Radiation Therapy for Laryngeal Cancer

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Journal of Singing, January/February 2018 Volume 74, No. 3, pp. 307–310 Copyright © 2018 National Association of Teachers of Singing EAD AND NECK MALIGNANCIES are not as common as other forms of cancer, but the effects, particularly of laryngeal cancer, on the voice can be severe and long lasting for a singer. Of all cancers in 2016, the National Cancer Institute reported rates of 3% for head and neck cancers and 0.8% for laryngeal cancer (SEER Data).¹ Radiation therapy plays an import role in the treatment of both early and advanced laryngeal cancers; however, it too can affect the voice. Singing teachers should be familiar consequences of radiation therapy. This article reviews radiation as a treatment modality and the short and long-term effects on vocal health.

WHAT IS LARYNGEAL CANCER?

The lifetime risk for developing laryngeal cancer is 1 in 277, and once diagnosed, the 5-year survival rate is 60.7% (SEER Data).² Squamous cell carcinoma is the most common type of malignancy encountered in the larynx, with smoking being the most common risk factor for developing this disease. However, there are other potential risk factors such as reflux and human papilloma virus. Presenting symptoms seen in patients with laryngeal cancer included referred otalgia (or ear pain), difficulties swallowing, hemoptysis (coughing up blood), hoarseness, and throat pain.

To understand the evaluation and treatment of laryngeal cancer, knowledge of the anatomy of the larynx is required. The larynx is divided into three subsites: supraglottis, glottis, and subglottis. The supraglottis includes the area above the true vocal folds from the epiglottis to the ventricle. The glottic structures include the true vocal folds, and the subglottis extends from just below the true vocal folds to the inferior border of the cricoid cartilage.³ Supraglottic and glottic tumors are much more common than subglottic tumors. Embryologically, the supraglottis has a separate origin from the glottis, explaining why supraglottic tumors typically do not traverse the ventricle to reach the glottis unless the paraglottic space is involved.⁴ The intrinsic ligaments create the paraglottic and pre-epiglottic spaces. Involvement of these spaces results in upstaging of the disease (worst outcome) and allows for transglottic spread.

Extent and location are important factors to consider when managing and evaluating laryngeal tumor. Laryngeal cancer can involve one or more of these subsites and can extend past the larynx. Cancer can spread to the neck, lung, and other locations in the aerodigestive tract. Head and neck cancer is stage-based on tumor size (T), nodal involvement (N), and distant metastasis (M). When classifying tumors, involvement of different subsites, vocal fold mobility, size of the tumor, cartilage invasion, and extralaryngeal extension must be taken into account. Diagnosis is made using radiographic, endoscopic, and pathologic evaluation of the lesions.

Surgery, chemotherapy, and radiation therapy are the mainstays of treatment for these cancers. Depending on the location and the stage of the disease, different treatment modalities are available. Radiation therapy or surgery can be used as single modality treatment for early stage tumors. Newer studies have suggested that late voice outcomes are comparable for both surgery and radiation therapy.⁵ For more advanced tumors, radiation therapy can be used in conjunction with chemotherapy as a curative or palliative treatment, and it also can be used as adjuvant therapy following surgery.⁶ For those patients with extensive cartilaginous invasion or extraglottic extension, radiation therapy may not be as effective as surgery. Depending on the types of radiation (palliative versus curative, adjuvant versus primary), different treatment protocols are utilized.

WHAT IS RADIATION THERAPY?

The goal of radiation therapy is to treat the field of disease and spare the normal tissue, and it is administered by a radiation oncologist. For head and neck cancer, typically external beam irradiation is used for treatment. Intensity-Modulated Radiation Therapy (IMRT) is a variation of external beam irradiation that helps spare normal, critical structures, particularly the spinal cord.⁷

Radiation therapy is fractionated over a several week course. There are varying schemes of radiation including conventional, hyperfractionated, hypofractionated, and accelerated fractionated. The typical schedule is a 5 to 7 week treatment with a total of 45 to 65 centigray (cGr) given. Fractionation is used to allow for repair of normal tissue, and it allows for reoxygenation of tumor cells making them more susceptible to the next dose of radiation therapy. In some cases giving concomitant chemotherapy boosts the effectiveness of radiation. If postoperative radiation therapy is given, it should usually be started within six weeks from surgery. There is a maximum dose for radiation therapy, so with recurrent disease treatment options may be limited.

RADIATION CHANGE TO THE LARYNX

There is an increasing focus to identify side effects of treatment and minimize their effects on patients. Radiation therapy, while anatomically preserving the structure of the larynx and other sites of treatments, causes numerous soft tissue and cellular changes that can impact the function of the larynx.⁸ Up to 92% of patients who receive radiation therapy for laryngeal cancer report dysphonia (poor voice quality).⁹

The side effects of radiation therapy range from more common and transient problems, such as soft tissue edema and sloughing of the mucosal layer (mucositis), to less common and more severe conditions like perichondritis of the laryngeal cartilages and necrosis of these cartilages.¹⁰

Some changes such as acute edema and disruption of soft tissue are due to the early effects of treatment. Early effects are attributed to cell death via damage to Deoxyribonucleic Acid (DNA) either directly by the radiation or via reactive oxygen species.¹¹ These soft tissue changes of edema and erythema can alter vocal fold properties, contributing to dysphonia. In many patients, edema and erythema subside following treatment, and patients' voices can regain quality that is close to baseline. However, secretory cells can be impacted during the acute effect phase. When the treatment area involves the larynx, the secretory cells within the saccule can be affected, leading to poor lubrication of the vocal folds and impairment of vibration and phonation.

