DEFINITIVE RADIOTHERAPY WITH INTERSTITIAL IMPLANT BOOST FOR SQUAMOUS CELL CARCINOMA OF THE TONGUE BASE

Omur Karakoyun-Celik, MD,1 Charles M. Norris, Jr, MD,2 Roy Tishler, MD,2,3 Anand Mahadevan, MD,4 John R. Clark, MD,5 Saveli Goldberg, PhD,1 Phillip Devlin, MD,3 Paul M. Busse, MD, PhD1

1 Department of Radiation Oncology, Massachusetts General Hospital, 100 Blossom Street, Cox 3, Boston, MA 02114. E-mail: pbusse@partners.org
2 Head and Neck Oncology, Dana Farber Cancer Institute, Boston, Massachusetts
3 Department of Radiation Oncology, Brigham and Women’s Hospital, Boston, Massachusetts
4 Department of Radiation Oncology, Beth Israel Deaconess Medical Center, Boston, Massachusetts
5 Medical Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts

Accepted 4 November 2004
Published online 22 February 2005 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/hed.20171

Abstract: Background. The purpose of this study was to examine the long-term outcome of a cohort of patients with unresected base of tongue carcinoma who received interstitial brachytherapy after comprehensive external beam radiation therapy.

Methods. Between 1983 and 2000, 122 patients with primary or recurrent squamous cell carcinoma of the oropharynx or oral cavity received interstitial brachytherapy as part of their overall management. Forty patients had primary, unresected carcinoma of the base of tongue and are the subjects of this analysis. The median age was 54 years. Fifty-four percent had T3 or T4 disease, and 70% had clinical or radiographic lymphadenopathy. Twenty-four (60%) received two to three cycles of neoadjuvant chemotherapy. The oropharynx, bilateral neck, and supraclavicular fossae were comprehensively irradiated, and the tongue base received a median external beam dose of 61.2 Gy (50–72 Gy). The primary site was then boosted with an interstitial 192Iridium implant by use of a gold-button single-strand technique and three-dimensional treatment planning. The dose rate was prescribed at 0.4 to 0.5 Gy/hr. The median implant dose was 17.4 Gy (9.6–24 Gy) and adjusted to reach a total dose to the primary tumor of 80 Gy. N2 to 3 disease was managed by a planned neck dissection performed at the time of the implant.

Results. The median follow-up for all patients was 56 months, and the overall survival rates were 62% at 5 years and 27% at 10 years. The actuarial primary site control was 78% at 5 years and 70% at 10 years. The overall survival and primary site control were independent of T classification, N status, or overall stage. Systemic therapy was associated with an improvement in overall survival (p = .04) and a trend toward increased primary site control with greater clinical response. There were seven documented late effects, the most frequent being grade 3 osteonecrosis (n = 2), grade 2 swallowing dysfunction (n = 2), trismus (n = 2), and chronic throat pain (n = 1).

Conclusions. In an era of greatly improved dose distributions made possible by three-dimensional treatment planning and intensity-modulated radiation therapy, brachytherapy allows a highly conformal dose to be delivered in sites such as the oropharynx. If done properly, the procedure is safe and delivers a dose that is higher than what can be achieved by external beam radiation alone with the expected biologic advantages. The long-term data presented here support an approach of treating advanced tongue base lesions that includes interstitial brachytherapy as part of the overall management plan. This approach has led to a 78% rate of organ preservation at 5 years, with a 5% incidence of significant late morbidity (osteonecrosis) that has
required medical management. © 2005 Wiley Periodicals, Inc.
*Head Neck* 27: 353–361, 2005

**Keywords:** brachytherapy; tongue base; interstitial implant

The therapeutic management of base of tongue carcinoma has largely shifted from surgery and postoperative radiation toward combined-modality approaches with an emphasis on organ preservation. This has been a common theme for many head and neck sites and is particularly important in the oropharynx because of the critical role of the tongue base function in processes such as swallowing, speaking, and the formation of a patent airway. Unlike tumors in the mobile tongue, tumors that arise posterior to the circumvallate papillae are not appreciated at an early stage. They are typically discovered because of vague symptoms, referred pain to the ear, or the development of lymphatic disease in the neck. Because of the extensive nature of these tumors at the time of diagnosis, a high radiation dose is required to have a chance of permanent disease control. However, the mandible poses a limitation to the amount of radiation that can be delivered, because external beam doses greater than 70 Gy carry a risk of osteoradionecrosis.

