Abstract: Background. The purpose of this study was to analyze factors influencing outcome in patients who received postoperative irradiation for advanced squamous cell carcinoma of the oral cavity.

Methods. Between October 1964 and November 2000, 226 patients with 230 previously untreated primary invasive squamous cell carcinomas of the oral cavity were treated postoperatively with continuous-course external beam irradiation. All patients had a minimum follow-up of 2 years (analysis, November 2002). No patient was lost to follow-up.

Results. The 5-year actuarial rates of locoregional control by pathologic American Joint Committee on Cancer stage were: stage I, 100%; stage II, 84%; stage III, 78%; and stage IV, 66%. Recurrence of cancer above the clavicles developed in 55 patients (24%). In multivariate analysis of locoregional control, positive margins, vascular invasion, perineural invasion, extracapsular extension, and T classification remained significant.

Conclusions. This article provides additional data defining relatively favorable and unfavorable groups of patients in the postoperative setting. Dose recommendations are re-examined and selectively increased for high-risk patients. © 2004 Wiley Periodicals, Inc. Head Neck 26: 984–994, 2004

Keywords: carcinoma; squamous cell; mouth; radiotherapy; mouth neoplasms; postoperative care

The rationale for postoperative radiotherapy (RT) is that it is most likely to be effective against microscopic deposits of cancer cells, which would progress and lead to locoregional recurrence if left unchecked.1 In 1989, our results were published on 134 patients who underwent postoperative irradiation for tumors of oral, pharyngeal, or laryngeal sites at the University of Florida. Included were 38 patients with oral cavity cancers. During the period covered in our initial review, the institutional policy was to use primary irradiation for most oral cavity cancers. In the early 1980s, the approach to oral cavity cancer changed at the University of Florida such that almost all patients were treated initially by operation with postoperative irradiation added as indicated by pathologic findings. The main reason for the change was to avoid the relatively high incidence of bone exposure and soft tissue necrosis observed in patients treated predominantly for oral tongue and floor of mouth cancers with interstitial irradiation. This series updates...
our experience to include 226 patients with oral cavity malignancies.

**METHODS AND MATERIALS**

Between October 1964 and November 2000, 226 patients with 230 previously untreated primary invasive squamous cell carcinomas of the oral cavity (excluding the lip) were treated postoperatively with continuous-course external beam irradiation in the University of Florida Department of Radiation Oncology. All living patients had a minimum follow-up of 2 years (analysis, November 2002). No patient was lost to follow-up. The mean and median follow-up times were 4.8 and 3.2 years, respectively.

Patients ranged from 15 to 85 years of age (mean, 60; median, 61). There were 167 men and 59 women.

Disease was staged according to the guidelines of the 1997 American Joint Committee on Cancer (AJCC)\(^2\) (Table 1). Stages IVA and IVB were grouped together for statistical analyses, because only two patients were initially seen with clinical stage IVB disease. Four patients had two synchronous oral cavity cancers. In each of these cases, only one TNM stage was assigned, corresponding to the most advanced lesion. Statistical analysis was done for 226 patients rather than 230 separate tumors.

All patients underwent a major cancer operation (e.g., partial glossectomy, maxillectomy, tongue-jaw-neck dissection) with or without neck dissection before irradiation. Patients referred for irradiation after excisional biopsy of early cancers were excluded. Most patients were treated in the 1980s and 1990s. Before that time, most early and moderately advanced oral cancers received pri-
mary irradiation. Irradiation was started as soon as feasible after surgery, usually within 4 to 6 weeks. No patient received chemotherapy except for palliation after tumor recurrence.

Indications for postoperative RT are listed in Table 2. Twelve patients had none of our usual indications for postoperative irradiation but were irradiated because the surgeon believed the patient was at high risk of local recurrence.

Margins of resection at the primary site were negative in 83 patients (37%), positive in 68 patients (30%), and “close/equivocal” in 75 patients (33%) (close [invasive or carcinoma in situ {CIS} ≤5 mm] in 41 [18%], initially positive but ultimately negative in 26 [12%], contained CIS or dysplasia in seven [3%], and uncertain in one [0.4%]). The latter grouping into the “close/equivocal” category was done because of the small number of patients in each category and because no significant difference was seen in local or locoregional control rates between the different subgroups.

