

Leading article

Elective management of the neck in oral cavity squamous carcinoma: current concepts supported by prospective studies

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Accepted 2 June 2008

Abstract

The incidence of occult cervical metastasis in oral cavity cancer, even in early stages, is significant, necessitating elective treatment of the neck in a majority of cases. There is no method of imaging or other examination that will detect microscopic foci of metastatic disease in cervical lymph nodes. Immunohistochemical and molecular analysis of neck specimens reveals the incidence of occult metastases to be higher than revealed by light microscopy with ordinary hematoxylin and eosin staining. The neck may be treated electively by surgery or irradiation. Surgery has the advantage of permitting pathological staging of the neck, avoiding unnecessary radiation treatment and indicating cases where adjuvant therapy should be employed. As oral cavity cancer rarely metastasizes to level V, a radical or modified radical neck dissection of all five node levels is not necessary. Selective dissection of levels I–III (“supraomohyoid neck dissection”) is the usual procedure of choice for elective dissection of the neck. Most of the relatively small number of isolated metastasis to level IV are from primary tumours of the tongue, which are known to produce “skip” metastases. Thus an “extended supraomohyoid neck dissection” of levels I–IV is recommended by some authors for elective treatment of the neck in tongue cancer. A number of recent prospective multi-institutional studies have demonstrated that sublevel IIB is rarely involved with isolated metastasis from oral cavity primary tumours, except from some tongue cancers. Thus it is justifiable to omit dissection of sublevel IIB in elective treatment of most cases of oral cavity cancer. Bilateral neck dissection should be performed in elective treatment of tumours involving midline structures, and in patients with ipsilateral neck metastasis.

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Keywords: Elective neck dissection; Supraomohyoid neck dissection; Node levels I–IV; Oral cavity cancer; Radiotherapy

Incidence of occult metastasis

Elective management of the neck in patients with squamous carcinoma of the oral cavity remains a controversial topic. The reported incidence of occult regional lymph node metastasis from such tumours varies from 6% to 46%.¹ Occult regional metastasis may be found even in cases with small primary tumours.¹ The reason for the variance in reported

incidence of metastasis is that traditional techniques of pathologic analysis of neck dissections may fail to detect isolated neoplastic cells and micrometastases. When new and highly sensitive investigations that may detect subpathological as well as subclinical disease are employed, the incidence of metastases detected has been found to be higher than previously indicated.^{2–15} These newer technologies include immunohistochemistry and molecular analysis.

Site of the tumour and nodal metastases

The oral cavity consists of the mucosa of the upper and lower lips, cheek mucosa, retromolar areas, upper and lower

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bucco-alveolar sulci (vestibule of mouth), upper alveolus and gingiva (upper gum), lower alveolus and gingiva (lower gum), hard palate, anterior two-thirds of the tongue, and floor of the mouth.¹⁶ The great majority of primary tumours of the oral cavity are squamous carcinomas but a variety of other pathological types can occur. The two most common subsites of the oral cavity involved by squamous carcinoma are the mobile (oral) tongue and the floor of the mouth. Tumours arising from each of these structures, including those found in patients with early (T1–T2) disease, have a significant propensity to metastasize to the regional lymph nodes.¹⁷ Although control of the primary tumour of the oral cavity, particularly in earlier stages, is often achieved, treatment failure frequently results from recurrence in cervical lymph nodes, even among patients who initially present with no clinical evidence of neck disease. Consequently, initial management must address the possibility of occult metastases.¹⁸ Early stage tongue and floor-of-mouth cancers have a significant incidence of occult cervical metastasis. Depth of invasion and tumour thickness are significant predictors of lymph node metastasis in these tumours.^{19,20} The risk of lymph node metastases for the other subsites is also significant in patients with intermediate and advanced mucosal tumours.²¹ Only lower alveolar ridge cancers have a low potential for neck metastases.²²

