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CLINICAL INVESTIGATION **Head and Neck**

DEVELOPMENT AND VALIDATION OF A STANDARDIZED METHOD FOR CONTOURING THE BRACHIAL PLEXUS: PRELIMINARY DOSIMETRIC ANALYSIS AMONG PATIENTS TREATED WITH IMRT FOR HEAD-AND-NECK CANCER

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Purpose: Although Radiation Therapy Oncology Group protocols have proposed a limiting dose to the brachial plexus for patients undergoing intensity-modulated radiotherapy for head-and-neck cancer, essentially no recommendations exist for the delineation of this structure for treatment planning.

Methods and Materials: Using anatomic texts, radiologic data, and magnetic resonance imaging, a standardized method for delineating the brachial plexus on 3-mm axial computed tomography images was devised. A neuroradiologist assisted with identification of the brachial plexus and adjacent structures. This organ at risk was then contoured on 10 consecutive patients undergoing intensity-modulated radiotherapy for head-and-neck cancer. Dose–volume histogram curves were generated by applying the proposed brachial plexus contour to the initial treatment plan.

Results: The total dose to the planning target volume ranged from 60 to 70 Gy (median, 70). The mean brachial plexus volume was 33 ± 4 cm^3 (range, 25.1–39.4). The mean irradiated volumes of the brachial plexus were 50 Gy (17 ± 3 cm^3), 60 Gy (6 ± 3 cm^3), 66 Gy (2 ± 1 cm^3), 70 Gy (0 ± 1 cm^3). The maximal dose to the brachial plexus was 69.9 Gy (range, 62.3–76.9) and was ≥60 Gy, ≥66 Gy, and ≥70 Gy in 100%, 70%, and 30% of patients, respectively.

Conclusions: This technique provides a precise and accurate method for delineating the brachial plexus organ at risk on treatment planning computed tomography scans. Our dosimetric analysis suggest that for patients undergoing intensity-modulated radiotherapy for head-and-neck cancer, brachial plexus routinely receives doses in excess of historic and Radiation Therapy Oncology Group limits. © 2008 Elsevier Inc.

Head-and-neck cancer, Brachial plexus, Radiotherapy planning, Intensity-modulated radiotherapy, Contouring.

INTRODUCTION

Concerns over the development of brachial plexopathy among head-and-neck cancer patients receiving intensity-modulated radiotherapy (IMRT) have prompted the Radiation Therapy Oncology Group to require brachial plexus contours with dose constraints ranging from 60 to 66 Gy on many recent protocols. Guidelines for contouring the brachial plexus on axial computed tomography (CT) imaging scans used for radiotherapy planning, however, are essentially nonexistent (Table 1). Furthermore, the Advanced Technology Consortium mandates that all clinical trials using IMRT must provide specific organ-at-risk (OAR) contouring instructions (1). Notably, variation in the configuration and volume of the brachial plexus contour can profoundly affect optimization of both IMRT and three-dimensional conformal treatment plans (2). The goal of this study, therefore, was to devise standardized contouring guidelines for the brachial plexus and to characterize the dose–volume histogram in several common treatment scenarios in an effort to validate the organ at risk.

METHODS AND MATERIALS

Anatomic texts books and radiologic data were reviewed for descriptions of the brachial plexus within the neck, supraclavicular fossa, and axilla (3, 4). As limited information was available on the identification of the brachial plexus using axial computed tomography (CT), sagittal and coronal magnetic resonance imaging (MRI)-based descriptions were used to identify the course of the brachial plexus through the neck and supraclavicular region on 3-mm axial computed tomography (CT) images (3, 4). A board-certified neuroradiologist (A.D.) assisted with identification of the brachial plexus,

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Table 1. Current RTOG protocols requiring brachial plexus contours

