Abstract: Purpose. The purpose of this review is to address the issue of unnecessary irradiation of the normal larynx.

Methods. We performed a literature review and dosimetry evaluation of intensity modulated radiotherapy (IMRT) techniques.

Results. Data suggest that matching conventional parallel opposed photon fields through adenopathy is a reasonable alternative to the common practice of unnecessarily irradiating the normal larynx to high doses. The dosimetry evaluation demonstrates that the laryngeal dose is much higher when the entire neck is included in the IMRT field as opposed to using a standard anterior low-neck field below the level of the thyroid notch.

Conclusions. Lateral opposed fields should not be extended to include the larynx to avoid matching fields through adenopathy. IMRT fields should not include the normal larynx when the laryngeal dose would be substantially lower with a technique that shields the larynx in an anterior low-neck field. © 2004 Wiley Periodicals, Inc. Head Neck 26: 257–264, 2004

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“The main obstacle to progress is not the acceptance of new ideas but the giving up of old ones.”

—John Maynard Keynes

Over a decade ago, the head and neck team from the University of Florida published an editorial titled “Unnecessary Irradiation of the Normal Larynx.”¹ The purpose of that editorial was to discourage the practice of including the normal larynx in the lateral opposed fields when the primary tumor site could be adequately covered by placing the inferior border of the lateral fields at the level of the thyroid notch (Figure 1A).

Thirteen years is a long time in a rapidly changing field such as radiation oncology. However, we raise the unnecessary laryngeal irradiation issue in 2003, because it is clear that unnecessary laryngeal irradiation is a practice that is still alive and well in the radiotherapy community. Both at national meetings and in our regional practice, we continue to see board-certified radiation oncologists treating patients with nasopharyngeal, oropharyngeal, or oral cavity primary tumors with parallel opposed fields similar to those shown in Figure 1B. Often, the rationale for unnecessary laryngeal irradiation is a concern about junctioning fields through gross neck disease, but it is not unusual to review cases in which the lateral fields include the larynx in the absence of neck disease simply because the
laryngeal dose is not considered during treatment planning. An additional reason to revisit the unnecessary laryngeal irradiation issue is that laryngeal dose is a factor that is often not discussed when comparing intensity modulated radiotherapy (IMRT) plans for patients with tumors not involving the larynx. Given this background, the purpose of this article is to review the two main issues that are at the heart of the unnecessary laryngeal irradiation controversy and to explain how these issues apply to IMRT field design. Throughout this article, the terms “match line” and “field junctions” refer to the area of the neck in which the radiotherapy fields that are used to treat the primary site touch the radiotherapy field that is used to treat the lower portion of the neck.

MODERATE-DOSE IRRADIATION DAMAGES THE LARYNX

Techniques that involve unnecessary laryngeal irradiation are often based on the concept that moderate-dose irradiation has little effect on laryngeal function. Probably the most systematic study of the toxicity of irradiating the normal larynx in patients with head and neck cancer was reported by Fung and colleagues from the University of Western Ontario. In this study, the authors evaluated the effect of radiotherapy on the larynx using videostroboscopy, aerodynamic measurement of speech, digital analysis of voice quality, and subjective voice quality survey instruments. Two groups of patients were studied. The control group consisted of 13 patients irradiated for stage I vocal cord cancer using radiotherapy fields that covered only the larynx (laryngeal cancer group). The study group consisted of 17 patients who had the normal larynx irradiated as part of their treatment for primary tumors not involving the hypopharynx or larynx (nonlaryngeal cancer group). The mean laryngeal dose was 61 Gy in the patients with laryngeal cancer and 50 Gy in the patients with nonlaryngeal tumors. The study demonstrated abnormal laryngeal function in all of the parameters evaluated for both groups of patients. Laryngeal function was significantly worse in the nonlaryngeal cancer group than in the group who received primary radiotherapy for an early vocal cord cancer. The authors conclude: “Previously it was thought that voice dysfunction was caused by direct laryngeal radiation damage in a dose dependent manner. It now seems that RT treatment volume also significantly impacts on vocal dysfunction. Furthermore, our findings suggest that wide-field head and neck RT might be more important than larynx-only radiation in determining voice quality.”

JUNCTIONING RADIOTHERAPY FIELDS THROUGH ADENOPATHY

When there is gross adenopathy at the level of the larynx, the decision to extend the primary-site fields to include the larynx is based on the view that the risk of underdosing cancer near the match line is greater than the risk of radiation damage to the larynx. There are two main ways one can evaluate the importance of dose uncertainty at the match line between the primary site and low-neck fields in this setting. The most powerful approach is to look at outcome data on large numbers of patients who have been irradiated with field arrangements that match the fields through high-risk areas of the neck when this is necessary to spare the larynx. There are many publications providing such data, but we are most comfortable with those from our institution. The bottom line is that the University of Florida data on hundreds of patients with long-term follow-up demonstrates that the rates of neck recurrence and complications with techniques that junction the primary and low-neck fields at the level of the thyroid notch regardless of the location of adenopathy are at least as low as those reported from other institutions where the larynx is included in the lateral fields.