Evaluation of the clinically negative (N0) neck

The work of Weiss et al.²³ has established a threshold of a 20% possibility of cervical metastasis as the indication for elective treatment of the neck in squamous cell cancer of the head and neck. Others have suggested that this threshold be lowered to 15%, because of the highly adverse impact of lymph node metastasis on survival once they become evident on clinical examination, and change in the risk–benefit ratio during the past two decades due to the use of more conservative surgical procedures.^{24,25}

The advent of modern methods of clinical, pathological and molecular analysis has indicated that the incidence of occult metastatic disease for most oral cavity cancers is higher than previously believed. Despite advances in imaging technology, none of the currently available imaging modalities is able to detect reliably the presence of micrometastases in the lymph nodes of clinically N0 necks.⁹ Twenty-five percent of tumour-positive elective neck dissection specimens of clinically N0 necks contain micrometastases smaller than 3 mm.²⁶ Many of these metastatic nodes are involved with tumour cells not visible on histological slides prepared with conventional hematoxylin and eosin staining, although they may be detected by immunohistochemistry and molecular analysis.^{8,12} Various immunohistochemical investigations have found micrometastases in 5–58% of patients who had no evidence of metastatic disease on routine pathological assessment.¹⁰ In addition, the use of molecular analysis permits detection of micrometastases in approximately 20% of patients staged pN0 by conventional light microscopy.^{27–30}

Thus the 15% to 20% threshold for consideration of elective treatment of the neck is exceeded far more often than was believed in the past.

At present no pretreatment study can replace the accuracy, and thus the requirement, of staging the neck pathologically. The goal of identifying subclinical disease without surgical intervention remains elusive.

Management of the neck – supraomohyoid (levels I–III) and extended supraomohyoid (levels I–IV) neck dissections

Elective neck dissection is the usual treatment of choice for oral cavity squamous carcinoma. Elective neck dissection allows accurate neck staging and determination of the need for other adjuvant therapies.

Clinical and pathological studies have supported the concept that modified radical neck dissection (levels I–V) comprises unnecessary overtreatment in the elective management of oral cavity squamous carcinoma. For example, in a multi-institutional prospective study designed to compare modified radical neck dissection with supraomohyoid neck dissection in the management of the clinically negative neck in patients with oral squamous carcinoma, the rates of recurrence and survival were similar in both groups of patients.³¹ Other clinical, pathologic and genetic studies have shown that level V is rarely involved in cancers of the oral cavity never in cases without clinical disease at other levels.^{8,32}

The efficacy of supraomohyoid neck dissection is based on the usual distribution of metastasis from oral cavity cancer. Scintigraphic studies have shown that the preferential pathway of lymphatic drainage from tongue cancer is to levels II–IV,³³ while the majority (88%) of metastatic submandibular lymph nodes (sublevel IB) measuring 1 cm or less in diameter occur in squamous carcinoma of the floor of mouth.³⁴

Supraomohyoid neck dissection consists of selective dissection of levels I–III including the submandibular gland, while preserving the spinal accessory nerve, the internal jugular vein and the sternocleidomastoid muscle. In cancers approaching or crossing the midline structures, bilateral neck dissection is indicated because the lymph nodes on both sides of the neck are at risk of containing metastases.³⁵ Koo et al.³⁶ advocate elective contralateral neck treatment with surgery or radiotherapy in patients with oral cavity squamous carcinoma with positive ipsilateral nodes, advanced stage primary tumours or primary tumours crossing the midline.

While dissection of level IV may expose the patient to some risk of chyle fistula, or even phrenic nerve injury, for patients with oral tongue cancer, inclusion of level IV in the dissection appears justified in view of known lymphatic drainage of the tongue and the higher incidence of “skip” metastases.^{33,37,38} Byers et al.³⁷ reported a high incidence (15.8%) of either level III or IV metastasis as the only manifestation of disease in the neck, without disease

in levels I and II, among 277 patients with oral tongue carcinoma. The dissection of levels I–IV is known as “extended” or “expanded” supraomohyoid neck dissection or antero-lateral neck dissection.³⁷ Salvage of patients who develop skip metastases, however, is poor, which may reflect a more aggressive biological tumour behaviour in these cases. If there is pathologic evidence of lymph node metastases in the neck dissection specimen, postoperative radiotherapy is often considered to be indicated.^{6,17} De Zinis et al.³⁸ found metastases in level IV in 15% of patients with squamous carcinoma of the oral cavity who had positive lymph nodes. Twenty-eight percent of the level IV nodes were skip metastases. In another study, occult metastases in level IV occurred in 5 of 49 patients with cancer of the oral cavity, staged N0.³⁹