All patients were treated with megavoltage photon beams, usually 60Co or 6 MV. The mean doses according to margin status in 218 patients who were treated by external irradiation alone (eight additional patients received an interstitial implant) were as follows: negative margins, 64.8 Gy; positive margins, 72 Gy; and close/equivocal, 66 Gy. No patient in this series was treated with intensity-modulated radiation therapy (IMRT).

All patients were treated with planned continuous-course external beam RT. Sixty-nine patients received twice-a-day irradiation at 1.2 Gy per fraction to a median dose of 74.4 Gy (range, 64 Gy–76.8 Gy). One hundred forty-nine patients were treated once daily to a median dose of 65 Gy (range, 21.6 Gy–70.5 Gy). Eight additional patients received an interstitial implant after external beam irradiation.

The posterior cervical and low-neck regions (unilateral or bilateral) were irradiated in most patients. All scars, needle tracks, and drain sites were bolused during irradiation with 0.5-cm–thick petrolatum gauze.

**Statistical Methods.** All statistical analyses were performed with SAS software (SAS Institute, Cary, NC). Univariate survival estimates were obtained by the Kaplan-Meier method. The log-rank statistic was used to detect differences between strata, and corresponding two-sided p values of less than .05 were interpreted as statistically significant. Cox regression was implemented for multivariate analyses. Specifically, backward selection was performed to attain the most parsimonious model for each endpoint of interest. Multiple imputation was implemented to allow the most unbiased estimates in the presence of explanatory variables with randomly missing information. Those patients not receiving a neck dissection were excluded from multivariate analyses.

The presence of severe complications was analyzed with logistic regression; those patients receiving an implant rather than external beam RT were excluded, because hyperfractionation was one of the covariates in this analysis.

**RESULTS**

**Local (Primary) Control.** The 5-year actuarial rate of primary site control was 83%. There was no significant difference (p = .16) in the 5-year local control rates according to tumor location within the oral cavity: oral tongue, 84%; retromolar trigone, 76%; floor of mouth, 85%; and other, 70%. There was a significant difference in local control according to margin status (p = .0004): positive, 63% (n = 68); negative, 82%; and close/equivocal, 92%. The difference in local control rates according to preoperative clinical T classification was also significant (p = .04): T1, 90%; T2, 88%; T3, 79%; and T4, 70%.

Local control rates did not correlate with clinical N status or with the number of lymph nodes involved in the pathologic neck dissection specimen. Five-year local control rates according to clinical N status were as follows (p = .96): N0, 79%; N1, 78%; and N2–N3, 84%. Local control according to the number of pathologically positive lymph nodes were as follows: none, 81%; one, 82%; two to three, 86%; four or more, 78% (p = .73).

**Regional (Neck) Control.** The 5-year rates of neck control by the number of positive lymph nodes at

<table>
<thead>
<tr>
<th>Table 2. Indications for postoperative radiation.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• T4 (Bone invasion/soft tissue of neck)</td>
</tr>
<tr>
<td>• Multiple positive nodes</td>
</tr>
<tr>
<td>• Extracapsular spread</td>
</tr>
<tr>
<td>• Perineural invasion</td>
</tr>
<tr>
<td>• Vascular invasion</td>
</tr>
<tr>
<td>• Margins, close (≤5 mm), positive, CIS/dysplasia, or initially positive but negative after re-excision</td>
</tr>
</tbody>
</table>

Abbreviation: CIS, carcinoma in situ.
Locoregional Control According to Primary Site. Five-year actuarial locoregional control rates according to primary site were as follows: oral tongue, 72%; floor of mouth, 78%; retromolar trigone, 75%; and other sites, 61% (p = .23).

Locoregional Control According to AJCC Stage. Five-year actuarial locoregional control rates according to clinical AJCC stage were as follows: stage I, 87%; stage II, 74%; stage III, 68%; and stage IV, 72% (p = .6).

Locoregional Control According to Margin Status. Five-year actuarial locoregional control rates according to margin status were as follows: negative margins, 77%; positive margins, 52%; and close/equivocal, 86% (p < .0001).

Locoregional Control According to Other Pathologic Variables. Five-year actuarial locoregional control rates were significantly worse in patients with ECE, perineural invasion, or pathologic T3 or T4 tumors. There were no significant differences in 5-year locoregional control rates in patients with vascular invasion, bone invasion, or poor differentiation (Table 3). In addition, the number of lymph nodes involved did not significantly affect 5-year locoregional control rates (p = .30): none, 78%; one, 75%; two to three, 74%; and four or more, 65%. Disease in 10 of the 12 patients with none of the usual indications for postoperative radiation was locoregionally controlled.

