Int. J. Radiation Oncology Biol. Phys., Vol. 58, No. 1, pp. 113–123, 2004

0360-3016/04/$–see front matter

doi:10.1016/S0360-3016(03)01453-6

CLINICAL INVESTIGATION **Head and Neck**

ROTTERDAM AND BRUSSELS CT-BASED NECK NODAL DELINEATION COMPARED WITH THE SURGICAL LEVELS AS DEFINED BY THE AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY

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Purpose/Objective: Rotterdam and Brussels have independently published guidelines for the definition and delineation of CT-based neck nodal Levels I–VI. This paper first reports on the adequacy of contouring of the Rotterdam delineation protocol. Rotterdam and Brussels differed slightly in translating the original surgical level definitions as proposed by the 2002 American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) to CT guidelines. To adapt to the surgical level definitions to come to a unifying concept, adjustments of both CT-based classifications are proposed.

Methods and Materials: The clinical neck nodal target volumes of patients irradiated in Rotterdam by three-dimensional conformal radiotherapy (3D-CRT) between December 1998 and March 2001 were reviewed. Thirty-four patients with N0 and 27 patients with N+ disease with primary tumors located in the oral cavity (n = 1) oropharynx (n = 24), hypopharynx (n = 7), and larynx (n = 29) were evaluated. Seven patients underwent unilateral (3 N0 patients, 4 N+ patients) and 54 underwent bilateral (31 N0 patients, 23 N+ patients) irradiation of the neck. In 11 N+ patients, 3D-CRT of the neck was followed by unilateral neck dissection. The dose to the primary and nonresected N+ necks was 70 Gy and to the N0 neck was 46 Gy. Neck levels were analyzed for adequacy of contouring, dose distribution, and patterns of relapse. The mean dose and the percentage of the volume receiving a minimum of 95% (V_{95}) or >107% (V_{107}) of the prescribed dose was computed.

Results: In 4 patients treated with bilateral 3D-CRT, contouring was not in concordance with the guidelines of the protocol. The V_{95} and V_{107} in the 81 adequately contoured N0 necks (63 irradiated N0 necks from 33 N0 patients, 18 irradiated N0 necks from 24 N+ patients) was 95.6% and 6.3%, respectively. For the 26 N+ necks (15 N+ necks from 13 N+ RT-only patients, 11 N+ necks from 11 preoperatively irradiated patients), the V_{95} and V_{107} was 94.6% and 6.7%, respectively. With a median follow-up of 29 months, in 4 (8.6%) of 46 patients treated by 3D-CRT only, regional relapse was found. An actuarial regional and locoregional relapse-free survival and disease-free survival rate at 3 years of 90%, 78%, and 68%, respectively, was observed. All regional relapses were observed in the N0 necks of patients with supraglottic laryngeal carcinoma. Taking the surgical 2002 AAO-HNS classification as a reference, adjustments are proposed for the Rotterdam and Brussels delineation protocols to arrive at a unified CT-based neck nodal classification.

Conclusion: Adequate dose coverage for the Rotterdam CT-based contours of the neck nodal levels was found. In the RT-only patients, only four failures were observed: one regional and three locoregional relapses. As a next step in optimizing the current Rotterdam and Brussels CT-based delineation protocols, adaptations are proposed to resolve the discrepancies compared with the 2002 AAO-HNS surgical classification. © 2004 Elsevier Inc.

Irradiation, Selective, Surgery, Neck Dissection, Node, Level, Delineation, CT-based, 3D-CRT, Intensity-modulated RT, Consensus guidelines.

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Acknowledgments—All team members of the Rotterdam and Brussels Head and Neck Cooperative Groups are kindly acknowledged for their dedication in patient care, in particular, for their support by taking part in the discussions on the validation of the consensus guidelines of the clinical neck nodal target. Discussions with Avraham Eisbruch on the concept of the current paper were much appreciated.

Received Dec 4, 2002, and in revised form May 7, 2003. Accepted for publication May 16, 2003.

INTRODUCTION

In state-of-the-art (organ preservation) radiotherapy (RT) for head-and-neck cancer, incorporating image-based technology is paramount. Three-dimensional conformal RT (3D-CRT), stereotactic RT, and intensity-modulated RT are currently realities to live by in most RT departments. Patients visit clinicians, asking about high-dose, high-precision RT, questions not infrequently based on information easily obtainable in an open society and/or by "surfing" the Internet. This type of technology is providing the radiation-oncology community with incentives and the means to improve on tumor control and normal tissue sparing (1–7). The need for sparing in this respect is of particular interest because meta-analyses have demonstrated the benefit of concomitant chemotherapy for local control and survival but, unfortunately, at the expense of significant associated extra toxicity (8–10). At present, similar findings seem to surface from ongoing meta-analyses regarding the efficacy and side effects of hyperfractionated/accelerated RT schedules (11). Fortunately, for better sparing, novel RT techniques such as intensity-modulated RT are available. Therewith, contouring of the primary tumor and neck target on CT images becomes essential. This paper focuses on neck delineation guidelines. As a next step, one could aim for maximally sparing the mucosa and salivary glands by irradiating only a selective number of adequately defined neck nodal levels.

The type of neck dissection one is performing depends on the surgical removal of the levels and nonlymphatic structures (types of selective neck dissection and types of modified radical neck dissections, respectively). These surgical procedures, as well as the corresponding nomenclature, are now standardized (12, 13). When delineating the neck target volumes on CT images (with or without image fusion using, for example, MRI or positron emission tomography), the standardization of CT-based level definitions is pivotal. That is, with the most recent surgical level definitions taken as a reference, one needs to define the clinical target volume (CTV) of the different neck nodal Levels I–VI accurately before specific neck target volumes can be (selectively) irradiated (14). For contouring, one is dependent on factors related to the imaging modalities *per se* and, possibly even more so, on the skills of the clinician with respect to the identification of image-based landmarks on CT (15). Also, in clinical practice, unknown primaries, distortion of the anatomy owing to large masses, and previous surgery (neck dissection) are potentially additional constraints in this respect.