The second approach to evaluating the potential risk of matching conventional radiotherapy fields through adenopathy is to look at studies of the dose distribution near match lines that have been done with computer modeling or measurements in tissue-equivalent phantoms. Since 1990,
there have been at least four articles in the *International Journal of Radiation Oncology Biology Physics* reporting the results of studies done specifically to evaluate the dose distribution close to the junction between opposed lateral and anterior fields as used to treat head and neck cancer.\(^7-10\) Some of these studies suggest that there may be a few millimeters of increased or decreased dose near field junctions in the neck. Because none of these dosimetry studies take into account the fact that patient position in the region of the neck match moves at least a few millimeters in an unpredictable pattern throughout treatment, the chance that dose inhomogeneities would impact clinical outcome is likely to be extremely low. For this reason, we view these studies from the physics laboratory as consistent with the clinical observation that the position of the field junction does not increase the risk of nodal recurrence.

**UNNECESSARY LARYNGEAL IRRADIATION WITH IMRT**

When using IMRT to treat a patient with a primary tumor of the nasopharynx, oropharynx, or oral cavity, there are three basic options in regard to the question of field matching and laryngeal irradiation: (1) avoid match line issues by including both the primary site and regional lymphatics, including those in the low neck in a single IMRT treatment plan; (2) use a conventional anterior low-neck field, but include the larynx in the IMRT fields to avoid placing the match line through positive nodes in the mid-neck; and (3) use a conventional anterior low-neck field, but place the inferior border of the IMRT field at the level of the thyroid notch, even when this means matching fields through positive nodes.

**Laryngeal Dose When the Larynx Is Included in the IMRT Fields.** When designing IMRT treatment plans, it is important to take into account the impact that including the larynx in the IMRT fields might have on laryngeal dose (options 1 and 2). When the larynx is included in the IMRT fields, it is possible to direct the inverse planning system to limit the dose to the larynx, but it is usually not possible to spare the larynx as much as when the larynx is blocked in the anterior low-neck field (option 3).

There are no published data that allow one to compare the dose-volume histograms for the larynx with conventional versus IMRT plans when the larynx in not involved with tumor. To demonstrate the increase in laryngeal dose that results from including the normal larynx in the IMRT fields, we generated two different treatment plans in a model patient with a stage T2N2b carcinoma of the tonsil with adenopathy extending to the level of the bottom of the cricoid cartilage. One treatment plan reproduced option 1 in which the IMRT fields covered the entire neck (Figure 3). The other treatment plan reproduced option 3 by matching the IMRT and anterior low-neck fields at the level of the middle of the thyroid notch (Figure 2).

Because the many parameters of head and neck IMRT delivery and dose specification are currently so heterogeneous among the centers that are currently publishing on this subject, it will not add value to present all of the details of the IMRT plan that we used to evaluate the laryngeal dose for this review. Our goal is to demonstrate the concept that the laryngeal dose is higher when it is included in the IMRT fields than when it is blocked in the anterior low-neck field. We planned IMRT with the Corvus system (Version 4.0R6, NOMOS corporation) and delivered IMRT with a six-beam arrangement using a multileaf collimator with 1-cm wide leaves. The dose was prescribed as has been reported by the University of California at San Francisco.\(^11\) A dose of 70 Gy at 2.12 Gy/fraction was prescribed to gross disease (including adenopathy) and a dose of 59.4 Gy at 1.8 Gy/fraction was prescribed to clinically negative areas. The larynx was contoured, and the plan was optimized to spare the larynx as much as possible with the requirement that the planning target volumes received 95% or more of the prescription dose (Figure 3).

For the treatment plan that blocked the larynx in the anterior low-neck field (option 3), we reproduced the larynx block and field borders typically used in our department in this setting (Figure 2). To generate a dose-volume histogram for the larynx, we contoured the larynx as was done for the IMRT plan and used a Pinnacle system (Version 6.0, ADAC Laboratories) to evaluate dose distribution. The entire low neck received 50 Gy at 2 Gy/fraction, and then the field size was reduced to boost the gross adenopathy at 2 Gy/fraction to a final dose of 70 Gy (Figure 2).