Table 3. Univariate analysis of 5-year locoregional control.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>% of locoregional control with listed factor (no. patients)</th>
<th>% of locoregional control without listed factor (no. patients)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3/T4 primary*</td>
<td>63 (133)</td>
<td>86 (93)</td>
<td>.0003</td>
</tr>
<tr>
<td>Positive margins</td>
<td>52 (68)</td>
<td>77 (83)</td>
<td>.0018</td>
</tr>
<tr>
<td>Perineural invasion</td>
<td>62 (83)</td>
<td>88 (40)</td>
<td>.003</td>
</tr>
<tr>
<td>ECE</td>
<td>61 (43)</td>
<td>87 (42)</td>
<td>.007</td>
</tr>
<tr>
<td>≥3 risk factors</td>
<td>63 (49)</td>
<td>79 (177)</td>
<td>.007</td>
</tr>
<tr>
<td>Bone invasion</td>
<td>67 (80)</td>
<td>76 (146)</td>
<td>.24</td>
</tr>
<tr>
<td>Vascular invasion</td>
<td>70 (49)</td>
<td>76 (46)</td>
<td>.40</td>
</tr>
<tr>
<td>Poor differentiation</td>
<td>76 (47)</td>
<td>72 (179)</td>
<td>.57</td>
</tr>
</tbody>
</table>

Abbreviation: ECE, extracapsular nodal spread.

*pT1, 88%; pT2, 86%; pT3, 64%; pT4, 63%.

Locoregional Control According to Number of Indications for Irradiation. Five-year actuarial locoregional control rates were significantly worse in patients with three or more indications for ad-
ministering postoperative irradiation (Figure 3). A steady decline was observed in the rates of locoregional control with an increase in the number of indications for administering postoperative irradiation (Table 4). On the basis of these findings, patients were divided into relatively “favorable” and “unfavorable” groups. Patients in the favorable group had fewer than three indications to receive irradiation; those in the unfavorable group had three or more indications.

Multivariate Analysis of Pathologic Variables Affecting Locoregional Control. A multivariate analysis of pathologic factors that might influence locoregional control is shown in Table 5. T classification, margin status, and the presence of ECE, vascular or perineural invasion were significant.

Time Analyses. Treatment time was analyzed in three ways to determine its influence on locoregional control. First, the interval (in days) between surgery and the beginning of irradiation was analyzed (Table 6). Data were analyzed by four time periods, which were chosen for statistical reasons to give near equal numbers of patients in each group. Patients were separated into low (≤ three indications for RT) and high (> three indications for RT) risk groups. There was a trend toward higher failure rates in high-risk patients whose irradiation was initiated more than 51 days after surgery (Figure 4). No trend was seen in low-risk patients (0–35 days, 23%; 36–42 days, 4%; 43–51 days, 30%; and >51 days, 17%). Second, the length of the overall “treatment package,” calculated from the date of surgery until the last day of irradiation, was analyzed for its prognostic impact (Table 6). In high-risk patients, there was a trend toward higher failure rates when the overall treatment time exceeded 101 days (Figure 5). For low-risk patients, the failure rates were not significantly different according to length of the overall treatment package (0–80 days, 19%; 81–90 days, 16%; 91–101 days, 28%; and >101 days, 17%). The length of the radiation course (in days) was analyzed for its potential impact on locoregional control. No trend was identified for either low-risk or high-risk patient groups.

Dose Analysis. Five-year locoregional control rates for patients who received 60 Gy or less (74%), > 60 to 65 Gy (84%), > 65 to 70 Gy (69%), or more than 70 Gy (63%) were similar because of patient selection (p = .07). Patients with positive margins received higher mean doses (72 Gy) than did those with negative margins (64.8 Gy), yet still had lower locoregional control rates (63% vs 82%) at 5 years. Conversely, patients with close/equivocal margins had the highest control rate (92%), their less favorable prognosis being offset by higher mean doses (66 Gy) (p = .0004).

Salvage of Locoregional Recurrence. Of 55 patients with locoregional failures, surgical salvage with or without additional irradiation was attempted in 17 (31%). Nine of 17 patients (53%)

![FIGURE 3. Locoregional control versus number of risk factors.](image)
were successfully salvaged, for an overall salvage rate of 16% (nine of 55 patients).