Rotterdam and Brussels have independently published guidelines for the definition and delineation of CT-based neck nodal Levels I–VI (1–3). The Rotterdam 3D conformal delineation protocol of the neck by Wijers *et al.* (2) has been used consistently since 1998 in our center. To use easy-to-depict anatomic landmarks, somewhat more generous boundaries for each level were implemented in this protocol as opposed to our original—anatomy-based—contouring guidelines by Nowak *et al.* (1). The adequacy of the guidelines for these contours still needs to be verified. Taking the contouring guidelines of Rotterdam and Brussels, it also became apparent that the translation of the original—surgical anatomy-based—level descriptions (12, 13, 16) to CT images showed discrepancies per level for each individual center. Obviously, for standardization these inconsistencies first need to be corrected. Therefore, we report on the adequacy of the Rotterdam CT-based neck level contouring guidelines as proposed by Wijers *et al.* in 1999 (2), in terms of the dose coverage and neck failure pattern. This paper should also be considered a preparatory report on the development of a universally applicable neck nodal delineation protocol in the case of elective (N0 neck). In this respect, we discuss in some detail the (small) adjustments needed to resolve the discrepancies between the current Rotterdam and Brussels delineation protocols in reference to the 2002 American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) surgical level definitions of the neck (16). It will thus serve as the basis for future communications on a definitive and detailed CT-based classification system of neck nodal Levels I–VI (17).

Table 1. Incidence and distribution of regional metastasis for Levels I–V for clinically N0 neck

	Levels involved (%)				
Tumor site	I	II	III	IV	V
Oral cavity	20	17	9	3	0.5
Oropharynx	2	25	19	8	2
Hypopharynx	0	13	13	0	0
Larynx	5	19	20	9	2.5

Patterns of cervical node metastases based on data from Shah (18), Bataini *et al.* (19), Lindberg (20), Chao *et al.* (21), Byers *et al.* (22), Shah *et al.* (23), and Candela *et al.* (24, 25).

METHODS AND MATERIALS

The Rotterdam protocol for RT of the (elective) neck is based on institutional preferences and clinical data sets as presented by many well-documented reports (18–26). For a brief summary of the neck (nodal) targets to be included in the treated volume for the different head-and-neck tumor sites, see Table 1 for N0 patients and Table 2 for N+ patients. The first part of this section deals with the adequacy of the Rotterdam CT-based neck level contouring guidelines in terms of dose coverage and neck failure patterns. For this part of the study, all patients with a primary tumor and unilateral or bilateral treatment of the neck by 3D-CRT were eligible. The neck was to be treated by elective, preoperative, or definitive 3D-CRT. The second part focuses on the Rotterdam and Brussels protocols in reference to the 2002 AAO-HNS surgical level definitions.

Table 2. Incidence and distribution of regional metastasis for Levels I–V for clinically N+ neck

	Levels involved (%)				
Tumor site	I	II	III	IV	V
Oral cavity	48	39	31	15	4
Oropharynx	15	71	42	27	9
Hypopharynx	10	75	72	45	11
Larynx	6	61	54	30	6
Nasopharynx*	13	95	60	21	44

Patterns of cervical node metastases from Shah (18), Bataini *et al.* (19), Lindberg (20), Chao *et al.* (21), Byers *et al.* (22), Shah *et al.* (23), Candela *et al.* (24, 25), and Sham *et al.* (26).

* Clinical distribution of neck nodes at presentation for cancer in nasopharynx (26).

Adequacy of Rotterdam CT-based contouring guidelines of the neck

Treatment techniques and 3D-CRT protocol. After joint consultation by the radiation-oncologist and head and neck surgeon, the tumors were staged according to the International Union Against Cancer/American Joint Committee on Cancer classification, 1997 edition (27). As part of the treatment planning procedure, a CT scan (ACQSIM, Marconi PQ5000) was acquired for contouring purposes. The CT scans were obtained with the patient in the supine treatment position, using an immobilizing PVC head cast. For the purpose of 3D-CRT, the CTV of the neck and primary tumor, as well as the critical normal tissues, such as the major salivary glands and spinal cord, were delineated on 5-mm CT slices. The CTV was expanded (automated) with an additional 3D margin of 5 mm to arrive at the planning target volume (32). The neck nodal levels were contoured according to the "simplified" Rotterdam protocol (2). This protocol allows for somewhat more generous margins because of the preset condition to choose "easy-to-identify CT-based landmarks" as opposed to our original 1999 protocol (1). For the dose distributions in the neck subvolumes, dose–volume histograms were computed. Computer planning was performed using the 3D Cadplan Treatment Planning System (version 3.1.2, Varian-Dosetek, Finland). To allow both for better sparing of the parotid glands and spinal cord, as well as for adequate target coverage, a noncommercial inverse-planning module "Optimize," developed in our institute, was implemented (29, 30).

Patients were generally irradiated with a 6-MV photon beam and/or high-energy electrons. Dose prescription and reporting were according to the International Commission on Radiation Units and Measurements Report 50 recommendations. According to the Rotterdam protocol, the node negative (N0) neck is electively irradiated to a dose of 46 Gy in the case of an estimated risk of >10% of occult neck nodal involvement (3, 28). For preoperative RT, a dose of 46 Gy is applied, and for definitive RT, after a first series of 46 Gy, the gross primary tumor, as well as the neck nodal masses, is irradiated to a dose of 70 Gy. The prescribed dose, according to the calculated dose fluency profiles of the treatment plan, was delivered by so-called missing tissue compensators, mounted on a multileaf collimator or by dynamic multileaf collimation. In most patients, the lower neck was treated by an abutted AP portal in conjunction with a midline shield, with the dose prescribed to a depth of 3 cm.

The techniques used were such that the junction line, if possible, did not overlie the tumor masses and/or the midline block did not in part shield the primary tumor. Finally, patients were immobilized on the treatment couch and irradiated by 3D-CRT techniques directed at the primary tumor and the upper neck. An electronic portal imaging device was implemented, according to our routine practice (protocol), once weekly to verify and, if necessary, correct for setup errors (31).