Protocol	Constraint	Contouring instructions
Head and neck		
RTOG 0435: Phase III, double-blind, placebo-controlled study to evaluate efficacy and safety of palifermin for reduction of oral mucositis in patients with locally advanced head-and-neck cancer receiving radiotherapy with concurrent chemotherapy	60 Gy (2 Gy/fx)	None provided
RTOG 0522: Concurrent accelerated radiation + cisplatin ± cetuximab for Stage III and IV head-and-neck cancer	60 Gy (2 Gy/fx)	None provided
RTOG 0615: chemoradiotherapy ± bevacizumab for locally advanced nasopharynx cancer	66 Gy (2 Gy/fx)	None provided
Lung		
RTOG 0236: Phase II trial of stereotactic body radiotherapy in treatment of patients with medically inoperable Stage I/II non–small-cell lung cancer	24 Gy (8 Gy/fx)	Major trunks of brachial plexus contoured using subclavian and axillary vessels as surrogate for identifying location of brachial plexus; this neurovascular complex is contoured starting proximally at bifurcation of brachiocephalic trunk into jugular/subclavian veins (or carotid/subclavian arteries) and following route of subclavian vein to axillary vein, ending after neurovascular structures cross second rib
RTOG 0412/SWOG S0332: Phase III trial of preoperative chemotherapy vs. preoperative concurrent chemotherapy and thoracic radiotherapy followed by surgical resection and consolidation chemotherapy in favorable prognosis patients with Stage IIIA non–small-cell lung cancer	60 Gy (2 Gy/fx)	None provided
RTOG 0617/NCCTG N0628/CALGB 30609: Phase III comparison of standard-dose (60 Gy) vs. high-dose (74 Gy) conformal radiotherapy with concurrent and consolidation carboplatin/paclitaxel in patients with Stage IIIA-IIIB non–small-cell lung cancer	66 Gy (2 Gy/fx)	None provided

Abbreviations: RTOG = Radiation Therapy Oncology Group; fx = fraction; SWOG = Southwestern Oncology Group; NCCTG = North Central Cancer Treatment Group; CALGB = Cancer and Leukemia Group B.