**Distant Metastasis.** Five-year actuarial distant metastasis-free survival by pathologic AJCC stage was as follows: stage I, 100%; stage II, 97%; stage III, 90%; and stage IV, 81% \((p = .07)\).

In patients with positive nodes, those with ECE had significantly lower distant metastasis–free survival rates (64%) than did those without ECE (95%, \(p = .001\)).

**Survival.** Actuarial 5-year absolute and cause-specific survival rates for the entire group were 47% and 67%, respectively.

Absolute 5-year survival rates by pathologic AJCC stage were as follows: stage I, 63%; stage II, 70%; stage III, 48%; and stage IV, 40% \((p = .03)\).

Node-positive patients with ECE had a significantly lower absolute survival rate (21%) than did those without ECE (58%; \(p = .0003\)).

Cause-specific survival rates at 5 years by pathologic AJCC stage are shown in Figure 6. Node-positive patients with ECE had a significantly lower 5-year cause-specific survival (38%) than those without ECE had (81%, \(p < .0001\)). There was a significant improvement in 5-year cause-specific survival for patients without perineural invasion (85%) compared with those in whom it was present (56%, \(p = .002\)).

A multivariate analysis of pathologic factors that might influence cause-specific survival is shown in Table 7. The presence of ECE or perineural invasion was significant.

**Postirradiation, Late Complications.** Complications of treatment were graded in severity as mild, moderate, or severe. Mild complications were those that healed spontaneously in 1 to 5 months and were most often small \((\leq 0.5 \text{ cm})\)
areas of soft tissue necrosis or bone exposure. Moderate complications were of longer duration and produced more disability, yet resolved after conservation measures to promote healing such as discontinuation of denture use, oral rinses, antibiotics, and, in some instances, hyperbaric oxygen, without requiring surgery. Severe complications required hospitalization, surgery, or both. Patients requiring a permanent gastrostomy tube were also coded as having a severe complication.

There were 58 mild and moderate complications (26%): 22 bone exposures, 21 soft tissue necroses, one small wound dehiscence, seven fistulas, and seven wound infections.

There were 33 severe injuries (15%): 14 osteoradionecrosis, seven permanent gastrostomies, four severe dehiscences, three fistulas, two soft tissue necrosis, one wound infection, one mandibular fracture, and one plate extrusion. The median dose was 66 Gy in patients with severe complications. Logistics regression showed no correlation with respect to total dose ($p = 0.81$) or fractionation ($p = 0.25$) (twice daily vs once daily) in patients experiencing severe complications.

**DISCUSSION**

The usual indications to give postoperative irradiation at the University of Florida for carcinoma of the oral cavity include one or more of the following pathologic findings related to the primary site: bone invasion or extension of tumor into the soft tissues of the neck (T4 primary); margins that are positive, close ($\leq 5$ mm), contain CIS or dysplasia, or that were initially positive (but ultimately negative after re-resection$^6$–$^9$) perineural invasion;$^{10}$–$^{12}$ vascular space invasion;$^{13}$ or multicentricity (scattered, discontinuous foci or islands of tumor adjacent to the primary site, making margins of resection uncertain).

Factors in the neck specimen for which postoperative irradiation is generally added include multiple positive lymph nodes$^{14}$–$^{17}$ or ECE.$^{13,16,18}$–$^{21}$ High risk of occult tumor in an undissected, clinically negative N0 neck is not an adequate reason to add adjuvant RT unless additional indications for treatment are present. The high-risk neck should be electively disected.

Some of these factors are more ominous than others. For example, early bone erosion of the mandible is not likely to have the same negative prognostic influence as positive margins. Factors thought to be particularly ominous are the presence of positive margins,$^{7,22,23}$ multiple indications for administering postoperative irradiation,$^{22,24,25}$ and/or ECE.$^{17,19}$–$^{21,23,25}$–$^{27}$ Although we have never used poor differentiation as the sole indication for postoperative irradiation, there are data to suggest it may significantly affect locoregional control,$^{13,17,24}$ and in otherwise borderline cases, poor differentiation might be a reason to add irradiation postoperatively.

