

Target volume delineation

Proposal for the delineation of the nodal CTV in the node-positive and the post-operative neck

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Abstract

Background and purpose: In 2003, a panel of experts published a set of consensus guidelines regarding the delineation of the neck node levels (Radiother Oncol, 2003; 69: 227-36). These recommendations were applicable for the node-negative and the N1-neck, but were found too restrictive for the node-positive and the post-operative neck.

Patients and methods: In this framework, using the previous recommendations as a backbone, new guidelines have been proposed taking into account the specificities of the node-positive and the post-operative neck.

Results: Inclusion of the retrostyloid space cranially and the supra-clavicular fossa caudally is proposed in case of neck nodes (defined radiologically or on the surgical specimen) located in levels II, and IV or Vb, respectively. When extracapsular rupture is suspected (on imaging) or demonstrated on the pathological specimen, adjacent muscles should also be included in the CTV. For node(s) located at the boundary between contiguous levels (e.g. levels II and Ib), these two levels should be delineated. In the post-operative setting, the entire 'surgical bed' should be included. Last, the retropharyngeal space should be delineated in case of positive neck from pharyngeal tumors.

Conclusions: The objective of the manuscript is to give a comprehensive description of the new set of guidelines for CTV delineation in the node-positive neck and the post-operative neck, with a complementary atlas of the new anatomical structures to be included.

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The implementation of three-dimensional conformal radiotherapy (3D-CRT) and intensity modulated radiation therapy (IMRT) permitting far greater control of dose distribution, requires optimal selection and delineation of target volumes and organs at risk. This is particularly important for the management of tumors in the head and neck region, where, with few exceptions (e.g. early stage laryngeal and oral cavity tumors), radiation oncologists previously were used to comprehensive treatment of all node levels in the neck. In recent years, however, more selective treatment of the neck nodes have been advocated, and few retrospective studies have demonstrated that such policy could lead to substantial reduction in the dose inflicted on critical organs at risk, such as the parotid glands, without jeopardizing loco-regional control [1-4]. However, sub-optimal selection and delineation of target volumes could easily jeopardize the clinical impact of the exquisite dose distributions produced.

Guidelines for the selection and the delineation of the neck node levels have been published over the past few years, and in 2003 a consensus was proposed and adopted by the major international cooperative groups [4-7]. Such guidelines, however, only concerned the node negative necks. For the node-positive and the post-operative neck, it was felt that these recommendations were too restrictive and that amendments were required. Recent retrospective IMRT series have indeed reported marginal recurrence in the neck of node-positive patients treated primarily or post-operatively with radiotherapy, illustrating the need for more comprehensive dose coverage in these clinical situations [8].

Within this framework, from the clinicians having worked previously on the consensus guidelines for the node-negative neck, a core group decided to review and amend the existing recommendations to take into account the specificities of the node-positive and the post-operative neck. Particular consideration was given to (1) cranial extension of level II,

and caudal extension of levels IV and Vb, (2) criteria for inclusion of additional non-lymphoid structures, and (3) inclusion in the CTV of nodal levels that are adjacent to clinically involved levels, and would not be considered at-risk in the N0 neck.

The objective of the present manuscript is to present the new set of guidelines for CTV delineation in the node-positive neck and the post-operative neck, together with a complementary atlas of the new anatomical structures to be included in the CTV.

Evidences for the need of specific guidelines in the node-positive and in the post-operative neck

A legitimate concern when selecting and delineating the target volumes in preparation of 3D-CRT or IMRT for head and neck squamous cell carcinoma (HNSCC) is that too tight target volumes might lead to unacceptable rate of marginal failures. For the node-negative neck, the proposed guidelines have reached a worldwide consensus [5]. For the node-positive neck, few data indicate that indeed the CTV might have to be extended in specific cases, which are detailed below.