One well-established method to treat the base of tongue to a dose in excess of 70 Gy is to use brachytherapy as a component of radiation treatment. There are a number of different isotopes and implant methods that have been used to achieve this end, but the unifying aspect of brachytherapy is the localization of dose in a conformal pattern that reflects the volumetric distribution of disease. An experienced brachytherapy team can perform these procedures with an acceptable level of morbidity, and the additional dose may contribute to an increased chance of cure and organ preservation.

This article reports on the long-term results of a population of patients treated with definitive radiation for unresected primary carcinoma of the base of tongue in which a portion of the total dose was delivered by interstitial 192Iridium. More than half the patients also received induction chemotherapy as subjects in phase II clinical trials at the Dana Farber Cancer Institute.

### PATIENTS AND METHODS

Between September 1983 and March 2000, 122 patients with primary or recurrent cancer of the oral cavity and oropharynx were treated at the Joint Center for Radiation Therapy with external beam radiation and an interstitial implant boost. Of these patients, 106 had primary cancers, whereas 16 had recurrent disease. Fifty-two patients had tumors of the mobile tongue, 52 of the base of tongue, 10 of the floor of mouth, five of the tonsil, and three of other sites. In this report, we evaluate the 40 patients with previously untreated primary squamous cell carcinomas of the tongue base. All procedures in this review followed the ethical standards on human experimentation and the Helsinki Declaration of 1975 and as revised in 1983.

A head and neck oncology team consisting of a radiation oncologist, medical oncologist, and head and neck surgeon evaluated all patients. Patients underwent a complete history and physical examination, including an examination under anesthesia, and were free of distant metastases at the time of their initial evaluation. There were 29 men and 11 women, with an age range of 37 to 86 years (median, 54 years). The distribution of patients according to the 1992 American Joint Committee on Cancer (AJCC) staging system is shown in Tables 1 and 2. There were eight T1, 11 T2, 16 T3, and five T4 primary tumors. The overall stage distribution was two stage II, 12 stage III, and 26 stage IV.

All patients were treated with radiation as the primary modality, with surgery reserved for salvage. Neck dissection was elective and generally reserved for patients with N2 or N3 disease. The external beam radiation therapy consisted of standard comprehensive lateral fields that included the primary site and regional lymphatics. Individualized blocks were designed to shield uninvolved normal tissue. The energy was 4 or 6 MV, and parallel-opposed lateral fields covered the oropharynx and neck up to the skull base. These fields were matched to an anterior field that covered the lower cervical and supraclavicular lymph nodes. The dose per fraction was 1.8 to 2.0 Gy daily; after

<table>
<thead>
<tr>
<th>T classification</th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
<th>Total no. patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>2</td>
<td>6</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>1</td>
<td>8</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>7</td>
<td>17</td>
<td>4</td>
<td>40</td>
</tr>
</tbody>
</table>

This table shows the distribution of patients by T and N classification according to the 1992 American Joint Committee on Cancer (AJCC) staging system.
44 to 45 Gy, a cord block was placed, and the posterior neck was irradiated with 6 to 9 MeV electrons. The anterior field was then treated to approximately 56 Gy, as was the posterior neck. In some cases, a second field reduction was designed to boost the tongue base to a median external beam dose of 61.2 Gy (range, 50–72 Gy). Unless involved, the low neck received 44 to 45 Gy. Acute reactions were self-limiting and managed symptomatically. Feeding gastrostomy tubes were routinely placed at the start of radiotherapy beginning around 1990. Treatment breaks were discouraged.

