Navigating External Beam Radiation Therapy for Head and Neck Cancer

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1. Squamous cell carcinomas of the head and neck generally arise from the
   a. Submucosal tissues.
   b. Major and minor salivary glands.
   c. Muscular tissues of the oropharynx.
   d. Mucosal lining of the upper aerodigestive tract.

2. The primary radiobiologic principles of radiation, known as the "4 Rs" of radiation therapy, are repair, repopulation, redistribution, and
   a. Recall.
   b. Radionecrosis.
   c. Reoxygenation.
   d. Radiosensitivity.

3. Intensity-modulated radiotherapy (IMRT) differs from conventional radiation planning techniques in that it
   a. More precisely identifies the target volume, so less dose is required for treatment.
   b. Involves the use of implanted fiducial markers to precisely localize the target volume.
   c. Delivers a higher-intensity dose, allowing for shorter periods of time required for daily treatment.
   d. Delivers beams of differing intensities from many angles and can better accommodate irregularly shaped tumors.

4. Mr. L, a 56-year-old man with tumor T3, N2, M0 (tumor, node, metastasis) squamous cell carcinoma of the right base of tongue, is receiving definitive IMRT to a total dose of 7,000 cGy over 35 treatments to the base of the tongue and bilateral neck. He tells you that amifostine has been mentioned to him and asks you if it is necessary. Your best response is
   a. Treatment to the right base of the tongue will spare the left parotid, and amifostine will not be needed.
   b. Should you develop acute xerostomia while on therapy, a short course of amifostine could be added for the last two weeks of treatment.
   c. Most patients do not experience xerostomia at this dose, but if this occurs at any time, pilocarpine and not amifostine will be prescribed to protect your parotid glands from further damage.
   d. Significant risk of parotid dysfunction is likely with this plan, and amifostine is recommended to reduce the amount of xerostomia you may experience following the completion of treatment.

5. Mr. L is ready to begin radiation therapy and has been scheduled for his first amifostine injection (via IV). The nurse should anticipate that he has been given a prescription for
   b. Oxycodone (OxylIR®, Purdue Pharmaceuticals, Stamford, CT).
   c. Dolasetron (Anzemet®, Aventis Pharmaceuticals, Bridgewater, NJ).
   d. Lisinopril (Zestril®, AstraZeneca, Wilmington, DE, or Prinivil®, Merck & Co., Inc., Whitehouse Station, NJ).

6. Mr. L now has received a total of 24 treatments (4,800 cGy). The radiation therapist asks you to see him today because he is complaining of significant nausea and vomiting despite administration of daily dolasetron, prochlorperazine, and lorazepam. He is unable to remain still during treatment because of nausea. You discuss which of the following options with him to improve his symptoms so he can continue treatment?
   a. Double the dolasetron dose to 100 mg every 12 hours.
   b. Continue radiation treatment, but discontinue amifostine.
   c. Change amifostine to an every other day dosing schedule.
   d. Change amifostine from IV administration to oral administration.

7. Mr. L’s wife has a long-standing history of hypothyroidism. She is concerned about her husband developing hypothyroidism following radiotherapy to his neck. The nurse explains to Mrs. L that
   a. This does not occur with IMRT.
   b. The possibility is diminished with the use of amifostine.
   c. This may develop several months after treatment is complete.
   d. The possibility is greatest in the immediate post-treatment period.

8. Mr. S is about to begin a course of primary radiation treatment to a dose of 5,600 cGy for clinical stage T2, N0, M0 laryngeal cancer. In preparing him for treatment, you plan to review which of the following with him?
   a. He will not experience mucositis, and dietary intervention will not be necessary.
   b. He will experience mild mucositis but should be able to tolerate a soft, bland diet.

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c. He will need a feeding tube for the duration of his treatment because of severe mucositis or esophagitis.
d. He will experience moderate mucositis and will need to supplement his diet with periodic tube feedings.

9. A patient diagnosed with which of the following would benefit most from an IMRT plan?
   a. Metastatic brain involvement
   b. Early-stage laryngeal carcinoma
   c. Limited-stage nasopharyngeal carcinoma
   d. Ethmoid sinus tumor with extension encasing the optic nerve

10. You have just completed teaching a patient who is about to begin head and neck radiation. To assess his understanding, you ask him to reiterate the main points you discussed. Which statement would identify the need for further clarification related to interventions throughout his treatment?
   a. I should see a dentist for a thorough evaluation before beginning treatment.
   b. Vitamin E supplements are important during radiation to prevent mucositis.
   c. Daily fluoride trays are an important part of oral care during and after treatment.
   d. Routine salt and soda oral rinses will help to alleviate discomfort associated with mucositis.