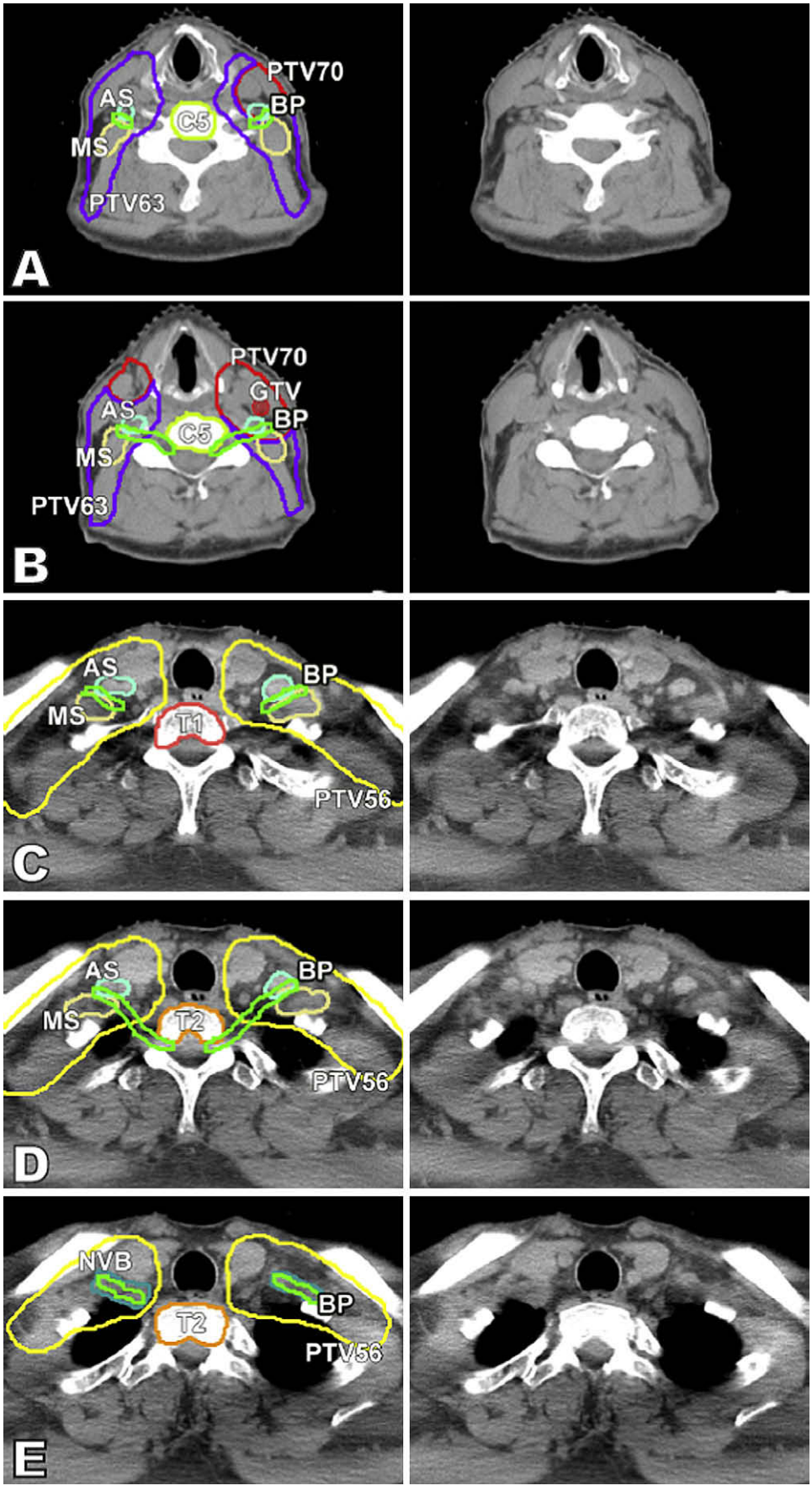
as well as adjacent structures, including the anterior and middle scalene muscles, the subclavian and axillary arteries and veins, and relevant cervical and thoracic vertebrae using noncontrast axial CT. The following step-by-step technique for contouring the brachial plexus on axial noncontrast CT was devised:

1. Identify and contour C5, T1, and T2.
2. Identify and contour the subclavian and axillary neurovascular bundle.
3. Identify and contour anterior and middle scalene muscles from C5 to insertion onto the first rib.
4. To contour the brachial plexus OAR use a 5-mm diameter paint tool.
5. Start at the neural foramina from C5 to T1; this should extend from the lateral aspect of the spinal canal to the small space between the anterior and middle scalene muscles.
6. For CT slices, where no neural foramen is present, contour only the space between the anterior and middle scalene muscles.
7. Continue to contour the space between the anterior and middle scalene muscles; eventually the middle scalene will end in the region of the subclavian neurovascular bundle.
8. Contour the brachial plexus as the posterior aspect of the neurovascular bundle inferiorly and laterally to one to two CT slices below the clavicular head.
9. The first and second ribs serve as the medial limit of the OAR contour.

Using these guidelines, the brachial plexus OAR was contoured on 10 consecutive head-and-neck cancer patients who were undergoing definitive or postoperative IMRT for locally advanced head-and-neck cancer. Examples of the OAR are shown in Figs. 1 and 2. The disease characteristics are listed in Table 2. The median radiation dose was 70 Gy (range, 60 to 70). The brachial plexus volumes and corresponding planning target volumes were recorded. In an attempt to verify the brachial plexus volume and location consistency for the 10 patients contoured in this study, dose–volume histogram curves were generated by applying the proposed brachial plexus contour to the initial treatment plan, and the percentage of the volume receiving ≥50, ≥60, and ≥66 Gy were determined.