Other authors have supported inclusion of level IV in elective dissection for tongue cancer, Woolgar⁴⁰ recommended that neck dissection should include level IV considering the “erratic” (unpredictable) pattern of metastasis of this cancer, and Hosai et al.⁴¹ routinely included dissection of level IV in the management of cancer of the tongue. The low incidence of failure (0.7%) outside the field of dissection found in their study supports this policy. Lydiatt et al.⁴² pointed out that supraomohyoid neck dissection removes approximately 60–70% of the nodes at greatest risk of metastasis, but this rises to 80–94% if level IV nodes are included in the dissection. Kerawala and Martin⁴³ advocated a policy of routinely extending the supraomohyoid neck dissection to level IV in patients with squamous carcinoma of the floor of the mouth to allow for adequate staging of the neck. Ahmed et al.⁴⁴ suggested removing level IV lymph nodes along with levels I, II and III in squamous carcinoma of oral cavity even when the tumours are small. Other authors have noted the occurrence of skip metastases to level IV, and recommend including this level in the dissection for tongue cancer.^{45,46}

To the contrary, Khafif et al.,⁴⁷ in an analysis including pathologic findings and clinical follow-up, found an incidence of only 2% metastasis to level IV in a cohort of 51 patients with T1–T3, N0 tongue cancer. These authors concluded that level IV need be included in the dissection only when there is intraoperative suspicion of metastasis in levels II or III.

Dissection of sublevel IIB?

The spinal accessory nerve courses through sublevel IIB, and dissection of this area may cause shoulder dysfunction. To determine whether sublevel IIB may be preserved in elective supraomohyoid neck dissection in patients with squamous carcinoma of oral cavity and no palpable lymph nodes, Lim et al.,⁴⁸ in 2004, prospectively studied 74 patients with clinically negative necks. While 24 patients (32%) had positive lymph nodes, only 4 (5.4%) had involvement of sublevel IIB. There was no instance of isolated metastasis to sublevel IIB without involvement of other lymph nodes in the supraomohyoid neck dissection specimens. All 4 patients with a

positive sublevel IIB lymph node had T2N0 tongue cancers (4 of 51), in which the location of the primary site was the lateral border of the oral tongue. The authors concluded that sublevel IIB metastasis was rare in their study, and nodal recurrence in this area after selective supraomohyoid neck dissection in squamous carcinoma of the oral cavity was extremely rare. Therefore, this region may be preserved in elective neck dissection in these patients.

In 2005, in a prospective study using molecular markers to identify metastatic disease, Elsheikh et al.⁴⁹ found metastasis to sublevel IIB in 5 (10%) of 48 patients with oral cavity cancer. As in the study by Lim et al.,⁴⁸ in all 5 cases the primary tumour was situated in the tongue (5 of 23), and there were no instances of isolated metastasis to sublevel IIB lymph nodes without involvement of other nodes in the supraomohyoid neck dissection specimens. Although 10% is higher than the incidence reported with primary tumours of other sites, this incidence is still below the generally accepted threshold for elective neck dissection. Nevertheless, an exception may be considered for primary tumours of the tongue. Elsheikh et al.⁴⁹ concluded that sublevel IIB may be preserved in elective supraomohyoid neck dissection in patients with squamous carcinoma of the oral cavity, except in cases of primary tongue cancer, where it should be included in the dissection.

In 2007, Bolzoni Villaret et al.⁵⁰ prospectively studied 54 oral cavity cancer patients with clinically negative necks. Only 1 (1.8%) had involvement of sublevel IIB.