**Answers**

**Question 1:** The correct answer is d, mucosal lining of the upper aerodigestive tract. Squamous cell carcinomas are the most common type of head and neck cancers, accounting for more than 90% of all head and neck carcinomas. Adenocarcinomas account for most of the remaining diagnosed solid tumors in the head and neck region (Carr, 2005). Squamous cell carcinomas may arise from the mucosal lining involving the nasopharynx (nose and paranasal sinuses), oropharynx (tonsils, soft palate, uvula, and base of the tongue), oral cavity (lips, oral tongue, floor of the mouth, alveolar ridge, retromolar trigone, and hard palate), hypopharynx (pyriform sinus, posterior pharyngeal wall, and postcricoid mucosa), and larynx (glottic, subglottic, and supraglottic regions) (Gosselin & Pavilonis, 2002). Choices a, submucosal tissues, and c, muscular tissues of the oropharynx, are incorrect because these more commonly represent invasion from primary mucosal origin and indicate disease extension. Choice b, major and minor salivary glands, also is incorrect. Most tumors involving the major salivary glands, which include the parotid, submandibular, and sublingual glands, are benign, with mucoepidermoid carcinomas accounting for most of the malignant tumors in these glands. Minor salivary glands, which are distributed widely throughout the upper aerodigestive tract, palate, buccal mucosa, base of the tongue, pharynx, trachea, cheek, lip, gingival, floor of the mouth, tonsils, palatal sinuses, nasal cavity, and nasopharynx, are more likely to be malignant than the major salivary glands (Simpson, 2004).

**Question 2:** The correct answer is c, reoxygenation. The “4 Rs” of radiotherapy are used to define the biochemical dynamics of cellular response to radiation (Hilderley, 1997) and guide the principles of radiation dosing and fractionation. Reoxygenation depends on the presence of oxygen in the nucleus of the cell when radiation is delivered to achieve tumor response to treatment (cell death). Tumor cells have varying degrees of oxygenation, and some are relatively hypoxic for reasons such as tumor burden, vascular supply, or metabolic state. When regression of tumor burden occurs, more oxygen is available to previously resistant hypoxic tumor cells, thus maintaining the ongoing efficacy of therapy (Hilderley). Choice a, recall, is incorrect. This refers to dermatitis in a previously treated radiation field, generally in response to administration of a precipitating agent such as certain chemotherapeutic agents or sun exposure. Choice b, radionecrosis, also is incorrect. This generally refers to the toxic effect of radiation on healthy tissues leading to tissue necrosis as a result of ischemia either acutely or as a late effect of treatment. All cells, including tumor cells, have varying degrees of radiosensitivity which, in some instances, can be modified by oxygenation or administering radiosensitizing medication to promote response to treatment. However, this property does not play a direct role in the cellular kinetic responses to therapy (McBride & Withers, 2004). Therefore, choice d, radiosensitivity, is incorrect.

**Question 3:** The correct answer is d, delivers beams of differing intensities from many angles and can better accommodate irregularly shaped tumors. IMRT is a modification of three-dimensional conformal planning, rather than an entirely new technique, that provides tighter beam conformity around irregularly shaped targets. By increasing the number of treatment fields used to approach the target, dosage is intensified in the target field and distributed across healthy tissues at a lower dose. As a result, dosages usually can be escalated to the target site while keeping radiation exposure to nearby healthy tissues in a safe range, thereby decreasing overall toxicity. IMRT is particularly helpful for irregularly shaped tumors or tumors in close proximity to critical structures unable to tolerate a high radiation dose. It is especially suited to treating head and neck tumors because it allows optimal doses to be delivered to the target field while lessening exposure to nearby critical structures (including the spinal cord, optic nerve, salivary glands, carotids, and thyroid). Some theoretical risk exists that low-dose exposure to radiation over a broader area of tissues may increase the development of secondary malignancies. However, this has not become apparent clinically (Glatstein, 2002). Choices a, more precisely identifies the target volume, so less dose is required for treatment, and b, involves the use of implanted fiducial markers to precisely localize the target volume, are incorrect. Visualization and localization of the target field are essential to delivering IMRT accurately. However, these are not features that distinguish IMRT from other forms of treatment planning. Improved accuracy of tumor imaging offered by advanced radiographic imaging contributes to better-defined field volumes with three-dimensional conformal and IMRT techniques. Implanted fiducial markers for field localization may be used with an IMRT plan to improve the accuracy of beam delivery but also may be used with other forms of treatment planning and are not unique to IMRT. Choice c, delivers a higher-intensity dose, allowing for shorter periods of time required for daily treatment, is incorrect. IMRT uses standard treatment doses and fractionation, with the advantage of less dose and toxicity to surrounding healthy tissues. It also may be given with a higher-intensity dose over fewer fractions (hypofractionated). Daily treatment times generally are longer than with standard fractionation techniques because of the increased number of treatment fields required.