RESULTS

The contours were successfully created for all patients using the proposed brachial plexus OAR guidelines. Table 2 lists the tumor characteristics, including disease site, stage, structures included in the gross tumor volume, and treatment parameters. Of the 10 patients, 4 had tonsil cancer, 3 had base of tongue cancer, 1 had an unknown primary, 1 had nasopharyngeal cancer, and 1 had esthesionueroblastoma. All patients had lymph node-positive disease. The total radiation dose was 60–70 Gy. Of the 10 patients, 6 received 70 Gy,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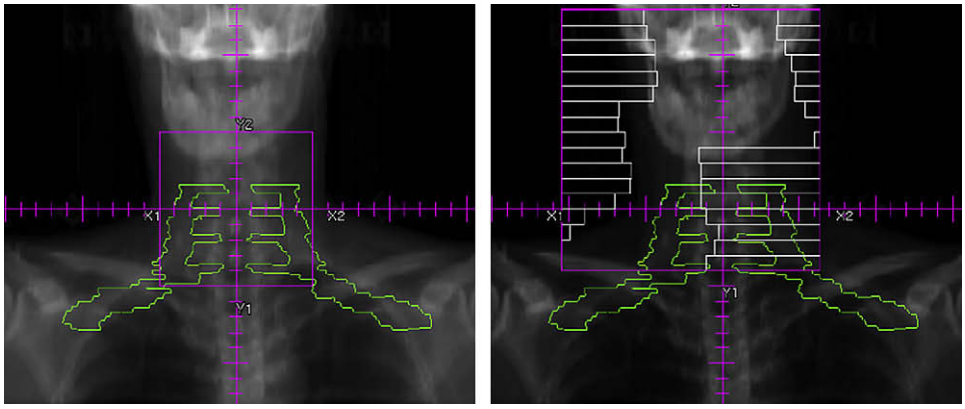

Fig. 2. Reconstructed coronal view of brachial plexus (BP) generated from contours shown in Fig. 1. This view provides visual approximation of total BP volume generated from our prescription.

3 received 66 Gy, and 1 received 60 Gy. All patients were treated in daily 2-Gy fractions.

The mean brachial plexus volume was 33 ± 4 cm^3 (range, 25.1–39.4). The mean irradiated volume of the brachial plexus receiving ≥50 Gy was 17 ± 3 cm^3 (with $52\% \pm 7\%$ of patients receiving >50 Gy), ≥60 Gy was 6 ± 3 cm^3 (with $16\% \pm 8\%$ receiving >60 Gy), ≥66 Gy was 2 ± 1 cm^3 (with $5\% \pm 4\%$ receiving >66 Gy), and ≥70 Gy was $0\% \pm 1\%$ (with $1\% \pm 2\%$ receiving >70 Gy). The mean maximal dose to the brachial plexus was 69.9 Gy (range, 62.3–76.9) and was >60, >66, and >70 Gy in 100%, 70%, and 30% of patients, respectively. The dose–volume curves for each patient are shown in Fig. 3. In general, patients with intact lymph node disease extending into Level III or IV were more likely to receive a high dose to the brachial plexus.

DISCUSSION

The brachial plexus begins at the ventral rami of the cervical nerve roots starting at the fifth cervical vertebra and continues inferiorly to include the nerve roots exiting the neural foramen of thoracic vertebra T1 (3, 4). It then passes inferolaterally between the anterior and middle scalene muscles to the subclavian artery and then laterally beneath the clavicle and into the axilla (3, 4).