The interstitial implant was typically performed approximately 4 weeks after the completion of external beam radiation to allow the acute mucosal reaction to subside. When indicated, the implant was performed at the time of a planned neck dissection. The median time between the external beam radiation therapy and implant was 25 days (range, 7–69 days). An elective tracheostomy was performed in all except one case, and patients received dexamethasone and broad-spectrum antibiotics before, during, and after the procedure. With respect to the catheter placement itself, the submental area was prepped and draped and the mandible and hyoid bone identified. A small skin incision was made, and stainless steel trocars were inserted through the submental skin and into the tongue base until the beveled end was visualized in the oropharynx. Blind-ended, single-leader nylon after loading catheters were threaded through the trocars until seated onto the dorsum of the tongue. The blind end of the catheter was a gold button, which served to anchor the catheter as well as shield the opposing wall of the oropharynx. A silk suture threaded through the gold button facilitated removal of the catheter and was placed outside of the oral cavity. The spacing of the catheters was approximately 1 cm apart at the dorsum of the tongue and was as uniform as possible through the volume plus a 1-cm margin. Lateral and anterior simulation films from a representative implant are seen in Figures 1 and 2. In this example, the catheters cover a pretreatment clinical tumor volume that was lateralized but extended from the circumvallate papillae to the vallecula.

Patients were simulated the day after implant with the placement of dummy seeds into each catheter, and films were taken at multiple angles. Typically, four or five seeds of $^{192}$Ir of equal strength (0.4–0.5 mg Ra eq/seed) 1 cm apart were loaded into each strand to produce a Quimby-like dose distribution. The distal-most end of the source strand contained a seed to maximize dose to the surface of the tongue. The median number of catheters was nine (range, 4–19), and the median amount of radioactivity was 18.1 mg Ra eq (range, 10.0–35.6 mg Ra eq). The number of seeds per catheter was four in most cases. In two instances, the primary disease extended outside the base of tongue and onto the tonsil. In these cases, the tongue and glossopharyngeal sulcus were implanted with $^{192}$Ir and the tonsil with $^{198}$Au seeds. Computerized three-dimensional treatment planning was used to generate isodose curves, which were reviewed in multiple dimensions. Dose rates

### Table 2. Overall stage distribution and number of patients who received induction chemotherapy.

<table>
<thead>
<tr>
<th>Overall stage</th>
<th>Total no. patients</th>
<th>No. patients with chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>III</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>IV</td>
<td>26</td>
<td>15</td>
</tr>
</tbody>
</table>

FIGURE 1. Lateral projection of a base of tongue interstitial implant. Gold buttons follow the contour of the dorsum of the tongue from the posterior mobile tongue to the vallecula. Smaller seeds are dummy sources showing the position of actual Iridium sources when afterloaded. A protective tracheostomy is in place.
that produced continuous isodose lines at the perimeter as well as the center of the implant volume were evaluated. With the catheter spacing and seed strength noted previously, the prescribed dose rate was to an isodose that completely covered the implant volume and was between 0.4 and 0.5 Gy/hr, whereas the center of the implant received approximately 0.8 Gy/hr or less. The catheters were loaded with 192Ir within 24 hours, secured with a stainless steel button in the submental area, and then removed at the completion of the implant. The median implant dose was 17.4 Gy (range, 9.6–24 Gy) and adjusted so the total dose to the base of tongue primary tumor was approximately 80 Gy (median 80 Gy; range, 70.8–86.4 Gy). There were no instances of acute bleeding or infection at the time of the placement or removal. The procedure did not add additional time to the length of stay for the neck dissection.

Twenty-four patients (60%) received two to three cycles of platinum-based induction chemotherapy, the most common regimen being continuous infusion cisplatinum, 5-fluorouracil, and leucovorin (10 patients). Of these patients, 16 achieved a complete response and eight a partial response. One patient with stage III disease received concurrent chemotherapy and external beam radiation therapy.

Survival and primary site control were calculated from the time of the date of the interstitial implant procedure. Actuarial survival curves were generated using the Kaplan-Meier method. Differences between survival curves were calculated for the entire period of observation. Outcomes in different groups were compared by the log-rank chi-square test. Multivariate analysis was performed with a Cox proportional hazards model.

RESULTS

At the time of analysis, 24 patients were alive and free of disease at a median follow-up of 68 months (range, 18–236 months). Five patients were alive but had either a recurrence or second malignancy. Five patients are known to have died of recurrent cancer, two from metastatic disease, one from a second malignancy, one from intercurrent disease, and two from causes that could not be ascertained. The overall survival rate for the entire population was 62% (± 9%) at 5 years and 27% (± 8%) at 10 years (Figure 3). The disease-free survival rate was 54% (± 10%) at 5 years and 18% (± 7%) at 10 years (Figure not shown). There was no relationship between T classification, N status, or overall stage and survival. Figure 4 shows an improvement in the overall survival
that was statistically significant ($p < .05$) in patients who received two to three cycles of induction chemotherapy, external beam radiation, and implant (24 patients) compared with those who received external beam radiation and implant (16 patients).