In 2008, Paleri et al.⁵¹ prospectively conducted a personal study and review of the literature to identify the incidence of occult metastases in the lymph nodes of sublevel IIB in upper aerodigestive tract squamous carcinoma among patients with clinically and radiologically stage N0 necks. This large cumulative series included 10 of the authors’ personal cases of oral cavity cancer, of which 4 were situated in the tongue [personal communication, 2007]. Only one tumour, localized at the floor of the mouth and adjacent alveolus (T4), presented isolated metastasis at sublevel IIB. On the basis of an incidence between 4% and 5% of metastasis at sublevel IIB in oral and oropharyngeal primaries, the authors recommended that this sublevel should be dissected in the elective treatment of oral cavity squamous carcinoma, unless it is evident that the patient will need postoperative irradiation. They concluded that there is no need to dissect sublevel IIB on the contralateral side.

Data from these four recent prospective analyses of neck dissection specimens, totalling 186 patients with N0 oral cancers, revealed a 5.9% incidence of positive nodes at sublevel IIB in cases of oral cavity squamous carcinoma. More prospective studies on this subject are needed given the disparate results in these reports concerning metastases to sublevel IIB from tongue cancers (0–21%).^{48–51} The highest percentage of lymph node metastases was detected in the study supported by molecular investigations. The risk of nodal disease in sublevel IIB is greater for tumours arising in the oropharynx compared with the oral cavity and larynx.⁴⁹ In any case, when considering the merits of preservation of

sublevel IIB, the benefit of preservation of accessory nerve function must be weighed against potentially reduced tumour control.⁵²

Irradiation

The work of Fletcher⁵³ established that elective irradiation of the N0 neck can produce results equivalent to those obtained by neck dissection. Thus radiation therapy is an alternative treatment to supraomohyoid neck dissection for elective treatment of the N0 neck. While neck dissection has the advantage of enabling histopathologic examination of the specimen as well as avoiding the complications of irradiation, and reserving radiation therapy for subsequent use if needed, and while most oral cavity tumors are treated surgically, there nevertheless are instances when the oral cavity primary tumour must be treated by irradiation. These include factors such as the patient's ability to undergo surgery and patient preference, particularly in cases of tongue cancer where brachytherapy plus external irradiation may be chosen in preference to hemiglossectomy.⁵⁴ In cases where the primary tumour is treated by irradiation, it is our practice, as well as that of many other surgeons, also to treat the neck with irradiation.⁵⁵ The reasons for this, in addition to the same factors that led to treatment of the primary tumour with irradiation, include the difficulty of administering subsequent irradiation to the same patient without producing areas of "geographic miss", or overlapping fields. The indications for elective irradiation of the neck are based on the same statistical thresholds as for surgical treatment of the neck.

Conclusions

Selective neck dissection, including lymph node levels I–III, is the type of lymph node dissection most commonly performed in cancer of the oral cavity with clinically N0 necks. When the lesion is localized in the tongue, there is evidence indicating that level IV is at risk, and this level should be included in the dissection ("extended" or "expanded" supraomohyoid neck dissection). There are conflicting data regarding the risk of disease in sublevel IIB, but a number of recent studies indicate that isolated metastasis rarely occurs in this region, except in a small number of tongue cancers. While further study is needed, omission of this sublevel from elective dissection of non-lingual oral cavity cancers appears justified.

Bilateral neck dissection is indicated in cancers involving midline structures, as well as for patients with positive ipsilateral nodes. Elective radiation therapy can provide adequate treatment of the clinically negative neck. It has the disadvantage of producing no information as to the actual stage of cervical lymph node disease, if any. Radiation of the neck is generally reserved for cases where the primary tumour is treated by the same modality.

