confirmed. Brushing the tongue can reduce the rate of development of biofilm on soft and hard tissue of oral cavity. Keeping a humidifier in the room, set at (least) 50%, especially at night, will help reduce moisture loss from the oral tissue from breathing at night. Breaking Vitamin E capsules in the mouth, up to 1200IU, or an oil bath (mixture of olive, coconut, and sesame) can provide some lubrication. It will be helpful to suggest the patient experiment with the products that give them the best result.

Standard of care for dental visits should be every three months depending on the risk level of every patient. These visits should include a prophylaxis, application of 5% fluoride varnish, or application of sodium diamine fluoride, and examination of tooth surfaces for tooth surface loss and

carious lesions. Carious lesions should be recorded to note any progression or reversals. The frequency of taking radiographs, including panoramic, should be increased to once a year as these patients are deemed "high risk" and carious lesions progress very rapidly in salivary hypofunction patients like those treated with radiation. Also, the oral cavity should be examined for candida and bacterial count because of dysbiosis. There is a positive association between salivary hypofunction and candida. There is growing evidence of candida lowering the oral pH and having a positive association with carious lesions. The patient's compliance to the at home regimens should be confirmed and re-emphasized at each visit.

The soft tissue and bone become hypovascular, hypocellular, and hypoxic at the site or at remote areas from the area of radiation. The decrease in capillary density with spontaneous necrosis of soft and bony tissue can result without any insult or injury to the tissue and the chances of soft tissue necrosis and osteoradionecrosis cannot be undermined. Non-healing ulcers of the soft tissue and exposition of bone maybe observed. Surgery involving bone, thickness of the bone, dosage of radiation, overlying mucosa, oral health, and hygiene may be factors for the development of osteonecrosis. Also, tooth/teeth extraction, invasive periodontal procedures and (intrabony) prosthetic appliances can induce soft tissue and osteonecrosis due to high mandibular bone density and lack of collateral blood supply. Soft tissue and osteonecrosis are susceptible to develop serious secondary infections that may be very painful, have suppuration and/or sequestration, and even cause pathological fractures. Treatment can range from rinsing with saline, oral and/or IV antibiotics, removal of sequestrum, bleeding of tissue, to more extensive surgical intervention.

Obtaining information from a radiation oncologist regarding field, dosage, and type of RT will determine whether any elective dental procedure, including extractions, requires hyperbaric oxygen treatment (HBO) to prevent complications even though some researches have shown no definite proof of benefit. Extractions in the areas of radiation can be avoided by treating a tooth endodontically and burying it inside gingiva.

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Dr. Athena Papas is the Erling Johansen Professor of Dental Research and the Head of the Division of Oral Medicine and Public Health Research at Tufts University School of Dental Medicine in Boston, Massachusetts. With expertise in the oral healthcare of the elderly and the medically compromised, Dr. Papas has devoted most of her professional career to this area of study and treatment. She specializes in the care of cancer, bone marrow transplant, geriatric, Sjögren's syndrome, xerostomic and medically compromised patients. She is a member of the medical advisory board of the Sjögren's Syndrome Foundation. Dr. Papas is a member of more than 15 professional organizations including The American Academy of Oral Medicine and The American Society of Geriatric Dentistry. Dr. Papas is a reviewer for Journal of Dental Research, Special Care in Dentistry, The New England Journal Of Medicine, Community Dentistry and Oral Epidemiology, along with 5 other journals. She has been the Dental Chairperson for the Massachusetts Public Health Association, a member of the professional advisory board for the Sjögren's Syndrome Foundation, Inc., former Dental Director of the New England AIDS Education & Training Center, in addition to participating in 14 other organizations. Dr. Papas has been the principal investigator of over 30 clinical trials and co-investigator of many more studies. In 2009, Dr. Papas was selected as the recipient of the International Association of Dental Research (IADR) Pharmacology-Therapeutics-Toxicology Research Award and is currently the President of PTT.

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Dr. Singh came from Nepal to the US in 1997. In Nepal, he worked as a general dentist and single handedly treated patients in the field. Dr. Singh has completed his Masters of Science in Dental Research and has worked on numerous research projects including NIDCR studies, and both industry and NIH sponsored Phase I-III clinical trials. Many of the research participants have come back to participate in other studies because of the relationship they have built with Dr. Singh.

His compassion for patients, strong clinical skills and knowledge are evident through his work in the Oral Medicine Clinic. He works with medically compromised patients suffering from autoimmune diseases, especially Sjögren's syndrome, radiation therapy patients with osteoradionecrosis of the jaw, BRONJ and HIV. He is very knowledgeable about the conditions and displays great clarity when explaining treatment options.

Dr. Singh has been doing the necessary preventive, restorative and other prosthetic dental work for all of the oral medicine studies and in the clinic, especially for the pre- and post-herapeutic radiation and hematopoietic stem cell patients, with excellent results.

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