Figures 2 and 3 show selected images demonstrating the increase in laryngeal dose resulting from including the larynx in the IMRT fields. Figure 4 plots the dose-volume histograms for the larynx when the larynx is included in the IMRT
field (option 1) and when the larynx is blocked in the anterior low-neck field (option 3). Even though the larynx is not completely shielded by the narrow larynx block typically used at the University of Florida, the dose to the central portion of the larynx is extremely low (~5 Gy, meaning <10% of

FIGURE 2. Laryngeal dose in a model patient with a stage T2N2b carcinoma of the tonsil with positive nodes on the right side at the level of the larynx. The primary site is irradiated with either IMRT or lateral opposed fields. The cervical lymphatics inferior to the primary site fields are treated with an anterior low-neck field. (A) Digitally reconstructed radiograph of the low-neck fields. The larynx was contoured and appears as a red color-wash structure. The larynx is shielded with a narrow midline block that does not cover the entire width of the larynx. In this model patient, the entire low-neck field received 50 Gy, and then the field size was reduced to boost the positive nodes on the right side of the larynx to 70 Gy. Irradiation was given with a 6-MV photon beam with source to axis distance of 100 cm. (B) Axial dose distribution at the level of the true vocal cords showing that the dose to the central portion of the larynx is extremely low when the larynx is shielded in the anterior low-neck field.

FIGURE 3. Dose distribution using IMRT as described in the text to treat the model patient with a stage T2N2b carcinoma of the tonsil with positive nodes on the right side at the level of the larynx. The plan was optimized to minimize the dose to the larynx while delivering 70 Gy to gross disease and 59.4 Gy to areas at risk for subclinical disease. (A) Coronal projection near the middle of the larynx. (B) Axial projection at the level of the true vocal cords. A comparison of Figure 2B and 3B shows that sparing of the central portion of the larynx is shielded in an anterior low-neck field.
the prescription dose), and the mean dose is approximately 17 Gy. When the larynx is included in the IMRT fields, the mean laryngeal dose is 35 Gy. When evaluating the importance of these mean doses (17 Gy vs 35 Gy), it is important to remember that we worked hard to keep the laryngeal dose as low as possible in optimizing our IMRT plan. The mean laryngeal dose of 35 Gy reported here does not represent what happens when the IMRT planning team is not sensitive to the unnecessary irradiation issue. In reviewing plans from other centers, it is not unusual to see IMRT treatment records that reflect a mean dose to the larynx of approximately 50 Gy when the larynx was included in the IMRT fields only to avoid field matching in the mid-neck.

Probably more important than mean dose is the proportion of the larynx receiving an extremely low dose, for example, 10 Gy. In this regard, the difference between the IMRT and anterior low-neck field plan is striking (Figure 4). Specifically, when the larynx is included in the IMRT fields, the entire larynx receives more than 10 Gy, whereas when the larynx is shielded in the low-neck field, approximately 45% of the larynx receives less than 10 Gy. The bottom line is that IMRT does a better job of sparing the larynx than when conventional lateral fields cover the larynx, but the laryngeal dose is still higher than when the larynx is shielded in the standard manner in an anterior low-neck field.

**CONCLUSIONS**

We began with a statement attributed to British economist John Maynard Keynes: “The greatest obstacle to progress is not the acceptance of new ideas but the giving up of old ones.” In our opinion, this statement explains the continued use of techniques that involve unnecessary laryngeal irradiation. It is human nature to resist change, especially when the consequences of making a mistake are high. However, at some point, leaving behind familiar practices becomes an essential element of progress.

The 1990 editorial explained why it is time to abandon the practice of delivering potentially damaging doses of irradiation to the larynx to avoid matching fields in the mid-neck. Over the past 13 years, many clinical outcome and dosimetry studies have been published that validate the concept that such practices constitute unnecessary laryngeal irradiation. Lateral opposed fields should not be extended to include the larynx to avoid matching fields through adenopathy. IMRT fields should not include the normal larynx when the laryngeal dose would be substantially lower with a technique that shields the larynx in an anterior low-neck field.

**REFERENCES**

EDITORIAL COMMENT: PROTECTING THE LARYNX

“What is the tolerance of the larynx?” A junior radiation oncology resident answers, “81.6 Gy if you use BID fractions,” and cites RTOG 90-03.1 The ambitious senior level resident objects, saying that 90-03 specifically excluded patients with laryngeal cancers because the standard of care with advanced laryngeal tumors required chemotherapy. The wise chief resident pontificates to rescue the junior, “But the RTOG did allow supraglottic laryngeal tumors as well as tumors of the pyriform sinus on 90-03, and all of these patients should have received full dose laryngeal irradiation.”