Patient characteristics. In Rotterdam, between December 1998 and March 1, 2001, 61 patients with histologically proven primary squamous cell carcinoma in the oral cavity ($n = 1$), oropharynx ($n = 24$), hypopharynx ($n = 7$), and larynx ($n = 29$) were irradiated by 3D-CRT techniques. Of the 61 patients, 46 (75%) had Stage III-IV disease. Three patients with a tumor in the hypopharynx (T1N1, T4N1, T4N0) and one with oropharyngeal cancer (T1N2b), that is five irradiated N0 and three irradiated N+ necks, were excluded from the analysis of dose coverage adequacy of the delineated neck nodal levels. The exclusion was based on the much too crudely performed contouring of the neck; that is, the physician in charge simply circled what was thought to be the neck target and did not delineate in concordance with the Rotterdam delineation guidelines available at the time (Fig. 1). None of these 4 patients, however, experienced local and/or regional relapse. The follow-up censor date was January 1, 2003. Forty-six patients were treated with 3D-CRT only to the primary and neck. In 10 patients (4 with tonsillar fossa, 5 with soft palate, and 2 with base of tongue tumors), treatment was given by 3D-CRT to the primary and neck, in conjunction with a fractionated high-dose-rate brachytherapy boost to the primary and ipsilateral neck dissection for the N+ neck (Rotterdam institutional protocol). One laryngeal cancer patient was treated to a full dose of 70 Gy for the primary tumor and neck node, followed by radical neck dissection because of slowly responding neck nodes.

Treatment outcome. For the analysis of dose coverage adequacy, the data set was limited to the first series of 57 patients treated by 3D-CRT to 46 Gy. Of these patients, 45 were men and 12 were women (mean age 61 years, range 41–82). Thirty-three patients had N0 and 24 had N+ disease. Seven patients underwent unilateral neck RT (3 N0, 4 N+ necks) and 50 patients underwent bilateral neck RT (78 N0, 22 N+ necks; Fig. 2). The percentage of the volume receiving a minimum of 95% (V_{95}) or >107% (V_{107}) of the prescribed dose was calculated for the 51 N0 and 24 N+ patients. For the tumor control computations, the 11 patients treated with 3D-CRT to the neck followed by neck dissection were excluded. For the remaining 46 patients treated

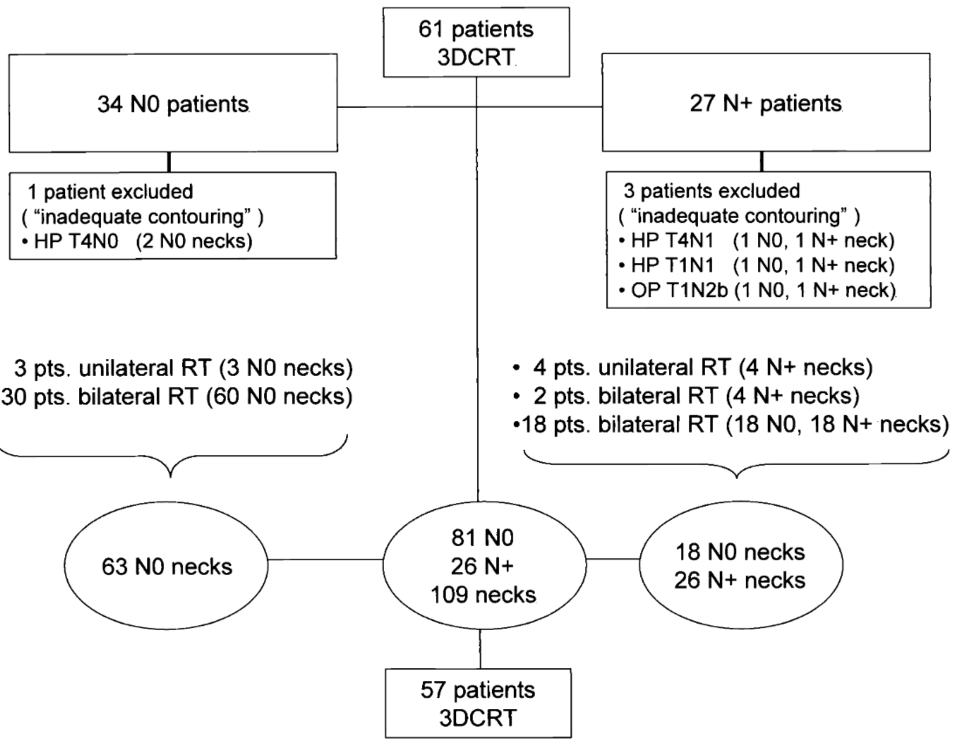

Fig. 1. Flow diagram of 61 patients treated with 3D-CRT between December 1998 and March 2001. Four patients were ineligible because the delineation was not coherent with the guidelines of the Rotterdam protocol. HP = hypopharynx.

with 3D-CRT only, the actuarial locoregional relapse-free survival, regional relapse-free survival, disease-free survival, and overall survival were calculated according to the Kaplan-Meier method.

We recorded the subjective and objective findings on preserving sufficient saliva production to analyze the effect on sparing of the major salivary glands by the implemented 3D-CRT techniques in a cohort of 26 laryngeal cancer patients included in this study. These data are a brief summary of the observations on a subset of patients treated with 3D-CRT previously reported by Braaksma *et al.* (33).

Rotterdam/Brussels delineation protocols in reference to the 2002 AAO-HNS surgical level definitions

The Rotterdam and Brussels delineation guidelines differed slightly in translating the surgical landmarks (anatomic boundaries) to CT (13, 16). Because the overall aim of this study was the standardization of the delineation of the neck nodal levels, this paper therefore also tried to eliminate these discrepancies to arrive finally at a unified CT-based neck delineation concept. For this reason, the Level I–VI contouring guidelines of both institutions were re-analyzed and meticulously compared with the 2002 AAO-HNS classification (surgical anatomy [16]), as well as to the image-based diagnostic classification system (radiologic anatomic structures) as proposed by Som *et al.* (15). This reanalysis, which resulted in a number of proposed adjustments (see "Results" and Table 3), was performed by a multidisciplinary team consisting of representatives of the medical specialties of radiation-oncology, ear, nose, and throat surgery, and radiology of both institutions.