Organ preservation, expressed as primary site control, was an important clinical endpoint and was analyzed in detail. The local control rate for the entire population is shown in Figure 5. The Kaplan-Meier estimate was 78% ($\pm$ 9%) at 5 years and 70% ($\pm$ 10%) at 10 years. There was no relationship between primary size as expressed by T classification and local control (Figure 6). Similarly, there was no demonstrable relationship between N status or overall stage and primary site control. In contrast with the results for overall survival, a benefit was not seen on local control with systemic therapy.

FIGURE 4. Kaplan-Meier estimate of overall survival in patients who received induction chemotherapy (24 patients, dashed line) and those who did not receive it (16 patients, solid line; $p = .05$).

FIGURE 5. Kaplan-Meier estimate of primary site local control for all patients.

FIGURE 6. Kaplan-Meier estimate of local control by T classification. The solid line shows T1 and T2 tumors; the dashed line shows T3 and T4 tumors.

FIGURE 7. Kaplan-Meier estimate of local control of the 24 patients who received induction chemotherapy and achieved either a complete response (CR, solid line) or partial response (PR, dashed line).
trend is seen toward better local control after a complete clinical response to induction chemotherapy ($p = .26$).

The addition of an interstitial implant to a planned unilateral or bilateral neck dissection did not add any additional morbidity to the surgical procedure other than the placement of a temporary tracheostomy. The catheters were removed at bedside without any incidence of bleeding or other complication. The acute mucosal reaction from the additional implant dose appeared 7 to 14 days after removal and was restricted to a confluent mucositis roughly the size of the area of the gold buttons on the dorsum of the tongue that peaked and regressed within 3 weeks. Patients rarely required additional pain medication during this time and were advised to follow the standard practices of postradiation oral hygiene.

There were no treatment-related deaths, and the risk of a long-term complication developing in this group of patients was low. The list of complications and level of severity are shown in Table 3. Most were grade 2 and managed without hospitalization or surgery. There were two patients with trismus, two with swallowing dysfunction, and one with chronic oropharyngeal pain. The most severe late effect was the development of osteonecrosis in two patients, one conservatively managed and the other treated with hyperbaric oxygen.

### DISCUSSION

The success of combined-modality therapy and accelerated fractionation regimens for organ preservation has led to their widespread use as primary therapy in the management of squamous cell head and neck malignancies.7–11 For these malignancies, particularly tongue base, organ preservation is an extremely important therapeutic endpoint, because the surgical procedures carry the expense of permanent dysfunction, anatomic loss, and occasionally disfigurement. Clinical trials have shown that dose intensity is an important factor for disease control. It is also widely recognized that morbidity is related to both dose and treatment volume, and efforts should be made to make the treatment volume as close as possible to the actual clinical target volume. Improvements in treatment planning and external beam radiation delivery such as three-dimensional conformal therapy and intensity-modulated radiation therapy have brought us closer to this goal. Despite these recent advances, one of the historically proven methods that has been used to achieve these ends is interstitial brachytherapy. By placing the appropriate radioisotope directly into the tumor and using three-dimensional treatment planning, a highly conformal dose of radiation can be delivered to structures like the base of tongue, while the rapid fall-off reduces the amount of radiation that is delivered to dose-limiting normal structures, which, in this case, is the mandible. In addition to conformal dose, brachytherapy has biologic advantages over conventional external beam radiation that may contribute to the overall effectiveness.