But is 81.6 Gy in 1.2 BID fractions harmless? There were 263 patients treated on the hyperfractionated arm, and 77 had either supraglottic laryngeal cancer or hypopharyngeal primary sites. Because 70% of the patients on the hyperfractionated arm had oropharyngeal or oral cavity cancers, let us assume that there were a few oropharyngeal cancers that involved the larynx but probably less than 100 patients had larynxes that received 81.6 Gy in 1.2 BID fractions. There were five RTOG grade 4 laryngeal “late” toxicities2 reported at least 90 days from the START of treatment. There were also 11 late grade 3 toxicities. However, with a mean follow-up of only 23 months, there were 70 and 40 grade 1 and 2 late laryngeal toxicities for the hyperfractionated patients for which we have data. Thus, with 81.6 Gy, laryngeal toxicity rates were quite high and might be the rule rather than the exception.

In this month’s Head & Neck, Dr. Amdur and his Gainesville colleagues argue against unnecessary laryngeal irradiation, a plea elegantly made by Drs. Mendenhall, Parsons, and Million in a 1990 editorial.3 Since that time, the advent of intensity modulated radiation therapy (IMRT) has added a new dimension to radiation treatment, particularly for head and neck cancer. The advantage of IMRT is that it better allows radiation oncologists to deliver a prescribed dose to the target volume while sparing critical normal tissues. However, what is often unstated is that the technology works by spreading the dose to the normal, noncritical, tissues. The good news about IMRT is that if you tell the treatment planning system that is important to keep the parotids below 27 Gy and the spinal cord below 45 Gy, the system will often do just what you ask. The bad news is quid pro quo. To get, you have to give. If we are sparing the parotids and limit the spinal cord dose, what tissues are receiving more radiation? We have learned that when attempting to spare the parotids and the spinal cord, the computer may recommend a plan that overdoses the mandible. Part of the learning curve is to adjust to the suggestions of the inverse planning systems; so we must now specify some limits for the mandible. But if we try to spare the parotids, the spinal cord, and the mandible, what will we overdose next?

The importance of the larynx and its ability to function cannot be overstated. Radiation oncologists may overestimate the tolerance of the larynx because of two peculiarities of laryngeal irradi-
ation: the already impaired laryngeal function seen in laryngeal cancer patients and the very small fields of radiation used to treat them. Most patients with laryngeal cancer have with vocal abnormalities, and it is because very small lesions produce such profound changes in the voice that many laryngeal cancers are found when they are diminutive. Naturally, many of the studies done on laryngeal irradiation have been done on patients with laryngeal cancers. When the radiation oncologists cure laryngeal cancers, voice quality often improves and thus our comfort level with laryngeal irradiation is high—too high. Radiation generally is not good for the larynx.

Regarding the importance of field size: as cited by Dr. Amdur and colleagues, Fung et al. evaluated the effects of the volume of tissue irradiated on patient morbidity. Thirteen patients with small glottic tumors treated with small radiation fields were compared with 17 patients with non-laryngeal tumors who were treated with large field irradiation. The patients who had small glottic cancers received higher mean doses to the larynx than did the patients with non-laryngeal cancers: 61 Gy vs 50 Gy, respectively. Unfortunately, there was increased supraglottic activity in the large field group, which could be expected, since small glottic fields do not cover the entire supraglottic region. However, despite the possibility that the small field patients had cancers that by invading past Reinke’s space into the intermediate and deep layers of the lamina propria might have interfered with the mucosal wave and despite the fact that these patients received higher doses of radiation to the larynx, voice quality was better compared with the non-laryngeal cancer patients treated with larger fields. Field size was important.

When radiation oncologists are treating patients with cancers of the oropharynx, nasopharynx, oral cavity, or paranasal sinuses with conventional, three field technique, laryngeal irradiation is unnecessary. But can we document the harm? Fung et al. examined 30 patients who had received “incidental” laryngeal irradiation who had no evidence of disease and were “out” at least a year after their treatment. Glottic closure, phase symmetry, and supraglottic activity were abnormal. Fundamental frequency was below the mean in 80% of patients when they were compared with age- and sex-matched controls. Looking at aerodynamics, there were statistically higher differential pressures in patients receiving more than 50 Gy. More ominous was the direct correlation between the time from radiation and voice impairment.

When treating with conventional technique, we have traditionally spared or limited the doses to the larynx and the trachea in the anterior field whenever there was no laryngeal or hypopharyngeal involvement and little risk of paratracheal nodal involvement. The primary purpose was to decrease acute toxicities of the irradiation, but now there are emerging data on the long-term dangers of laryngeal irradiation. To deliver the prescribed doses accurately to multiple target volumes while sparing critical structures, IMRT increases the volume of tissue receiving some irradiation. As we move forward in conformal radiation techniques, it is essential to remember that particularly with larger radiation fields, the larynx remains a very critical structure.

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