RESULTS

Adequacy of the Rotterdam CT-based contouring guidelines of the neck

With a median follow-up of 29 months, 5 of 57 patients experienced relapse: one local, one regional, and three locoregional relapses (Fig. 2). The 3 patients with locoregional recurrence developed regional relapse after the local relapse. All regional relapses were observed in the adequately contoured contralateral N0 necks of 4 patients with supraglottic laryngeal carcinoma in Level II, the transition zone of Levels II–III, Level III, and Level IV. Three of the 4 patients with neck recurrence died of disease after a salvage attempt. One patient with neck recurrence was cured and was alive without evidence of disease at the last follow-up visit. No explanation was found for the regional relapses in patients with supraglottic laryngeal cancer only, even after extensive dose distribution analyses. If one excludes the 10 patients with neck dissection after preoperative RT to a dose of 46 Gy or 70 Gy (1 patient), four neck relapses (8.6%) were seen in the contralateral N0 necks of RT-only patients. All patients with relapse had supraglottic laryngeal cancer. For the 46 patients treated with 3D-CRT only, the 3-year actuarial regional recurrence-free survival, locoregional recurrence-free survival, disease-free survival,

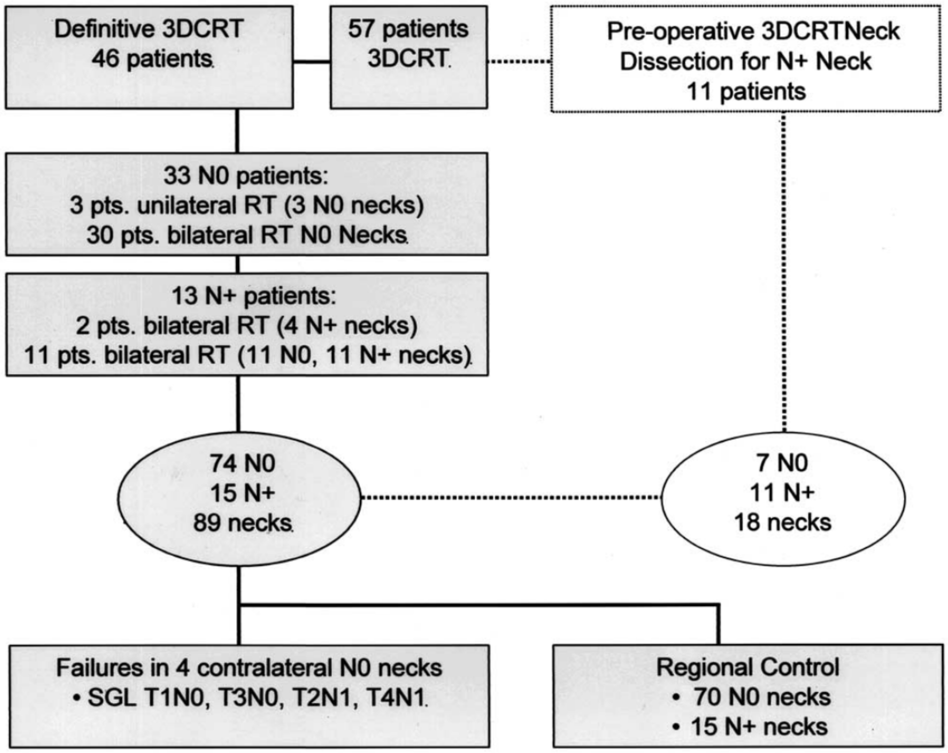

Fig. 2. Flow diagram of 57 eligible patients; 46 were treated with 3D-CRT only and 10 with a combination of preoperative RT to the neck (46 Gy), followed by neck dissection (for N+ disease) and a high-dose-rate brachytherapy boost to the primary. One patient with cancer in the larynx was treated with 70 Gy followed by neck dissection. Only four locoregional failures were observed; all four regional failures occurred in the contralateral N0 neck of patients with supraglottic laryngeal carcinoma.

and overall survival rate was 90%, 78%, 68%, and 73%, respectively (Fig. 3). The mean V_{95} and V_{107} was 95.7% (SD 4.6) and 6.1% (SD 7.2), respectively, for the 81 N0 necks (51 patients; Figs. 4 and 5), and 94.7% (SD 4.2) and 6.3% (SD 6.0) for the 26 N+ necks (24 patients; Figs. 4 and 5). The observed dose distributions in the irradiated patients with regional relapse were in the same range (mean V_{95} of 99% and mean V_{107} of 3%).

Table 3. Summary of adaptations resulting in Rotterdam Brussels consensus protocol for Levels I–VI (see text)

Level	Cranial	Caudal	Anterior	Posterior	Lateral	Medial
IA						
IB				Posterior edge SubMG		
IIA	Caudal edge lateral process C1		Posterior edge SubMG	Posterior edge IJV		Medial ICA
IIB	Caudal edge Lateral process C1	Posterior edge IJV				Deep cervical muscles
III		Inferior edge cricoid	Anterior edge SCMM	Posterior edge SCMM		Medial ICA/deep cervical muscles
IV	Inferior edge cricoid	2 cm superior SC joint	Anteromedial edge SCMM	Posterior edge SCMM		Medial ICA/paraspinal muscles
VA	Cranial edge hyoid	Inferior edge cricoid	Posterior edge SCMM	Anteromedial border Trapezius muscle		Paraspinal muscles
VB	Inferior edge cricoid	Transverse cervical vessels	Posterior edge SCMM	Virtual horizontal line anterior medial border trapezius muscle		Paraspinal muscles
VI	Caudal edge thyroid*	Sternal manubrium		Common carotid artery	SCMM	Trachea

Abbreviations: SubMG = submandibular gland; IJV = internal jugular vein; ICA = internal carotid artery; SCMM = sternocleidomastoid muscle; SC = sternoclavicular.

* In some cases, a head-and-neck surgeon does not extend resection of Level VI cranially to level of hyoid bone (2002 AAO-HNS classification), and caudal edge of thyroid gland is considered the most cranial boundary (personal/institutional preference).