Because of the high incidence of regional spread in base of tongue primary tumors, we believe an interstitial implant is not sufficient therapy by itself and should be used in conjunction with comprehensive external beam radiation. Less commonly, brachytherapy has been used as primary site therapy and combined with neck dissections.12

In the setting of oropharynx, the external beam dose to the adjacent structures and lymphatics must be high enough to eradicate subclinical spread that frequently spreads beyond the tongue base itself, and for that reason, at least in this series, external beam doses approached 60 to 70 Gy and were often defined by protocol. The implant dose was therefore limited to a confined boost to bring the overall dose to the tongue base to 80 Gy and is somewhat lower than in other series (Table 4). The proportion of overall dose that is delivered through brachytherapy did vary within our series; however, it was not directly associated with outcome as was observed in the oral tongue, where a greater proportion of dose delivered through interstitial techniques produced a better outcome.22 The importance of a high overall dose was demonstrated by Crook et al.,13 where a local control rate of 79% (26 of 33) was seen in patients with T1 or T2 primary tumors who received total doses of 75 Gy or more, but only 50% (four of eight patients) in patients who received 70 Gy or less. An overall dose of 80 Gy or more is easily

### Table 3. Late effects.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trismus</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swallowing dysfunction</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic throat pain</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteonecrosis</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
</tbody>
</table>
achievable with brachytherapy to this site, particularly if the tumor is centrally located.

The data presented in this study relate the experience of using an interstitial implant as part of the total radiation treatment plan. In more than half the cases, the overall course of therapy incorporated induction chemotherapy through phase II clinical trials. The primary site control rate, 78% at 5 years, compares favorably with other recent clinical experiences (Table 4), especially when the primary T classification is taken into account; 21 (53%) of 40 patients had T3 or T4 tumors. In a comparable series of 41 patients from Stanford University treated with brachytherapy as a boost after comprehensive external beam radiation, Gibbs et al\(^{20}\) report a strikingly similar 5-year local control rate of 82% with an acceptable long-term complication rate of 7% soft-tissue necrosis or ulceration and 5% osteoradionecrosis. Long-term data from Memorial Sloan-Kettering Cancer Center also demonstrate this approach can lead to an 89% primary site control rate,\(^{17}\) with an acceptable level of morbidity and high level of function.\(^{23}\) A sizable experience has also been reported by Puthawa et al, with an 83% rate of primary control. The data from major brachytherapy centers in France (Table 4) add to the collective experience and support the use of interstitial techniques to conformally increase dose and contribute to organ preservation. Where noted in Table 4, the Paris system\(^{21}\) was used to prescribe dose.

It is interesting to note the lack of a relationship between staging parameters typically associated with outcome and primary site control in this series; however, it is worth noting that the number of patients is relatively small, and patients were not randomly assigned to receive chemotherapy. A statistically significant relationship was not seen between T classification, N status, or overall stage and survival or local control. There are a number of possible explanations for this outcome. A high proportion of patients received neoadjuvant chemotherapy, all of whom achieved either a complete or partial response. Irrespective of the initial volume of disease at the time of staging, a complete response or partial response after chemotherapy places patients at a similar level of residual disease at the start of radiation. Alternatively, the high overall dose that was able to be achieved using brachytherapy techniques could equalize the effectiveness of this therapy across T classifications as overall local control rates reach 80% to 90%.\(^{18}\) A demonstrable effect that was statistically significant in this series was a higher overall survival (\(p < .05\))

---

**Table 4.** Extent of disease, treatment parameters, primary site control, and incidence of soft tissue and bone necrosis among various institutions.