There are not that many retrospective studies detailing the pattern of relapse in the neck after IMRT treatment for pharyngo-laryngeal squamous cell carcinomas. Eisbruch et al. reported a series of 135 patients treated bilaterally from 1994 to 2002 with 3D-CRT or IMRT for primary tumors mainly located in the oropharynx ($n=80$) and without node metastasis in the contralateral neck [8]. With a median follow-up of 32 months (range: 6-107 months), 21 patients had a loco-regional recurrence of which four were marginal. Some of the marginal recurrences were observed in the node-positive side of the neck near the base of skull above the upper limit of delineation. The explanation of such nodal involvement so high in the neck for non-nasopharyngeal primaries may lie in the fact that invaded node(s) in level II may induce a retrograde lymph flow thus carrying tumor cells in nodes not deemed to be invaded higher up in the neck [9]. Thus, although only few data are available, it may sound legitimate in case of infiltration of the upper part of level II to include in the CTV the fatty space around the jugulo-carotid vessels up to the jugular foramen. From an anatomic point of view, this space belongs to the upper most aspect of the retrostyloid fossa [10]. In the consensus guidelines, this space was purposely not included in level II, whose cranial edge was set at the level of the lateral process of the first cervical vertebra (C1) [5]. Indeed, recurrences near the base of skull are not typically observed in node-negative patients (see review in [4]). On this particular issue, the consensus recommendations are in contradiction with the upper limit of level II adopted by Som et al., who proposed to extend this level up to the base of skull irrespective of the neck nodal status [11].

Similarly, in case of infiltration of the lower neck, it may be appropriate to include in the CTV the fatty space caudal to levels IV and Vb down to the clavicle, which from an anatomical point of view belongs to the supraclavicular fossa [12]. In the consensus guidelines, following the surgical

practice, the caudal limit of level IV was arbitrarily set at 2 cm cranial to the sterno-clavicular joint, whereas the cervical transverse vessels defined the caudal limit of level Vb [5]. Again, these limits were adopted, as lower neck recurrences are typically not observed in node-negative patients (see review in [4]). This is also in contradiction with the proposal of Som et al., who adopted the clavicle as the lower limit of levels IV and Vb irrespective of the neck nodal status [11].

In the node-positive neck, an important factor to consider is the probability of capsular rupture and extracapsular extension (ECE). The risk of ECE is directly proportional to the size of the lymph node, typically being on average 26% (range 20-40%) for nodes smaller than 1 cm in diameter, and 81% (range 75-95%) for bulky nodes more than 3 cm in diameter (see review in [13]). In case of ECE, it was reported for rather small nodes, that cells typically infiltrate in fatty spaces within 1 cm from the capsule [14]. Thus, for patients who have large nodes (i.e. more than 3 cm in diameter), or for patients for whom the CT or MRI is clearly indicative of muscular infiltration, irrespective of the size of the node, it appears that additional adjacent structures at risk of tumor infiltration (e.g. the sterno-cleido-mastoid and/or paraspinal muscles) should also be included in the CTV. It is known that muscular fascias are strong barriers against muscle infiltration. When the fascia has been disrupted, the whole muscle is at risk as tumor cells easily propagate in the fatty tissue along the muscular fibers. Whether the entire muscle should be included in the CTV, or only a portion of it in the immediate vicinity of the node, is still a matter of debate.

In the post-operative situation, there are even fewer data on which one could build specific recommendations for CTV delineation. However, it seems logical to try to cover at least the entire operative bed. Also, as already discussed for the node-positive neck, the CTV may need to be extended cranially or caudally to include the retrostyloid space or the supraclavicular fossa, respectively. Last, additional structures may also need to be included in the CTV based on the pathologic findings, as already discussed above in case of ECE.

Guidelines for CTV selection and delineation in the node-positive neck

Based on the few data summarized in Section 2, recommendations can be proposed for the delineation of the nodal CTV in the node-positive neck. Because head and neck IMRT is still in its infancy, it seems appropriate to be generous in target volume delineation until more data are available on the pattern of recurrence after selective treatment. The following recommendations are based on the consensus guidelines already published for the delineation of the CTV in the N0 neck, which remain the foundation for the node-positive neck [5]. It is not the purpose of this manuscript to define what a node-positive neck is, but any lymph nodes with a smaller diameter larger than 1 cm on CT or MRI, or with a central necrosis irrespective of the size will be considered as involved

Table 1

Space	Cranial	Caudal	Anterior	Posterior	Lateral	Medial
Retrostyloid	Base of skull (jugular foramen)	Upper limit of level II	Parapharyngeal space	Vertebral body/ base of skull	Parotid space	Lateral edge of RP nodes
Supraclavicular fossa	Lower border of level IV/Vb	Sterno-clavicular joint	SCM m.; skin; clavicle	Anterior edge of posterior scalenus m.	Lateral edge of posterior scalenus m.	Thyroid gland/ trachea

SCM, sterno-cleido-mastoid; RP, retropharyngeal.