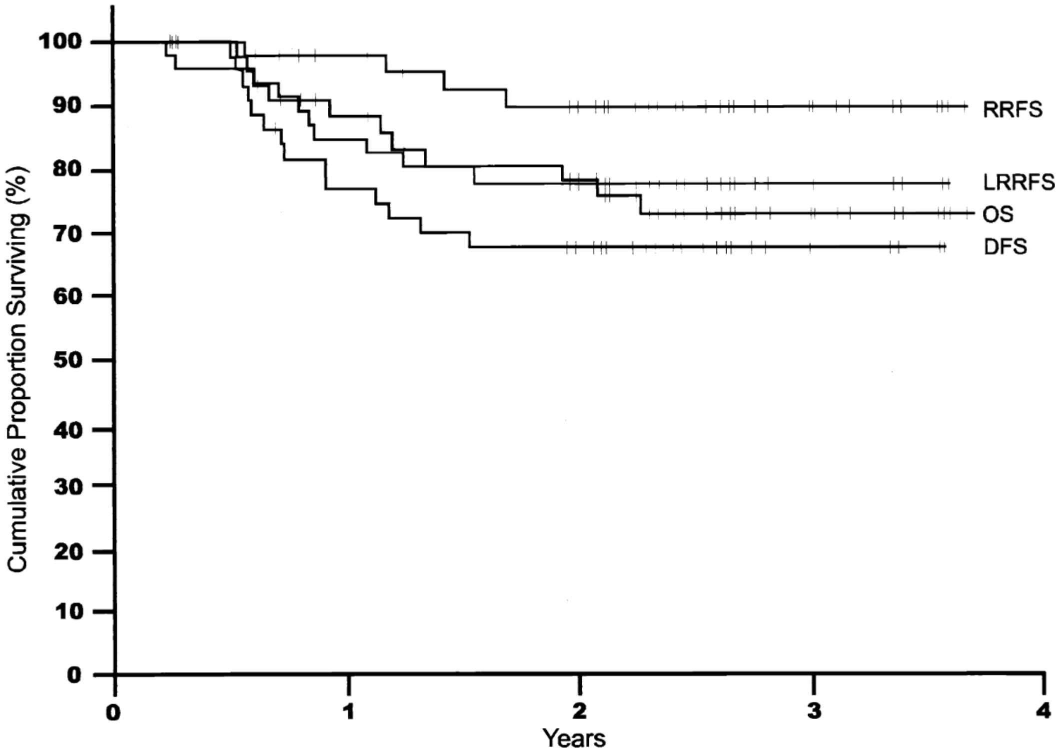

Fig. 3. For the 46 patients treated with 3D-CRT only, a 3-year actuarial regional relapse-free survival (RRFS), locoregional relapse-free survival (LRRFS), disease-free survival (DFS), and overall survival (OS) rate of 90%, 78%, 68%, and 73%, respectively, was found.

Rotterdam/Brussels delineation protocols in reference to 2002 AAO-HNS surgical level definitions

Table 3 summarizes the proposed adaptations needed to reach a consensus that complies in detail with the surgical anatomy-based level definitions of the 2002 AAO-HNS classification (16). Figure 6 depicts on an axial CT slice, taken at the level of the upper neck, the nodal Levels IA, IB, II, and V, contoured according to the Rotterdam guidelines (solid black line in the right neck) and the Brussels guidelines (solid black line in the left neck) delineation protocol.

On the same slice, the stipulated white line demarcates the contours of the Levels IA, IB, IIA, IIB, and VA when defined by the Rotterdam/Brussels unifying concept (i.e., the "consensus proposal"; see also adaptations proposed as summarized in Table 3). Figure 7 similarly shows, on an axial CT slice at the level of the cricoid (mid-neck), the

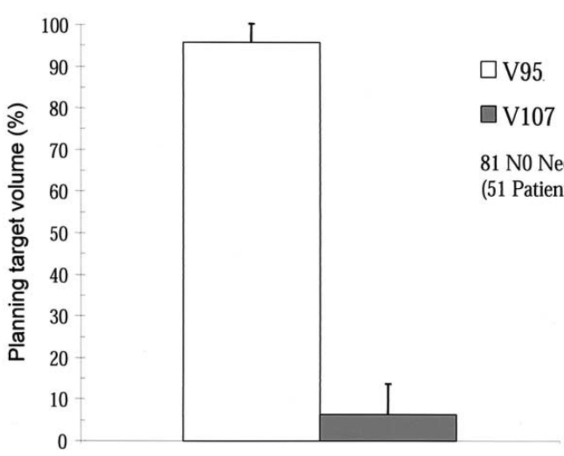

Fig. 4. Dose–volume histograms representing V_{95} or V_{107} of prescribed dose. Mean V_{95} and mean V_{107} for the 81 N0 necks (51 patients) was 95.7% (standard error 4.6) and 6.1% (standard error 7.2), respectively.

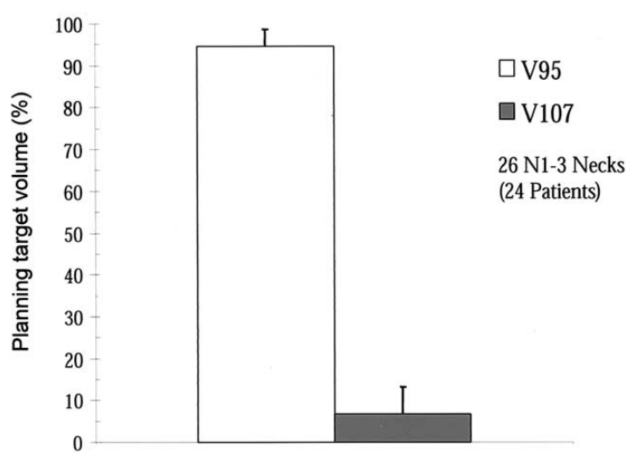

Fig. 5. Dose–volume histograms representing V_{95} or V_{107} of prescribed dose. Mean V_{95} and mean V_{107} for 26 N+ necks (24 patients) was 94.6% (standard error 4.1) and 6.3% (standard error 6.6), respectively.