<table>
<thead>
<tr>
<th>First author, year</th>
<th>No. patients</th>
<th>% patients with T3–4</th>
<th>Median EB Dose, Gy</th>
<th>Median implant Dose, Gy</th>
<th>Technique</th>
<th>Chemotherapy</th>
<th>Primary control</th>
<th>Time point</th>
<th>Osteonecrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Housset,(^{13}) 1987</td>
<td>29</td>
<td>0</td>
<td>45</td>
<td>30–35(^*)</td>
<td>Loop</td>
<td>None</td>
<td>80%</td>
<td>8 y</td>
<td>3%</td>
</tr>
<tr>
<td>Puthawala,(^{14}) 1988</td>
<td>70</td>
<td>74%</td>
<td>45–50</td>
<td>20–25</td>
<td>GB-V(^{\dagger})</td>
<td>None</td>
<td>83%</td>
<td>5 y(^{\dagger})</td>
<td>3%</td>
</tr>
<tr>
<td>Crook,(^{12}) 1988</td>
<td>48(^{\S})</td>
<td>0</td>
<td>48.6</td>
<td>32(^{*})</td>
<td>Loop/Hairpin</td>
<td>None</td>
<td>75%</td>
<td>5 y</td>
<td>6%</td>
</tr>
<tr>
<td>Lusinchi,(^{15}) 1989</td>
<td>108</td>
<td>47%</td>
<td>45</td>
<td>43.8</td>
<td>Loop</td>
<td>None</td>
<td>64%</td>
<td>5 y</td>
<td>None</td>
</tr>
<tr>
<td>Horowitz,(^{16}) 1986</td>
<td>20</td>
<td>45%</td>
<td>54</td>
<td>27</td>
<td>GB-V(\S)</td>
<td>25%</td>
<td>90%</td>
<td>5 y</td>
<td>None</td>
</tr>
<tr>
<td>Harrison,(^{17}) 1998</td>
<td>68</td>
<td>28%</td>
<td>54</td>
<td>20–25</td>
<td>Loop</td>
<td>13%</td>
<td>89%</td>
<td>5 y</td>
<td>3%</td>
</tr>
<tr>
<td>Demanes,(^{18}) 2000</td>
<td>25</td>
<td>48%</td>
<td>54</td>
<td>19.2–36.9</td>
<td>GB-V(\S)</td>
<td>None</td>
<td>92%</td>
<td>5 y</td>
<td>None</td>
</tr>
<tr>
<td>Robertson,(^{19}) 2001</td>
<td>20</td>
<td>35%</td>
<td>50–54</td>
<td>28.7</td>
<td>Loop</td>
<td>None</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Gibbs,(^{20}) 2003</td>
<td>41</td>
<td>50%</td>
<td>50</td>
<td>26</td>
<td>Loop(\S)</td>
<td>5%</td>
<td>82%</td>
<td>5 y</td>
<td>5%</td>
</tr>
<tr>
<td>Karakoyun-Celik,(^{#}) 2005</td>
<td>40</td>
<td>54%</td>
<td>61</td>
<td>17.4</td>
<td>GB-V(\S)</td>
<td>60%</td>
<td>78%</td>
<td>5 y</td>
<td>5%</td>
</tr>
</tbody>
</table>

Abbreviations: EB, external beam radiation; NR, not reported.\(^{*}\)Paris system.\(^{21}\)\(^{\dagger}\)Gold Button-Volume.\(^{\S}\)Median follow-up.\(^{\#}\)Fourty-one patients received external beam radiation and implant, seven patients received implant alone.\(^{\S}\)\(^{\dagger}\)Iodine-temporary.\(^{#}\)Present series.
observed in patients who first underwent chemotherapy followed by definitive radiation compared with those patients who did not receive chemotherapy (Figure 3). For primary site control, however, no improvement was seen with chemotherapy, although among the patients who received chemotherapy, there was a trend toward a better outcome as a function of clinical response (Figure 6).

The approach taken for the patients in this study produced a high rate of primary site control with a limited number of adverse events. The base of tongue is well vascularized and the risk of long-term complication is low, as shown in Table 4. The most common long-term reaction is soft tissue ulceration or necrosis that almost always responds to conservative medical management. Occasionally, with an incidence of approximately 5%, this can progress or a patient independently has focal osteonecrosis develop. This is a more serious problem but also can be managed medically, with hyperbaric oxygen, or with surgery. The other late reactions seen in our patients, swallowing difficulty and chronic pain, are seen after combined-modality regimens with a high external beam dose to large oropharyngeal fields. As the rate organ preservation and local control approaches 80% to 90% for base of tongue cancers, the incidence of late reactions, even osteonecrosis, is very acceptable.

In summary, we believe that the addition of an interstitial brachytherapy boost to the tongue base as a planned part of combined-modality therapy is worthwhile and has led to an excellent rate of primary site control in this series of patients, 54% of whom had T3 or T4 tumors. The procedure itself, although complicated, is not associated with an increased operative risk and carries an acceptable level of late morbidity. Further refinements and the potential for an improvement in dose homogeneity may be possible with high-dose rate brachytherapy [HDR], although the correct relationship between HDR, total dose, and fractionation schedule and conventional low-dose rate brachytherapy has yet to be determined.

REFERENCES