References

1. Capote A, Escorial V, Muñoz-Guerra MF, Rodríguez-Campo FJ, Gamallo C, Naval L. Elective neck dissection in early-stage oral squamous cell carcinoma – does it influence recurrence and survival? *Head Neck* 2007;**29**:3–11.
2. Ambrosch P, Brinck U. Detection of nodal micrometastases in head and neck cancer by serial sectioning and immunostaining. *Oncology (Williston Park)* 1996;**10**:1221–9.
3. Enepekides DJ, Sultanem K, Nguyen C, Shenouda G, Black MJ, Rochon L. Occult cervical metastases. Immunoperoxidase analysis of the pathologically negative neck. *Otolaryngol Head Neck Surg* 1999;**120**:713–7.
4. Hamakawa H, Takemura K, Sumida T, Kayahara H, Tanioka H, Sogawa K. Histological study on pN upgrading of oral cancer. *Virchows Arch* 2000;**437**:116–21.
5. Barrera JE, Miller ME, Said S, Jafek BW, Campana JP, Shroyer KR. Detection of occult cervical micrometastases in patients with head and neck squamous cell cancer. *Laryngoscope* 2003;**113**:892–6.
6. Byers RM, Clayman GL, McGill D, Andrews T, Kare RP, Roberts DB, Goepfert H. Selective neck dissections for squamous carcinoma of the upper aerodigestive tract: patterns of regional failure. *Head Neck* 1999;**21**:499–505.
7. Yoshida K, Kashima K, Suenaga S, Nomi N, Shuto J, Suzuki M. Immunohistochemical detection of cervical lymph node micrometastases from T2N0 tongue cancer. *Acta Otolaryngol* 2005;**125**:654–8.
8. Yamazaki Y, Chiba I, Hirai A, Satoh C, Sakakibara N, Notani K, Iizuka T, Totsuka Y. Clinical value of genetically diagnosed lymph node micrometastasis for patients with oral squamous cell carcinoma. *Head Neck* 2005;**27**:676–81.
9. Ferlito A, Shaha AR, Rinaldo A. The incidence of lymph node micrometastases in patients pathologically staged N0 in cancer of oral cavity and oropharynx. *Oral Oncol* 2002;**38**:3–5.
10. Devaney KO, Rinaldo A, Ferlito A. Micrometastases in cervical lymph nodes from patients with squamous carcinoma of the head and neck: should they be actively sought? Maybe. *Am J Otolaryngol* 2007;**28**:271–4.
11. Rhee D, Wenig BM, Smith RV. The significance of immunohistochemically demonstrated nodal micrometastases in patients with squamous cell carcinoma of the head and neck. *Laryngoscope* 2002;**112**:1970–4.
12. Ferlito A, Partridge M, Brennan J, Hamakawa H. Lymph node micrometastases in head and neck cancer: a review. *Acta Otolaryngol* 2001;**121**:660–5.
13. Woolgar JA. Micrometastasis in oral/oropharyngeal squamous cell carcinoma: incidence, histopathological features and clinical implications. *Br J Oral Maxillofac Surg* 1999;**37**:181–6.
14. Stoeckli SJ, Pfaltz M, Steinert H, Schmid S. Histopathological features of occult metastasis detected by sentinel lymph node biopsy in oral and oropharyngeal squamous cell carcinoma. *Laryngoscope* 2002;**112**:111–5.
15. Ferlito A, Rinaldo A, Devaney KO, Nakashiro K, Hamakawa H. Detection of lymph node micrometastases in patients with squamous carcinoma of the head and neck. *Eur Arch Otorhinolaryngol* 2008 Jun 4. [Epub ahead of print].
16. International Union Against Cancer (UICC). *TNM Classification of Malignant Tumours*. 6th ed. New York, NY: Wiley-Liss; 2002.
17. Robbins KT. Indications for selective neck dissection: when, how, and why. *Oncology (Williston Park)* 2000;**14**:1455–64, discussion 1467–1469.
18. Silver CE, Moisa II. Elective treatment of the neck in cancer of the oral tongue. *Semin Surg Oncol* 1991;**7**:14–9.
19. Spiro RH, Huvos AG, Wong GY, Spiro JD, Gnecco CA, Strong EW. Predictive value of tumor thickness in squamous carcinoma confined to the tongue and floor of the mouth. *Am J Surg* 1986;**152**:345–50.
20. Shiga K, Ogawa T, Sagai S, Kato K, Kobayashi T. Management of the patients with early stage oral tongue cancers. *Tohoku J Exp Med* 2007;**212**:389–96.