[15]. Although this manuscript only discusses the issue of delineation of the node levels and adjacent spaces, it might be appropriate to re-emphasize on the fact that treatment of selected neck levels (e.g. levels I-III or II-IV) has only been advocated for node-negative side of the neck and extended to patients with a single small node (i.e. N1) (see review in [4,16]). For all other neck stages (i.e. \geq N2a), comprehensive treatment of all levels with

or without inclusion of level VI and the retropharyngeal nodes is recommended.

- In case of involvement of upper level II (IIa or IIb) with one or more lymph nodes, it is recommended to extend the upper border of level II to include the retrostyloid space up to the base of skull (Table 1 and Fig. 1).

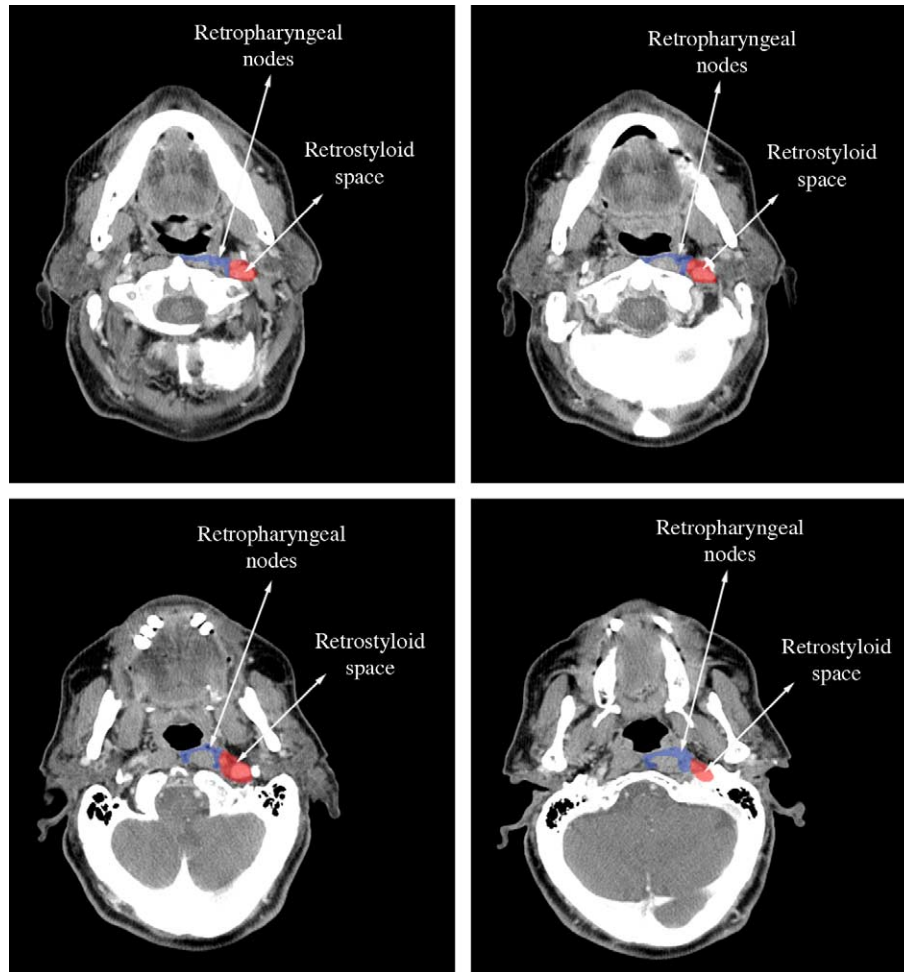


Fig. 1. Axial CT images of the upper neck of a patient with a T1N0M0 glottic SCC. The examination was performed on a dual-detector spiral CT (Elscent Twin, Haifa, Israel) using a slice thickness of 2.7 mm, an interval reconstruction of 2 mm and a pitch of 0.7. Contrast medium was injected intravenously at a rate of 2 ml/s with a total amount of 100 ml. Sections were taken from the level of C1 (cranial limit of level II) to the base of skull. The retrostyloid space was drawn using the radiological boundaries detailed in Table 1. The retropharyngeal nodes were delineated as already published (Grégoire, 2003). The delineated areas correspond to the CTV, and thus do not include any security margin for organ motion or set-up inaccuracy.