This series shows statistically significant correlations on univariate analysis between locoregional control and T classification (T1 and T2 vs T3 and T4), pathologic AJCC stage, ECE, perineural invasion, margin status, and the number of indications for postoperative radiation (Table 3). Multivariate analysis shows T classification, margin status, and the presence of ECE, vascular or perineural invasion to be independent predictors of locoregional control (Table 5).

**Table 7. Multivariate analysis of pathologic variables affecting cause-specific survival.**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECE</td>
<td>.0001</td>
</tr>
<tr>
<td>Perineural invasion</td>
<td>.0205</td>
</tr>
<tr>
<td>T classification</td>
<td>.0612</td>
</tr>
<tr>
<td>Vascular invasion</td>
<td>.2040</td>
</tr>
<tr>
<td>Differentiation</td>
<td>.2599</td>
</tr>
<tr>
<td>Bone invasion</td>
<td>.5086</td>
</tr>
<tr>
<td>Overall stage</td>
<td>.4521</td>
</tr>
<tr>
<td>N status</td>
<td>.6982</td>
</tr>
<tr>
<td>Margins</td>
<td>.8837</td>
</tr>
</tbody>
</table>

Abbreviation: ECE, extracapsular nodal spread.
follows: ECE, 31% and 66% \((p = .03)\); positive margins, 41% and 49% \((p = .04)\); and ECE and positive margins, 0% and 68% \((p = .001)\). A multivariate analysis of local control was performed evaluating the impact of T classification, N status, use of postoperative RT, the number of positive nodes, the number of nodes with ECE, primary site, microscopic and macroscopic ECE, and margin status. For the local control endpoint, use of postoperative RT \((p = .0001)\), macroscopic ECE \((p = .0001)\), and margin status \((p = .09)\) were of independent significance. Disease-free survival at 3 years was 25% after surgery alone and 45% after combined-modality treatment \((p = .0001)\). Cause-specific survival rates at 3 years were 41% for surgery alone and 72% for surgery and postoperative RT \((p = .0003)\). Multivariate analysis of cause-specific survival showed postoperative RT \((p = .0001)\) and the number of nodes with ECE \((p = .0001)\) significantly influenced this endpoint. Two irradiated patients experienced mandibular necrosis; one was treated with hyperbaric oxygen treatments and the other with conservative management.

Lundahl et al.\(^2\) reported a series of 95 patients with node-positive squamous cell carcinoma who were treated with a neck dissection and postoperative RT at the Mayo Clinic. A matched-pair analysis was performed with a series of patients treated with surgery alone; 56 matched pairs of patients were identified. The rates of recurrence in the dissected neck (relative risk \([RR] = 5.82; p = .0002)\), recurrence in either side of the neck \((RR = 2.21; p = .0052)\), and death from any cause \((RR = 1.67; p = .0182)\) were significantly higher for patients treated with neck dissection alone.

Thus, it seems for patients who are at high risk for locoregional failure after surgery, postoperative RT significantly improves disease control above the clavicles as well as survival.

**Factors Affecting Locoregional Control.** Data from the University of Florida,\(^2\) the Radiation Therapy Oncology Group (RTOG) 73-03 trial,\(^2\) and The University of Texas M. D. Anderson Cancer Center\(^2\) all suggest locoregional control rates after postoperative irradiation are lower for oral cavity primary tumors than for other head and neck primary sites. Zelefsky et al.\(^3\) noted that among patients with oral cavity primary tumors, those with oral tongue lesions fared the worst \((p = .03)\). In this series, there were no significant differences according to primary site within the oral cavity.

Another treatment-related issue that may influence the likelihood of cure is beam energy. Data exist in the literature suggesting better control in the neck with \(^{60}\)Co and 4-MV than with 6-MV photons, although local and locoregional control is just as good or better with 6-MV beams.\(^3\) Thus, most patients can be adequately treated with 6-MV photons. A beam spoiler may be added to increase the surface dose for patients believed to be at particularly high risk for tumor in the subcutaneous tissues.

**Salvage of Patients with Locoregional Recurrence.** In this series, 55 patients (25%) who were treated had recurrence above the clavicles develop. Seventeen underwent salvage surgery with or without additional RT. Nine of 17 (53%) were successfully salvaged, for an overall salvage rate of 16% (nine of 55).