21. Byers RM, Wolf PF, Ballantyne AJ. Rationale for elective modified neck dissection. *Head Neck Surg* 1988;**10**:160–7.
22. Byers RM, Newman R, Russell N, Yue A. Results of treatment for squamous carcinoma of the lower gum. *Cancer* 1981;**47**:2236–8.
23. Weiss MH, Harrison LB, Isaacs RS. Use of decision analysis in planning a management strategy for the stage N0 neck. *Arch Otolaryngol Head Neck Surg* 1994;**120**:699–702.
24. Pitman KT. Rationale for elective neck dissection. *Am J Otolaryngol* 2000;**21**:31–7.
25. Pillsbury 3rd HC, Clark M. A rationale for therapy of the N0 neck. *Laryngoscope* 1997;**107**:1294–315.
26. van den Brekel MWM, van der Waal I, Meijer CJLM, Freeman JA, Castelijns JA, Snow GB. The incidence of micrometastases in neck dissection specimens obtained from elective neck dissections. *Laryngoscope* 1996;**106**:987–91.
27. Brennan JA, Mao L, Hruban RH, Boyle JO, Eby YJ, Koch WM, et al. Molecular assessment of histopathological staging in squamous-cell carcinoma of the head and neck. *N Engl J Med* 1995;**332**:429–35.
28. Hamakawa H, Fukizumi M, Bao Y, Sumida T, Onishi A, Tanioka H, et al. Genetic diagnosis of micrometastasis based on SCC antigen mRNA in cervical lymph nodes of head and neck cancer. *Clin Exp Metastasis* 1999;**17**:593–9.
29. Cortesina G, Martone T, Galeazzi E, Olivero M, De Stefani A, Bussi M, et al. Staging of head and neck squamous cell carcinoma using the MET oncogene product as marker of tumor cells in lymph node metastases. *Int J Cancer* 2000;**89**:286–92.
30. Nieuwenhuis EJ, Leemans CR, Kummer JA, Denkers F, Snow RH, Brakenhoff RH. Assessment and clinical significance of micrometastases in lymph nodes of head and neck cancer patients detected by E48 (Ly-6D) quantitative reverse transcription-polymerase chain reaction. *Lab Invest* 2003;**83**:1233–40.
31. Brazilian Head Neck Cancer Study Group. Results of a prospective trial on elective modified radical classical versus supraomohyoid neck dissection in the management of oral squamous carcinoma. *Am J Surg* 1998;**176**:422–7.
32. Dias FL, Lima RA, Kligerman J, Farias TP, Soares JR, Manfro G, Sa GM. Relevance of skip metastases for squamous cell carcinoma of the oral tongue and the floor of the mouth. *Otolaryngol Head Neck Surg* 2006;**134**:460–5.
33. De Cicco C, Trifirò G, Calabrese L, Bruschini R, Ferrari ME, Travaini LL, Fiorenza M, Viale G, Chiesa F, Paganelli G. Lymphatic mapping to tailor selective lymphadenectomy in cN0 tongue carcinoma: beyond the sentinel node concept. *Eur J Nucl Med Mol Imaging* 2006;**33**:900–5.
34. DiNardo LJ. Lymphatics of the submandibular space: an anatomic, clinical, and pathologic study with applications to floor-of-mouth carcinoma. *Laryngoscope* 1998;**108**:206–14.
35. Rigual NR, Wiseman SM. Neck dissection: current concepts and future directions. *Surg Oncol Clin N Am* 2004;**13**:151–66.
36. Koo BS, Lim YC, Lee JS, Choi EC. Management of contralateral N0 neck in oral cavity squamous cell carcinoma. *Head Neck* 2006;**28**:896–901.
37. Byers RM, Weber RS, Andrews T, McGill D, Kare R, Wolf P. Frequency and therapeutic implications of “skip metastases” in the neck from squamous carcinoma of the oral tongue. *Head Neck* 1997;**19**:14–9.