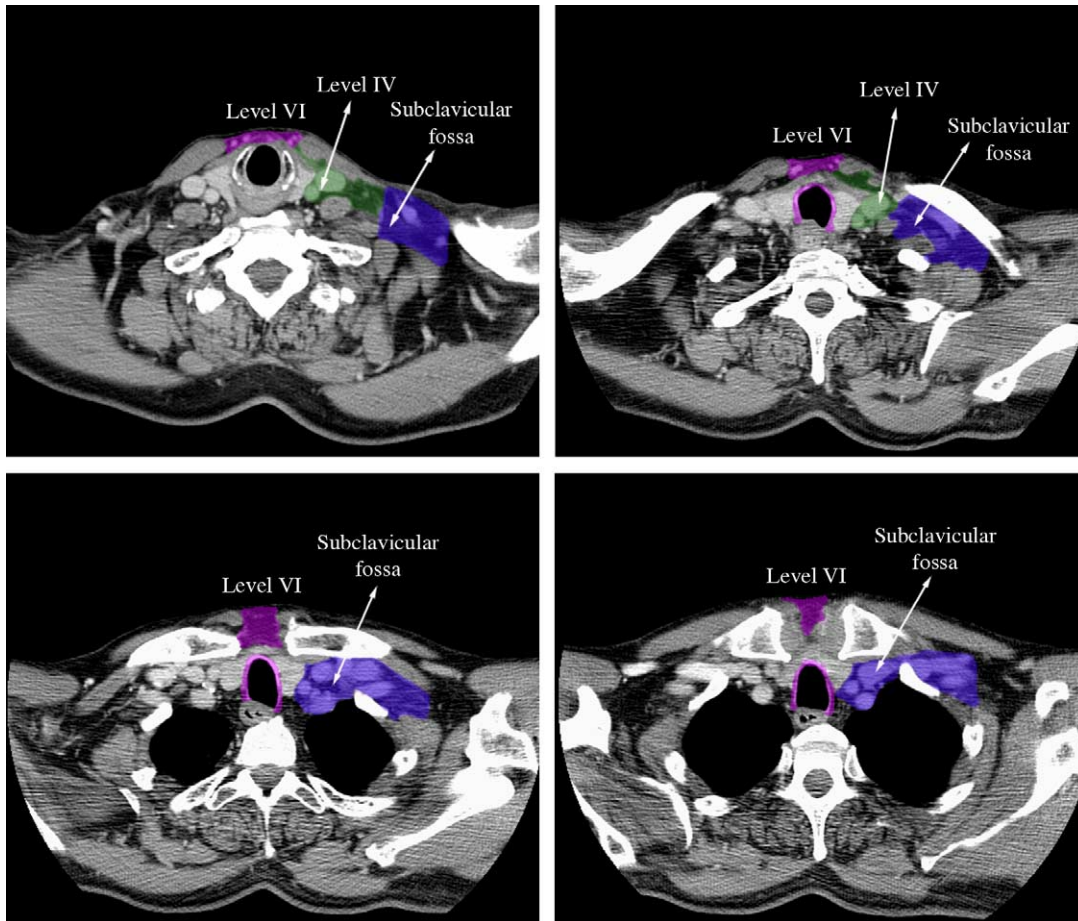


Fig. 2. Axial CT images of the lower neck of a patient with a T1N0M0 glottic SCC. The examination was performed on a dual-detector spiral CT (Elscent Twin, Haifa, Israel) using a slice thickness of 2.7 mm, an interval reconstruction of 2 mm and a pitch of 0.7. Contrast medium was injected intravenously at a rate of 2 ml/s with a total amount of 100 ml. Sections were taken from the caudal end of level IV to the cranial aspect of the sterno-clavicular joint. The supraclavicular fossa was drawn using the radiological boundaries detailed in Table 1. Levels IV and VI nodes were delineated as already published (Grégoire, 2003). The delineated areas correspond to the CTV, and thus do not include any security margin for organ motion or set-up inaccuracy.