Radiation also causes long-term effects mostly related to fibrosis and underlying vascular damage. Vascular damage causes localized hypoxia and ischemia of affected tissues leading to necrosis of tissue or permanent alteration of the underlying architecture of the larynx.¹² This is particularly important for the vocal folds, which rely on specific composition within their layers to achieve adequate voice quality.¹³ Often, injury to the superficial lamina propria may provoke a local response of the body to produce and densely deposit collagen within this layer,¹⁴ inhibiting proper vibration.

Alterations within the lamina propria of the vocal fold often manifest as vocal fold scarring. A patient may present with a breathy, weak, or harsh voice. Stroboscopy will show stiff vocal folds, a reduced mucosal wave, poor vibratory function of the vocal fold, and glottic insufficiency.¹⁵ There also may be permanent dysfunction of the mucus glands, leading to impaired vocal fold lubrication. Often, patients may develop compensatory hyperfunction in efforts to improve vocal quality.

Damage to the laryngeal cartilages, in particular the arytenoids, may manifest as poor vocal fold motion and positioning.¹⁶ Radiation therapy also causes muscular atrophy or "wasting," affecting the intrinsic laryngeal muscles, and also impairing vocal fold motion and positioning.

Studies examining functional voice outcomes following radiation therapy have been limited. In these studies, voice quality decreased immediately after radiation therapy for up to about one year, at which time voice may begin to approach baseline or pretreatment measurements.¹⁷ Still, patients who have received radiation therapy have overall decreased intensity, pitch range, and maximum phonation range, which all can affect singing ability.¹⁸ A significant number of patients (44– 80%) perceive longer term poor voice quality and look for treatments to help improve their laryngeal function.¹⁹

IMPROVING VOICE QUALITY AFTER RADIATION

A previously irradiated larynx is predisposed to laryngitis caused by fungal organisms. Up to 75% of head and neck cancer patients may be colonized by a particular species of fungus (yeast) called *candida albicans*.²⁰ Laryngoscopy may reveal diffuse, white plaques coating laryngeal mucosal surfaces. There should be a high suspicion for fungal laryngitis in these patients, and there should be a low threshold to consider treatment. Fungal laryngitis usually can be treated effectively with a three-week course of an antifungal, such as fluconazole.

Unfortunately, the majority of vocal fold changes due to radiation therapy are irreversible and progressive, meaning many patients will have life-long effects. Hyperbaric oxygen (HBO) therapy has been shown to maintain favorable functional outcome and reduce the progressive changes specifically for chondroradiation (cartilage) necrosis.²¹ Systemic medications to minimize radiation therapy side effects are being studied, as well.

Vocal hygiene is an important means of improving functional voice outcomes of patients who have undergone radiation therapy. Damage to secretory cells within the laryngeal saccule contributes to the dryness and poor lubrication of the vocal folds. Increased oral hydration or humidification can help improve vocal fold lubrication. There are medication options to increase secretions and lubrications, but they are few in number and are not always effective.²²

Proton pump inhibitors (anti-reflux medication) have commonly been used as prophylaxis in those who have laryngeal inflammation and irritation, but little research has been done to examine their role in the irradiated population. Studies have suggested a relationship between laryngopharyngeal reflux and laryngeal cancer, although some experts feel that these studies have not provided conclusive evidence because of confounding factors.²³

Speech-language pathologists provide voice rehabilitation services that can improve vocal quality. Voice rehabilitation has been shown to improve self-perceived and subjective vocal and communicative function of patients following therapy. In part, voice therapy may reduce muscle tension dysphonia seen in many irradiated patients. There also may be some improvement in the elasticity and flexibility of the larynx following voice therapy.²⁴

For patients who are not satisfied or do not find improvement from voice therapy, there are various surgical interventions for vocal fold scarring, but few studies focus specifically on scarring secondary to radiation therapy.²⁵ The possibility of recurrence and poor wound healing from radiation effects must be considered in this population. Steroid injections and laser treatments have been utilized, but multiple treatments are frequently needed before benefit is seen.²⁶ Depending upon the extent and severity, epithelial freeing techniques and laryngeal resurfacing may be utilized. If glottic insufficiency is present, medialization procedures such as thyroplasty and injection can be considered. Depending upon the extent of the scar, medialization may result in strained voice. Researchers continue to investigate tissue engineering as a means of improving scar; many growth factors and other substances are being tested.

Treatment of head and neck cancers, in particular laryngeal cancer, is aimed at curing disease, but also preserving laryngeal function. This includes maintaining voice quality as well as the functional role of the larynx in breathing and swallowing. Despite efforts to minimize adverse effects, they frequently occur. Short and long term changes in the larynx are seen, as well as delayed effects. Progress continues to be made in the treatment and management of laryngeal cancer, but singing teachers should understand that radiation has consequences, and that in some cases, it may lead to worse voice quality than surgical treatment.

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