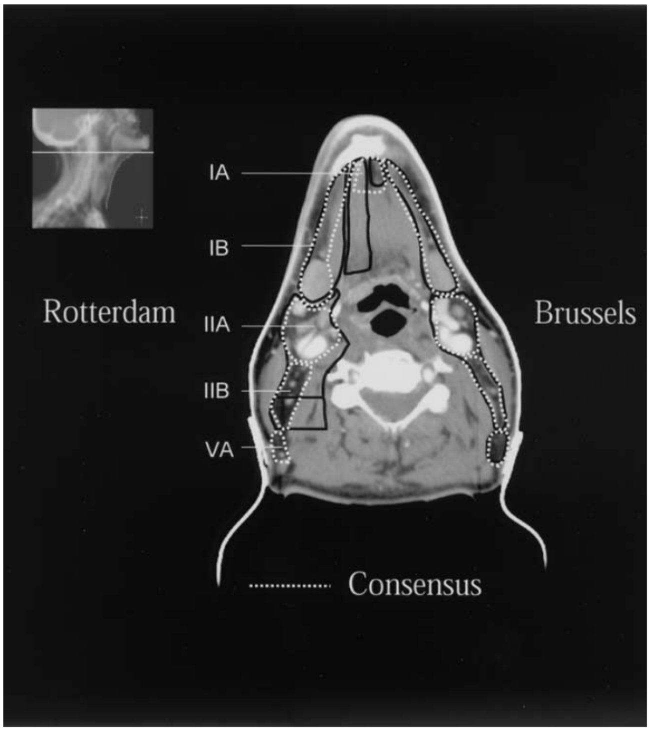

Fig. 6. Axial CT slice, taken in upper neck region, with Levels IA, IB, II, and V (solid black lines), contoured according to "simplified" Rotterdam (right neck) (2) and Brussels (left neck) (3) delineation protocols. Rotterdam and Brussels delineation protocols were meticulously compared with, and adapted to, surgical level definitions as defined by 2002 AAO-HNS classification (16), arriving at so-called Rotterdam/Brussels consensus protocol (this paper). Stipulated white lines (both necks) demarcate contours of levels and sublevels when defined by Rotterdam/Brussels consensus proposal, illustrating contours of Levels IA, IB, IIA, IIB, and VA.

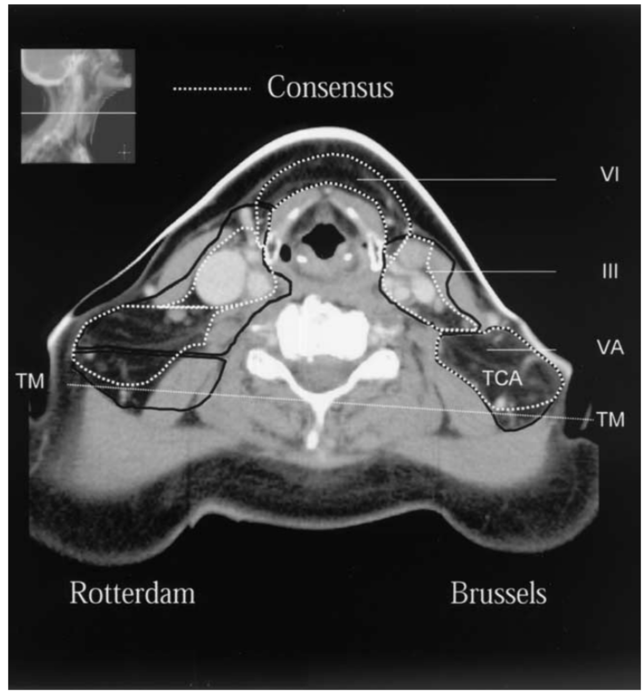

Fig. 7. Axial CT slice, taken in region of mid-neck (level of cricoid) with nodal Levels III, V, and VI (solid black lines), contoured according to "simplified" Rotterdam (right neck) (2) and Brussels (left neck) (3) delineation protocols. Stipulated white lines (both necks) demarcate contours of same levels and sublevels when defined by Rotterdam/Brussels consensus proposal (see also Fig. 6). Virtual horizontal line between anteromedial heads of trapezius muscles (TM) demarcates posterior boundary of Level VB (see text for details).

contours for Levels VI, III, and V. Figure 8 shows the contours for Levels VI, IV, and VB for the lower neck. For the Rotterdam/Brussels consensus guidelines, the superior level of the neck to be contoured is taken at the caudal edge of the lateral process of the first cervical vertebra (C1). The most caudal CT slice of the neck for Level IV to be contoured is taken 2 cm above the sternoclavicular joint. The most caudal CT slice for Level VB to be delineated is the point at which the transverse cervical arteries can be identified. The posterior boundary of Level VB is, in practice, difficult to define accurately, in particular at the most caudal region of the neck. For the Rotterdam/Brussels consensus report on the neck, the posterior boundary of Level VB is arbitrarily demarcated by a virtual horizontal line drawn between anteromedial heads of the trapezius muscles (Figs. 7 and 8). Figure 9 displays a lateral digitally reconstructed radiograph of the CTV of Levels I–VI.

DISCUSSION

In the past decade, we have seen the emergence of more effective (hyperfractionated/accelerated) fractionation schedules and concomitant chemotherapy. Meta-analyses have shown altered fractionation schemes and concomitant chemotherapy in cancer of the head and neck improving locoregional tumor control and survival, albeit at the cost of increased toxicity. The prevention of these side effects, such as long lasting acute and late Grade 3–4 mucosal toxicity and the dry mouth syndrome, have therefore become of paramount importance (8–11, 36, 37). Delivering adequate doses of radiation selectively to a tumor while at the same time preventing the surrounding normal tissues from receiving unnecessary radiation (therapeutic ratio) is a fundamental principle in RT. In surgery, the different types of neck dissection are based on this "sparing" or "selective" principle (12, 16). Similarly, this can be envisaged for image-guided RT. The need for tailoring RT to the precise extent of the disease underscores the pivotal importance of establishing universal acceptable definitions and delineation guidelines for the primary tumor and neck. This paper is a first step in the standardization of the clinical target volume of the neck. Historically, in 1981, Shah *et al.* (34) advocated the use of a simple compartmental classification system of the neck (levels). In 1998 and 2002, Robbins *et al.* (13, 16) presented the modified/updated 1991 AAO-HNS guidelines on the standardization of terminology for lymph node groups at risk of tumor metastasis. The boundaries of each of the lymph node