- In case of involvement of level IV or Vb with one or more lymph nodes, it is recommended to extend the lower border to include the supraclavicular fossa in the CTV (Table 1 and Fig. 2).
- When an involved lymph node abuts a muscle (e.g. sterno-cleido-mastoid or para-spinal) and/or show clear radiological indication of muscular infiltration, it is recommended to include this muscle at the vicinity of the node in the CTV, at least for the entire invaded level and at least with a 1 cm margins in all directions (Fig. 3).
- When an involved lymph node is located at the boundary with another level, which was not intended to be part of the CTV, it is recommended to extend the CTV to include this adjacent level (Fig. 4). This recommendation will only apply to patients with a single lymph node (N1), and for whom a selective treatment may be advocated, e.g. an oropharyngeal SCC with a N1 node in level II at the boundary with level Ib; an oral cavity tumor with a N1 node in level III at the boundary with level IV.

Recommendations for CTV selection and delineation in the post-operative neck

In the post-operative situation, there are even fewer data on which one could build specific recommendations for CTV delineation. It should be understood that the indications for post-operative irradiation on the one hand, and the selection—and consequently the delineation—of the CTV in the post-operative setting on the other hand should follow institutional guidelines jointly established by head and neck surgeons and radiation oncologists to guarantee treatment consistency and avoid over—or under-treatment of the neck. In particular, for early stage tumors, a general rule that favors an a priori single modality approach should be promoted. When a surgical approach is favored as primary treatment, adequate quality control on both the surgical procedure and the pathological analysis is a prerequisite for the use of specific guidelines for the delineation of the CTV in the post-operative neck. Indeed, in absence of unambiguous information on the surgical procedure and comprehensive report of the pathological



Fig. 3. Axial CT slice at mid level II of a patient with a T2N3M0 SCC of the right base of tongue treated by concomitant chemo-radiation. The right level II necrotic lymph node (solid line) showed typical features of extra-capsular spread with likely infiltration of the sternocleidomastoid muscle. The CTV included the ipsilateral levels Ib-V. Due to the likely infiltration of the SCM muscle, the CTV was enlarged to include this muscle at the entire level II (dashed line).

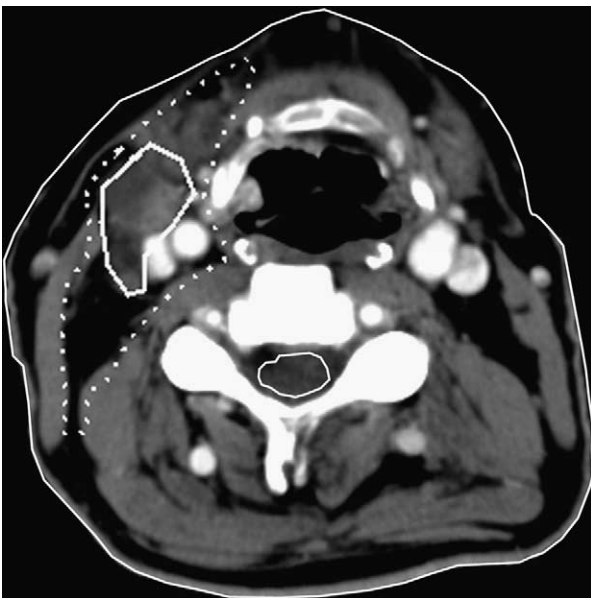


Fig. 4. Axial CT slice at the caudal edge of the sub-mandibular gland of a patient with a T2N1M0 SCC of the right base of tongue. Although only node levels II-IV were selected on the ipsilateral neck, the level Ib was also included in the CTV (dashed line) due to the close proximity of the node (solid line) to the sub-mandibular gland.

analysis, a too selective selection and delineation of the CTV may lead to an unacceptable high rate of loco-regional recurrences. As already mentioned, head and neck IMRT is still in its infancy, and it will not be inappropriate to be generous in target volume delineation until more data are available on the pattern of recurrence after selective treatment. As for the node-positive neck, the consensus guidelines established for the N0 neck will remain the foundation of these recommendations [5].