**Question 4:** The correct answer is d, significant risk of parotid dysfunction is likely with this plan, and amifostine is recommended to reduce the amount of xerostomia you may experience following the completion of treatment. With the advent of IMRT, some patients with head and neck cancer may not necessarily require amifostine. Therefore, each patient’s treatment plan must be evaluated carefully to assess parotid involvement. The parotid glands are responsible for approximately 60% of all saliva production. Saliva also is produced in smaller amounts by the submandibular and sublingual glands (Eisbruch, Ship, Kim, & Ten Haken, 2001). Xerostomia significantly impacts quality of
life by altering speech, taste, and chewing... The correct answer is choice b, he will experience mild mucositis but should be able to tolerate a soft, bland diet.

Amifostine at a daily dose of 200 mg/m², given via IV approximately 15–30 minutes prior to radiation, has been demonstrated to significantly reduce the incidence of acute moderate to severe xerostomia from 78% to 51% and late xerostomia from 57% to 34% (Brizel et al., 2000). Even with amifostine, many patients still may experience chronic xerostomia. Choice a, treatment to the right base of the tongue will spare the left parotid, and amifostine will not be needed, is incorrect. Use of IMRT will reduce the dose to the contralateral parotid considerably but, depending on the final outcome of the treatment plan, may not necessarily limit it sufficiently. Even with the use of IMRT, scatter radiation is not eliminated completely. Parotid recovery may be possible with radiation doses less than 2,000 cGy or partial parotid dosing. However, at the dose described, adequate parotid recovery cannot be guaranteed until the final treatment plan is reviewed. Choice b, should you develop acute xerostomia while on therapy, a short course of amifostine could be added for the last two weeks of treatment, is also incorrect. Amifostine has been shown to be more effective when initiated just prior to a patient’s first radiation treatment and continued throughout the course of treatment. The degree of parotid damage is a cumulative effect of radiation dose received, and an attempt at partial protection by adding amifostine for a limited time would yield a subtherapeutic response (Brizel et al.). Many patients experience oral changes during treatment (including thickening of saliva, taste changes, and xerostomia). The primary intent of amifostine is to prevent complications associated with chronic parotid dysfunction. Choice c, most patients do not experience xerostomia at this dose, but if this occurs at any time, pilocarpine and not amifostine will be prescribed to protect your parotid glands from further damage, also is incorrect. At a dose of 7,000 cGy, even to a unilateral treatment field, significant xerostomia is likely. Pilocarpine does not protect the salivary glands from fibrosis and long-term dysfunction. However, it does help to stimulate salivary production and can be used during or after treatment in an attempt at symptomatic relief of xerostomia (Johnson et al., 1993; LeVeque et al., 1993). Amifostine is the drug of choice to minimize permanent damage to a patient’s parotid glands as a result of radiation therapy.