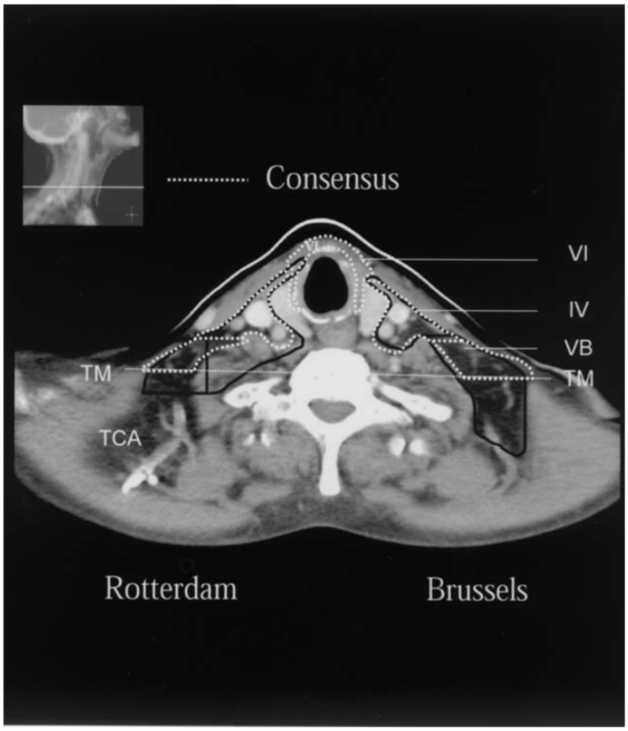

Fig. 8. Axial CT slice, taken in region of lower neck (level of supraclavicular fossa) with nodal Levels IV, V, VI (solid black lines), contoured according to "simplified" Rotterdam (right neck) (2) and Brussels (left neck) (3) delineation protocols. Stipulated white lines (both necks) demarcate contours of same levels and sublevels, when defined by Rotterdam/Brussels consensus proposal (see also Fig. 7). Virtual horizontal line between anteromedial heads of trapezius muscles (TM) demarcates posterior boundary of Level VB (see text for details).

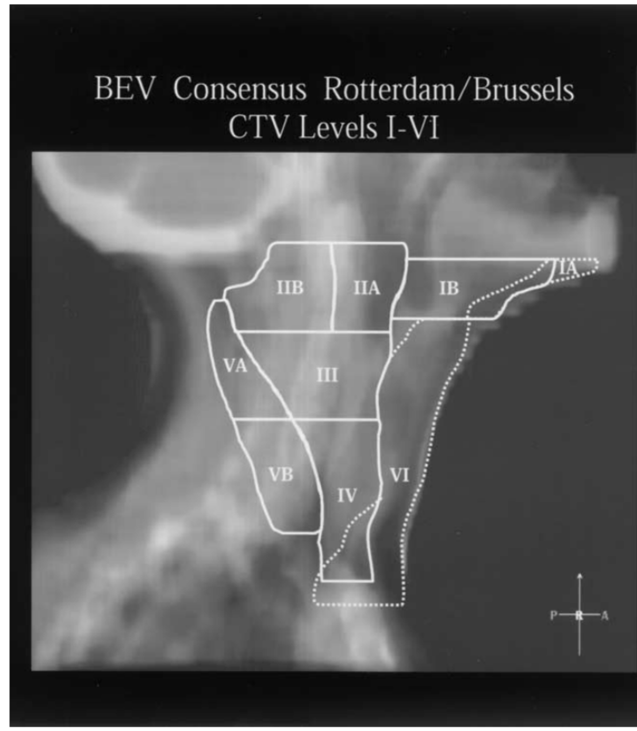

Fig. 9. Lateral view of digitally reconstructed radiograph of CTV of Levels I–VI.

groups to be removed surgically in a particular type of neck dissection are discussed in detail (13, 16). When classifying cervical lymphadenopathy, Som *et al.* (15) recommended a series of radiologic parameters to be taken into account as well.

CT and MRI (positron emission tomography) are advised as an adjunct to the existing American Joint Committee on Cancer/International Union Against Cancer and AAO-HNS 2002 classifications, in particular for the difficult to palpate (deeply situated, clinically inaccessible) lymph nodes. Finally, classifying the neck node status of patients must be done in a multimodality, multidisciplinary approach (i.e., an ear, nose, and throat surgeon, a head-and-neck–dedicated radiologist, and a radiation-oncologist should preferably be involved). The basis for the Rotterdam/Brussels consensus report (this preparatory paper) on the CT-based neck level contouring guidelines is the result of such a multidisciplinary team approach.

Determination of clinical neck nodal target volume

The determination of the CTV of the neck is based on data taken from the literature; given its retrospective nature and that the clinical information was collected over long periods, this is at best Class 3 evidence (nonrandomized studies, mostly of a retrospective nature). Although the metastatic pattern seems to be orderly and "predictable," the true incidence and/or distribution of metastatic cells to the different levels is multifactorial and thus difficult to estimate accurately. The chance of having (occult) regional metastasis in the neck, depends on many prognostic factors, such as the extent of the primary site, as well as its laterality and depth of infiltration. Also, the accuracy of the diagnostic means (palpation, CT, MRI, ultrasound-guided fine needle aspiration cytology) is often operator dependent (38). Additionally, surgeons do not always strictly adhere to their (selective) procedures to the precise definitions as proposed by the 2002 AAO-HNS. Also, ill-defined RT fields are often used postoperatively to compensate for potential irradical surgery. In this respect, even in their 2002 publication, Chao *et al.* (21) take a pragmatic approach in establishing a treatment protocol for neck node metastasis for the different primary tumor sites. They compiled data sets from the literature covering periods of 28 years (1972–2000) (21). The same holds for the review by Grégoire *et al.* (3). In trying to demonstrate the orderly and predictable pattern that metastatic spread of cancer cells tends to follow in the neck, the data from Lindberg (20), Bataini *et al.* (19), Byers *et al.* (22), and Shah (18, 23) were averaged out and tabulated in a single table. More so, the Rotterdam Head and Neck cooperative group, given the type of retrospective data available at the time, similarly relied on historical data sets to construct treatment protocols. Tables 1 (N0) and 2 (N+) provide a summary of some of the literature findings.