- The entire operative bed should be covered, especially in case of ECE, as tumors cells might have spilled during surgery. Surgeons usually do not clip the operative bed, but it can be estimated from the surgical protocol together with the pattern of 'tissue inflammation' and edema that can be seen on the planning CT.
- In case of pathological involvement of level II (IIa or IIb), irrespective of the size and the number of invaded lymph nodes, it is recommended to extend the upper border of level II to include the (typically) un-dissected retro-styloid space up to the base of skull (Table 1 and Fig. 2).
- In case of pathological involvement of level IV or Vb, irrespective of the size and the number of invaded lymph nodes, it is recommended to include the supraclavicular fossa in the CTV (Table 1 and Fig. 2).
- When a pathological lymph node abuts or invades a muscle (e.g. paraspinal muscle, subhyoid muscle) routinely not removed even in a radical or modified radical neck dissection, it is recommended to include this muscle into the CTV, at least for the entire invaded level.
- When a pathological lymph node is located at the boundary with a level which has not been dissected (e.g. a selective dissection of levels II-IV for an oropharyngeal SCC with a pN1 node in level II at the boundary with level Ib; a selective dissection of levels I-III for an oral cavity tumor with a pN1 node in level III at the boundary with level IV), it is recommended to extend the CTV to include the adjacent level (e.g. levels Ib and IV in the two previous examples). In fact, this recommendation will only apply to patients with a single involved lymph node (pN1) for whom post-operative radiotherapy is considered (e.g. because of a capsular rupture) and for whom selective treatment may be advocated.
- As already published, in case of pharyngeal tumors with pathological lymph node involvement, retropharyngeal lymph nodes delineated according to the published guidelines should be included in the CTV [4,5]. Considering the rare involvement of the medial retropharyngeal nodes, it may be reasonable to only outline the lateral retropharyngeal nodes alone (i.e. medial to the carotid arteries) [17,18]. This may enable partial sparing of the pharyngeal constrictor muscles, whose dysfunction following intensive chemo-RT may be a major cause of late dysphagia [19].

Conclusions

Adequate selection and delineation of target volumes is a prerequisite for successful IMRT and 3D-CRT. The proposed guidelines intended to extend the existing recommendations

for the node-negative neck to the node-positive and the post-operative neck. Such new guidelines were based more on logical assumptions than on definitive data, which are unfortunately still lacking. Interestingly, application of these guidelines somehow matches the field size that one was used to draw (i.e. from the clavicle to the base of skull) in 2D-radiotherapy for similar clinical cases. It should be re-emphasized that, as already discussed for the node-negative neck, these recommendations do not apply to a neck previously irradiated and/or which benefited from previous surgery, as the lymphatic pathways may have changed and become unpredictable [9].

The present proposal did not discuss the dose level that should be associated with the newly defined CTVs. In the primary setting, it is assumed that such comprehensive neck CTV will receive a prophylactic dose—whatever it may be—and that a therapeutic dose will be given to the involved neck level (or part of it) only. It is beyond the objective of this proposal to discuss these various options in details. However, based on recently published data on the pattern of cell migration from a lymph node with capsular rupture, one might propose to use a 5-10 mm margin from the GTV, providing that the newly created CTV—so-called ‘boost CTV’—is encompassed in the prophylactic dose CTV [14]. In the post-operative setting, there is still ongoing debate whether the full operative bed should receive a prophylactic dose, with a boost dose being only applied to the neck node levels with pathological infiltration, or whether the entire neck should received a full dose. Again, it was not the purpose of this manuscript to discuss the merits of the various options.

Implementation of the proposed guidelines in the daily practice of radiation oncology should contribute to reduced treatment variations from patient to patient and help to conduct multi-institutional clinical trials or retrospective studies. Lastly, although guidelines are designed to apply to the vast majority of patients, more than ever, oncologic knowledge, experience and judgment are prerequisites for appropriate use of the recommendations proposed in this manuscript.