**Question 5:** Choice c, dolasetron (Anzemet), is the correct answer. Amifostine is moderately emetogenic when given via IV with or without concurrent chemotherapy. Daily premedication with a serotonin reuptake inhibitor is appropriate (Boccia, 2002; MedImmune Oncology, Inc., 2003). Although amifostine is independently emetogenic, nausea is more significant in patients receiving concurrent chemotherapy. Other antiemetics, such as prochlorperazine or lorazepam, also may be used in conjunction with a serotonin reuptake inhibitor for management of breakthrough nausea but generally are insufficient on their own. Choice a, cetirizine (Zyrtec), is incorrect. Amifostine premedication with a histamine antagonist for prevention of local hypersensitivity reactions is appropriate for subcutaneous administration of amifostine but is not required with IV use. Choice b, oxycodone (OxyIR), is incorrect because this is given commonly for symptomatic relief of painful oropharyngeal mucositis related to radiation therapy, which will develop gradually as treatment continues. This would not be anticipated at the beginning of treatment. Choice d, lisinopril (Zestril or Prinivil), also is incorrect. Amifostine is likely to cause transient hypotension. Therefore, use of antihypertensive medications must be assessed prior to beginning therapy, and patients may be advised to hold any routine blood pressure medications until after amifostine has been administered. Additionally, patients should be instructed to maintain adequate hydration and increase oral fluid intake by at least 500 cc prior to amifostine administration and maintain at least one liter of oral fluid intake throughout the day (MedImmune Oncology, Inc., 2001; Werner-Wasik et al., 2001). IV hydration prior to amifostine administration may be required for patients who are unable to maintain adequate oral hydration during treatment.

**Question 6:** The correct answer is b, continue radiation treatment, but discontinue amifostine. In the event that significant nausea persists despite optimal hydration and antiemetics, discontinuation of amifostine may be necessary. Subcutaneous administration of amifostine is associated with less nausea and sometimes is better tolerated than IV administration. However, the U.S. Food and Drug Administration has yet to approve subcutaneous administration of amifostine. Studies evaluating toxicity and efficacy of subcutaneous amifostine are ongoing. A risk of local hypersensitivity reactions of the skin also is associated with the subcutaneous route. Therefore, daily premedication with a histamine antagonist, such as cetirizine, is prudent, along with alternating administration sites and close skin monitoring (MedImmune Oncology, Inc., 2001). Choice a, double the dolasetron dose to 100 mg every 12 hours, is incorrect because this exceeds the recommended dolasetron dosing limits (Aventis Pharmaceuticals, 2001). Choice c, change amifostine to an every other day dosing schedule, is incorrect. Amifostine concentrations in healthy tissues are negligible 24 hours after administration because of the drug’s short half-life. Therefore, daily dosing is required to maintain optimal cytoprotective effects. Choice d, change amifostine from IV administration to oral administration, is incorrect. Oral amifostine currently is not available. Amifostine is approved only for IV administration, with current trials evaluating the efficacy of subcutaneous administration.

**Question 7:** The correct answer is c, this may develop several months after treatment is complete. Clinical or subclinical hypothyroidism may occur in as much as 30% of patients who have received head and neck irradiation, and the highest risk is in patients receiving high doses to the cervical spine area (Jereczek-Fossa et al., 2004). This tends to be a late complication of treatment and may not develop for several months following its completion. Serum thyroid-stimulating hormone levels should be checked at 6- to 12-month intervals. Thyroid replacement therapy should be initiated if evidence of hypothyroidism as a consequence of radiation therapy is present (Jereczek-Fossa et al.). Choice a, this does not occur with IMRT, is incorrect. IMRT may reduce doses encountered by surrounding healthy tissues but does not eliminate radiation effects on these tissues. Choice b, the possibility is diminished with the use of amifostine, also is incorrect. Amifostine offers some protection of parotid tissue, may decrease the severity of mucositis and esophagitis associated with radiotherapy, and has been shown to decrease the incidence of pneumonitis and pulmonary fibrosis with thoracic irradiation (Andreassen, Grau, & Lindegaard, 2003). However, no evidence currently suggests that amifostine reduces the harmful effects of radiation on thyroid tissue. Choice d, the possibility is greatest in the immediate post-treatment period, is incorrect. Although early onset of hypothyroidism may occur in the first three months following treatment completion, the condition generally is considered a late effect, with peak occurrence two to three years following radiotherapy treatment (Jereczek-Fossa et al.).