Finally, the specificity and selectivity of diagnostic

Table 4. Rotterdam/Brussels consensus on retropharyngeal node delineation compared with classic surgical boundaries (3, 12, 16, 35)

	Surgery (AAO-HNS)	Rotterdam/Brussels CT-based consensus
Cranial	Base of skull	Base of skull
Caudal	Corpus third cervical vertebra (C3)	Cranial edge body hyoid
Anterior	Pharyngeal wall constrictor muscles	Pharyngeal wall constrictor muscles levator veli palatini muscles
Posterior	Prevertebral fascia	Prevertebral fascia and muscles (Mm. longus colli/longus capiti)
Lateral	Medial edge carotid artery (superior node = node of Rouviere)	Medial edge carotid artery (superior node = node of Rouviere)
Medial	1 or 2 nodes in midline	1 or 2 nodes in midline

Abbreviation: AAO-HNS = American Academy of Otolaryngology–Head and Neck Surgery.
For evidence of retropharyngeal adenopathy as a predictor of outcome in cancer of the head and neck, see Grégoire *et al.* (3), Shah *et al.* (34), and McLaughlin *et al.* (35).

means have greatly improved, in particular since the routine use of CT, MRI, and ultrasound-guided fine needle aspiration cytology (38). In fact, this can have a significant impact on the neck CTV and/or treatment-related morbidity in the near future (28).

CT-based contouring guidelines of the lymph nodal levels of neck

As shown by the data taken from the literature, for selective image-guided elective RT of the neck, the accurate determination of the clinical target volume is extremely important but, to date, remains a complex multifactorial issue to resolve (see previous section). In the case of elective RT of the neck, we also know from our own nationwide inventory that standardization is lacking in the definition and delineation of areas that need elective treatment, and consequently, field geometry for similar types (stages) of disease varies widely (39). In 1999, to try and solve this problem, Nowak *et al.* (1) from our institute proposed guidelines for the delineation of the neck nodal levels. These CT-based guidelines were originally a one-to-one translation from the surgical descriptions (cadaver studies) of neck nodal levels onto CT. Contrary to these original "tight boundaries," to establish a reproducible delineation procedure in a teaching hospital, the contours of each level were taken more generously by using easy-to-identify demarcating CT landmarks ("simplified" protocol by Wijers *et al.* [2]). Although these original CT-based level definitions were derived from studies without significant distortion of the neck tissue, from our clinical experience, we believed that one could implement similar guidelines in the case of limited-size pathologic neck nodes. This was one of the reasons for the contouring guidelines to be verified (first aim of this paper). The data of all patients treated with 3D-CRT between December 1998 and March 2001 to the primary and unilateral or bilateral neck, with the neck contoured in concordance with the Rotterdam "simplified" guidelines, were analyzed. The outcome of this analysis indicated that adequate dose distributions were achieved; the V_{95} and V_{107} in the N0 and N+ necks was 95.6% and 6.3% and 94.6% and 6.7%, respectively (Figs. 4 and 5). Only four locoregional relapses were observed in the N0 necks, with no recurrences in the N+ necks; 1 of the 4 patients was salvaged.

For the 46 3D-CRT–only patients, a 3-year actuarial locoregional relapse-free survival and regional relapse-free survival rate of 78% and 90%, respectively, was observed (Fig. 3). Although excellent results were obtained in terms of dose coverage and regional tumor control rates, the follow-up was, however, still limited. Furthermore, 3D-CRT did not lead to sufficient sparing (33). Given the regional control rate of 90% and the need for better sparing, we believed it was appropriate to embark on investigating the implementation of the tighter boundaries of our original—anatomy-based—level descriptions (1). This seemed reasonable, because the "simplified" definitions originated in essence from the more conformal boundaries as proposed by Nowak *et al.* (1). Moreover, the other frequently referred to classification system on CT-based neck nodal delineation in the literature, the one published by Grégoire *et al.* (3), also described boundaries that were in general somewhat tighter compared with the one proposed by Wijers *et al.* (Figs. 6–8) (2). However, it was found that the reports by Nowak *et al.* (1) and Grégoire *et al.* (3) not only differed from the one used in Rotterdam ("simplified") at the time, but also differed when compared with the surgical and diagnostic level definitions, as described by Robbins *et al.* (16) and Som (15), respectively. Taking the surgical 2002 AAO-HNS neck classification as a reference (gold standard), adjustments were proposed for the Rotterdam and Brussels protocols to arrive finally at a unified concept for CT-based neck nodal delineation. That is, by reanalyzing the boundaries, taking, in particular, the newly introduced surgical sublevels into account, the inconsistencies have been corrected (Table 3). A prime example of the relevance of some of the proposed adaptations presented in Table 3, is the cranial boundary of Levels IIA and IIB. These cranial borders are now positioned at the "level" of the caudal edge of the lateral process of the first cervical vertebra (C1). This is lower, as is frequently seen with RT portals drawn on conventional lateral X-ray films. Its relevance is given by its lower position relative to the lower part of the parotid gland, thus, potentially being more sparing. It goes beyond saying that this unified concept with the new clinical target volumes of the neck (Fig. 9) still has to be validated at some point in the future. Finally, to be complete, the boundaries of the retropharyngeal nodes, with data from papers by McLaughlin *et al.* (35) and Grégoire *et al.* (3), are also summarized in Table 4.

Future directives

Eventually, in the future, this Rotterdam/Brussels consensus proposal has to be validated in patients treated effectively by high-dose, high-precision RT, such as intensity-modulated RT. A detailed account of the delineation guidelines based on the Rotterdam/Brussels consensus proposal for the N0 neck and N+ neck, or in the case of postoperative neck RT, is in press. It will be submitted in full as a CT atlas covering the whole neck in 2-mm CT slices (17).

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