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References

- [1] Chao KS, Ozyigit G, Tran BN, Cengiz M, Dempsey JF, Low DA. Patterns of failure in patients receiving definitive and post-operative IMRT for head-and-neck cancer. *Int J Radiat Oncol Biol Phys* 2003;55:312-21.
- [2] Dawson LA, Anzai Y, Marsh L, et al. Patterns of local-regional recurrence following parotid-sparing conformal and segmental intensity-modulated radiotherapy for head and neck cancer. *Int J Radiat Oncol Biol Phys* 2000;46:1117-26.
- [3] Eisbruch A, Foote RL, O’Sullivan B, Beitler JJ, Vikram B. Intensity-modulated radiation therapy for head and neck cancer: emphasis on the selection and delineation of the targets. *Semin Radiat Oncol* 2002;12:238-49.
- [4] Grégoire V, Coche E, Cosnard G, Hamoir M, Reyckler H. Selection and delineation of lymph node target volumes in head and neck conformal radiotherapy. Proposal for standardizing terminology and procedure based on the surgical experience. *Radiother Oncol* 2000;56:135-50 [Review].
- [5] Grégoire V, Levendag P, Ang KK, et al. CT-based delineation of lymph node levels and related CTVs in the node-negative neck: DAHANCA, EORTC, GORTEC, NCIC, RTOG consensus guidelines. *Radiother Oncol* 2003;69:227-36.
- [6] Nowak PJ, Wijers OB, Lagerwaard FJ, Levendag P. A three-dimensional CT-based target definition for elective irradiation of the neck. *Int J Radiat Oncol Biol Phys* 1999;45:33-9.
- [7] Wijers OB, Levendag PC, Tan T, et al. A simplified CT-based definition of the lymph node levels in the node negative neck. *Radiother Oncol* 1999;52:35-42.
- [8] Eisbruch A, Marsh LH, Dawson LA, et al. Recurrences near base of skull after IMRT for head-and-neck cancer: implications for target delineation in high neck and for parotid gland sparing. *Int J Radiat Oncol Biol Phys* 2004;59:28-42.
- [9] Fisch U. Lymphography of the cervical lymphatic system. London: WB Saunders; 1968.
- [10] Paturet G. *Traité d’anatomie humaine. Tome I: ostéologie-arthrologie-myologie.* Paris, France: Masson; 1951.
- [11] Som PM, Curtin HD, Mancuso AA. An imaging-based classification for the cervical nodes designed as an adjunct to recent clinically based nodal classifications. *Arch Otolaryngol Head Neck Surg* 1999;125:388-96.
- [12] Rouvière H. *Anatomie humaine descriptive et topographique.* Sixth ed. Paris: Masson et Cie; 1948. p. 539-43.
- [13] Chao KS, Wippold FJ, Ozyigit G, Tran BN, Dempsey JF. Determination and delineation of nodal target volumes for head-and-neck cancer based on patterns of failure in patients receiving definitive and postoperative IMRT. *Int J Radiat Oncol Biol Phys* 2002;53:1174-84.
- [14] Apisarnthanarax S, Elliott DD, El Naggar AK, Asper JA, Yang T, Chao KC. Determining optimal clinical target volume margins in head-and-neck cancer based on microscopic extracapsular extension of metastatic neck nodes. *Int J Radiat Oncol Biol Phys* 2006;64:678-83.
- [15] Curtin HD, Ishwaran H, Mancuso AA, Dalley RW, Caudry DJ, McNeil BJ. Comparison of CT and MR imaging in staging of neck metastases. *Radiology* 1998;207:123-30.
- [16] Clayman GL, Frank DK. Selective neck dissection of anatomically appropriate levels is as efficacious as modified radical neck dissection for elective treatment of the clinically negative neck in patients with squamous cell carcinoma of the upper respiratory and digestive tracts. *Arch Otolaryngol Head Neck Surg* 1998;124:348-52.
- [17] Bussels B, Hermans R, Rijnders A, Van den Bogaert W. Retropharyngeal nodes in squamous cell carcinoma of the oropharynx: implications for target volume delineation. *Radiother Oncol* 2004;73:S179.
- [18] Poon I, Fischbein N, Lee N, et al. A population-based atlas and clinical target volume for the head-and-neck lymph nodes. *Int J Radiat Oncol Biol Phys* 2004;59:1301-11.
- [19] Eisbruch A, Schwartz M, Rasch C, et al. Dysphagia and aspiration after chemoradiotherapy for head-and-neck cancer: which anatomic structures are affected and can they be spared by IMRT? *Int J Radiat Oncol Biol Phys* 2004;60:1425-39.