**Question 8:** The correct answer is choice b, he will experience mild mucositis but should be able to tolerate a soft, bland diet.
Radiation to the larynx at this dose generally is well tolerated. If a patient presents with hoarseness from the disease, it actually may improve over the first week or two of therapy. However, recurrent hoarseness should be expected because of laryngeal inflammation induced by treatment as the radiation dose accumulates (Mendenhall et al., 2004). Toward the end of therapy, patients usually develop some degree of sore throat. Nonsteroidal anti-inflammatory drugs usually are sufficient for pain relief. Occasionally, however, narcotic analgesics may be required for pain management. Altering a patient’s diet to soft, bland foods as tolerated is helpful in maintaining nutritional requirements during this short period. Nurses also must evaluate for smoking and alcohol use because continued use during and after treatment may predispose a patient to more significant laryngeal edema (Mendenhall et al.). Therefore, the use of alcohol and tobacco products during radiation should be discouraged strongly. Healing will occur gradually over the two to three weeks following treatment, allowing the return of normal eating habits, although laryngeal edema may take several months to completely resolve (Mendenhall et al.). Choice a, he will not experience mucositis, and dietary intervention will not be necessary, is incorrect because most patients receiving this type of treatment experience some degree of throat discomfort prior to completing therapy and should be informed of this at the onset of treatment. Choices b, c, and d, he will need a feeding tube for the duration of his treatment because of severe mucositis or esophagitis, and he will experience moderate mucositis and will need to supplement his diet with periodic tube feedings, are incorrect. Many patients who undergo head and neck radiotherapy do require percutaneous endoscopic gastrostomy tube placement to maintain nutritional status because of significant stomatitis or esophagitis depending on the treatment fields, dose delivered, and administration of chemotherapeutic agents. However, the anticipated dose and relatively small treatment field required to treat a T2 laryngeal cancer generally are well tolerated and do not require feeding tube placement.

**Question 9:** The correct answer is choice d, ethmoid sinus tumor with extension encompassing the optic nerve. Treatment of this tumor is difficult because of its irregular shape and its proximity to the optic nerve, which is a dose-limiting structure. An attempt to treat the disease with an optimal dose, while limiting risk of radiation-induced blindness, is best achieved by an IMRT plan. Choice a, metastatic brain involvement, is incorrect. In this case, the goal is to treat the entire brain diffusely by means of whole brain radiotherapy because the potential exists for microscopic disease in the central nervous system, which usually responds favorably to radiation and reduces the risk of subsequent central nervous system recurrence. IMRT is not appropriate for treatment of such a broad field in this instance. Choice b, early-stage laryngeal carcinoma, is incorrect because this can be treated using conventional external beam radiation techniques and generally is well tolerated and does not necessitate the use of IMRT. Choice c, limited-stage nasopharyngeal carcinoma, also is incorrect. Although this patient would benefit to some degree from an IMRT plan, the risk of damage to critical structures is not as great as a tumor encasing the optic nerve.

**Question 10:** The correct answer is choice b, vitamin E supplements are important during radiation to prevent mucositis. The risks and benefits of antioxidant use during radiation therapy continue to be explored. Although cellular death in response to radiation therapy is partly a result of the radiation effect on DNA, the majority of its efficacy is an indirect response to the formation of intracellular hydroxyl radicals. The presence of free radical scavengers, such as vitamin E and other antioxidants, may protect healthy tissue against radiotoxicity. However, anti-oxidants also may reduce the effect of free radicals on target DNA in carcinogenic cells, raising the potential for suboptimal treatment. Actual impact of antioxidant use on treatment efficacy has been difficult to quantify. Until additional research supporting the use of antioxidants during radiotherapy is completed, antioxidants should be used with caution (Hamilton, 2001). Choice a, I should see a dentist for a thorough evaluation before beginning treatment, is incorrect. This is necessary to ensure optimal dental health prior to the start of treatment. A thorough oral examination should be performed and decayed teeth extracted prior to the start of radiotherapy. Radiation effects on the mandible put patients at significant risk for osteoradionecrosis if extraction is required after treatment. Choice c, daily fluoride trays are an important part of oral care during and after treatment, is incorrect because patients with xerostomia are at higher risk for dental caries from thickened saliva, which promotes plaque formation on teeth and creates an effective substrate for bacterial growth (Iwamoto, 1997). Patients should have ongoing dental follow-up after radiation therapy, where recommendations for fluoride treatments may be prescribed. Choice d, routine salt and soda oral rinses will help to alleviate discomfort associated with mucositis, is incorrect. Mouth rinsing is helpful in removing debris and maintaining moisture in the oral cavity, thereby reducing irritation and inflammation. Although many mouth rinses are used routinely, efficacy of any one mouth rinse over another has not been demonstrated clearly. However, mouth rinses that contain alcohol should be avoided because they can cause an increase in xerostomia (Haas & Kuehn, 2001; Iwamoto; Shih, Miaskowski, Dodd, Stotts, & MacPhail, 2002).

**References**