Fifty-eight of 240 patients (24%) treated with surgery and postoperative RT at M. D. Anderson Cancer Center had a locoregional recurrence develop.\(^2\) Thirty-six patients underwent salvage therapy with surgery alone or combined with chemotherapy (11 patients), RT alone or combined with chemotherapy (three patients), or chemotherapy alone (22 patients). Only one of 58 patients (2%) was a “long-term survivor” 22 months after salvage therapy.

**Analysis of Time and Dose Factors.** Intuitively, it seems residual microscopic nests of tumor would be able to regrow in proportion to the length of time between surgery and the beginning of RT. However, the available data are mixed on this issue.\(^2,27\) – 40 This study demonstrates a decrease in locoregional control for patients with three or more risk factors with surgery–RT intervals greater than 51 days (Figure 4). Several authors have also suggested a correlation between tumor control and the length of RT, the latter being altered by the dose per fraction and/or number of fractions per day.\(^2,25,40\) No such trend was detected in this series. These two indices (ie, the surgery–RT interval and the length of the radiotherapy course) combine to give the overall treatment time, defined as the time from surgery to the last day of irradiation. Data exist in the literature correlating overall treatment time with local control, at least for high-risk patients.\(^40\) This study demonstrates a decrease in locoregional control for patients having three or more risk factors with overall treatment times greater
than 101 days (Figure 5), although the difference is not statistically significant.

The previously mentioned data and common sense indicate irradiation should begin as soon as healing is complete; it can often be started within 3 to 4 weeks of surgery. If irradiation is delayed until gross recurrence has occurred, the chance for successful salvage by irradiation is only 5% to 10%. 7,44,45 If healing is not complete by 6 weeks, data from earlier University of Florida series 43,46 show irradiation can often be safely initiated, and approximately two thirds of patients will heal spontaneously during or after irradiation. Patients at high risk (≥ three risk factors) for recurrence and/or those whose surgery–RT interval has been prolonged (>7 weeks) should be considered for altered dose/fractionation schemes that shorten the length of the RT course, thereby decreasing the overall treatment time.

**Adjuvant Chemotherapy and Future Directions.**

The issue of whether chemotherapy is beneficial concomitantly with postoperative irradiation for head and neck cancer was recently resolved with the publication of two randomized trials (RTOG 9501 and EORTC 22391). 47,48 Each of these showed an improvement in locoregional control and disease-free survival with cisplatin (100 mg/M²) given on days 1, 22, and 43 of the radiotherapy regimen. 47,48 Prior to that, two publications showed a similar benefit using concomitant chemoradiation, although an earlier review of the RTOG 9501 data that appeared in abstract form was inconclusive. 49–51 Severe acute effects are seen more frequently with concomitant treatment compared with postoperative radiation alone. Although none of the patients in this series received chemotherapy, our current policy is to consider concomitant cisplatin in selected high-risk cases.

IMRT has been used postoperatively at other institutions. 52–56 We currently use IMRT mainly to treat de novo head and neck tumors definitively with irradiation. It is used sparingly in the postoperative setting, mainly because of concerns about the dose distribution to skin and subcutaneous tissues, which may be at more risk after surgery. As the role of IMRT evolves, its use may increase in postoperative situations. We continue to favor more conventional beam arrangements when feasible, to optimize dose distributions to the skin and subcutaneous tissues at risk.

The data presented herein suggest a strikingly negative effect on locoregional control when peri-neural spread, ECE, and/or positive margins are present. More than one third of patients continue to have treatment failure above the clavicles when any of these three factors exist. An improvement in locoregional control was seen in patients with positive margins treated twice daily to doses of 74.4 Gy or higher. We will likely consider the same aggressive treatment for patients with oral cavity lesions with perineural and/or ECE, as well. Conversely, consideration should be given to re-resection in cases in which the final margins contain invasive cancer if the site of positivity can be accurately determined and another operation performed without adding excessively to the morbidity. Our current recommendation for patients with oral cavity primary tumors who require postoperative irradiation is to deliver 64 to 66 Gy at 2 Gy per fraction for relatively favorable situations and 74.4 to 76.8 Gy in 62 to 64 fractions, twice a day, for unfavorable scenarios. Concomitant cisplatin should be considered in high-risk cases. We recognize that these dose-fractionation recommendations for high-risk patients are not strictly supported by our data or by randomized data published elsewhere in the literature. 25,40 However, we believe these guidelines are justified in view of the unsatisfactory rates of locoregional control seen in this unfavorable subset of patients.

**REFERENCES**