38. De Zinis LO, Bolzoni A, Piazza C, Nicolai P. Prevalence and localization of nodal metastases in squamous cell carcinoma of the oral cavity: role and extension of neck dissection. *Eur Arch Otorhinolaryngol* 2006;**263**:1131–5.
39. Crean SJ, Hoffman A, Potts J, Fardy MJ. Reduction of occult metastatic disease by extension of the supraomohyoid neck dissection to include level IV. *Head Neck* 2003;**25**:758–62.
40. Woolgar JA. Pathology of the N0 neck. *Br J Oral Maxillofac Surg* 1999;**37**:205–9.
41. Hosai AS, Carrau RL, Johnson JT, Myers EN. Selective neck dissection in the management of the clinically node-negative neck. *Laryngoscope* 2000;**110**:2037–40.
42. Lydiatt DD, Robbins KT, Byers RM, Wolf PF. Treatment of stage I and II oral tongue cancer. *Head Neck* 1993;**15**:308–12.
43. Kerauola C, Martin IC. Extending the supraomohyoid neck dissection in squamous cell carcinoma of the floor of mouth. *Head Neck* 1998;**20**:434 (Letter to the Editor).
44. Ahmed MU, Khawar A, Ahmed J, Ajmal M, Bangash WK, Akhter MR. Occult metastasis in carcinoma of oral cavity. *J Coll Physicians Surg Pak* 2007;**17**:313–5.
45. Ferlito A, Mannarà GM, Rinaldo A, Politi M, Robiony M, Costa F. Is extended selective supraomohyoid neck dissection indicated for treatment of oral cancer with clinically negative neck? *Acta Otolaryngol* 2000;**120**:792–5.
46. Ferlito A, Shaha AR, Rinaldo A, Pellitteri PK, Mondin V, Byers RM. Skip metastases” from head and neck cancers. *Acta Otolaryngol* 2002;**122**:788–91 (Guest Editorial).
47. Khafif A, Lopez-Garza JR, Medina JE. Is dissection of level IV necessary in patients with T1-T3 N0 tongue cancer? *Laryngoscope* 2001;**111**:1088–90.
48. Lim YC, Song MH, Kim SC, Kim KM, Choi EC. Preserving level IIb lymph nodes in elective supraomohyoid neck dissection for oral cavity squamous cell carcinoma. *Arch Otolaryngol Head Neck Surg* 2004;**130**:1088–91.
49. Elsheikh MN, Mahfouz ME, Elsheikh E. Level IIb lymph nodes metastasis in elective supraomohyoid neck dissection for oral cavity squamous cell carcinoma: a molecular-based study. *Laryngoscope* 2005;**115**:1636–40.
50. Bolzoni Villaret A, Piazza C, Peretti G, Calabrese L, Ansarin M, Chiesa F, Pellini R, Spriano G, Nicolai P. Multicentric prospective study on the prevalence of sublevel IIb metastases in head and neck cancer. *Arch Otolaryngol Head Neck Surg* 2007;**133**:897–903.
51. Paleri V, Kumar Subramaniam S, Oozeer N, Rees G, Krishnan S. Dissection of the submuscular recess (sublevel IIb) in squamous cell cancer of the upper aerodigestive tract: Prospective study and systematic review of the literature. *Head Neck* 2008;**30**:194–200.
52. Elsheikh MN, Rinaldo A, Ferlito A, Fagan JJ, Suárez C, Lowry J, Paleri V, Khafif A, Olofsson J. Elective supraomohyoid neck dissection for oral cavity squamous cell carcinoma: is dissection of sublevel IIb necessary? *Oral Oncol* 2008;**44**:216–9.
53. Fletcher GH. Elective irradiation of subclinical disease in cancers of the head and neck. *Cancer* 1972;**29**:1450–4.
54. Botstein C, Silver C, Ariaratnam L. Treatment of carcinoma of the oral tongue by radium needle implantation. *Am J Surg* 1976;**132**:523–4.
55. Ferlito A, Silver CE, Rinaldo A, Smith RV. Surgical treatment of the neck in cancer of the larynx. *ORL J Otorhinolaryngol Relat Spec* 2000;**62**:217–25.