Although few studies have analyzed the potential for iatrogenic injury from irradiation of the brachial plexus, it is likely that this structure receives a significant dose in many common treatment settings, particularly those involving treatment of head-and-neck and apical lung tumors. Radiation-induced brachial plexopathy is a potentially debilitating constellation of symptoms that includes upper extremity parasthesia, weakness, and motor dysfunction and is a late complication of radiotherapy to the neck and supraclavicular region. Effective treatments of radiation-induced brachial plexopathy are lacking, and the condition is generally considered irreversible (5). To our knowledge, the present report represents the first to attempt to quantify and analyze the doses received by the brachial plexus among patients treated for head-and-neck cancer. The published data on radiation-induced brachial plexopathy consists primarily of reports of patients irradiated for breast cancer using supraclavicular and axillary fields, with the development depending largely on the total dose and fraction size (6–8). The consensus recommendations on brachial plexus dose tolerance by Emami *et al.* (9) considered the brachial plexus and cauda equina together and suggested a value for a 5% risk at 5 years of 62, 61, and 60 Gy and a value for a 50% risk at 5 years of 77, 76, and 75 Gy for one-third, two-thirds, and the whole organ, respectively.

In our preliminary dosimetric analysis, all 10 patients received brachial plexus doses of ≥60 Gy (mean maximal dose, 69.9 Gy), with 70% and 30% of patients receiving a dose of >66 and 70 Gy, respectively. Of the 7 patients who received a dose >66 Gy, all had nodal disease extension into Level III or IV of the neck, with high- or intermediate-dose planning target volumes in close proximity to the brachial plexus contour. Similarly, the 3 patients who had received a dose >70 Gy had presented with tumor near to, or abutting, the brachial plexus.

Our dosimetric analysis provides initial validation that this brachial plexus contouring technique can be consistently applied to radiotherapy planning CT scans in a standardized and reproducible manner. Although the dose–volume histogram shown in Fig. 3 was unable to resolve the spatial differences

Fig. 1. Axial sections from C5 to T1 vertebral levels showing brachial plexus (BP) contours. (A) C5 vertebrae level. BP at C5 level is located between middle scalene (MS) and anterior scalene (AS) muscles. In this example, BP is completely encompassed by planning target volume (PTV)70 and PTV63. (B) C5 vertebral level. BP nerve roots were contoured from lateral border of neural foraminae to lateral border of scalene muscles. BP closely abuts gross tumor volume, with significant volume lying within PTV70 and PTV63. (C) T1 vertebral level. BP contour lies between scalene muscles and, in this patient, is entirely encompassed by PTV56. (D) T2 vertebral level. As with more rostral vertebral levels, BP nerve roots were contoured from lateral border of neural foramina to lateral border of scalene muscles. Note, significant portion of BP within PTV56. (E) T2 vertebral level. Inferior to scalene muscles, subclavian neurovascular bundle can be used as reference for BP contour.

Table 2. Tumor, target, and dose characteristics

Pt. No.	Stage	Site	GTV	Dose
1	T4aN2b	Right tonsil	Right tonsil, right nasopharynx, right Level 2-3 and left Level 2-3 lymph nodes	70 Gy; 2 Gy/d
2	T1N2c	Left base of tongue	Left base of tongue, left Level 2 and right Level 2 nodes	70 Gy; 2 Gy/d
3	T3N2b	Right tonsil	Right tonsil, right Level 2-3 and left Level 2 nodes	70 Gy; 2 Gy/d
4	T1N2c	Left base of tongue	Left base of tongue, right Level 2 nodes	70 Gy; 2 Gy/d
5	T4N2c	Nasal cavity	Right nasal cavity, maxillary sinus, bilateral sphenoids, bilateral ethmoids, right retropharyngeal nodes, right frontal lobe, right orbit, right Level 2-3 nodes	66 Gy; 2 Gy/d
6	T4N1	Nasopharynx	Bilateral nasopharynx, clivus, bilateral cavernous sinus, left retropharyngeal nodes, right Level 5 nodes	70 Gy; 2 Gy/d
7	pT0N1	Unknown primary	CTV only	60 Gy; 2 Gy/d
8	pT3N2b	Right tonsil	CTV only	66 Gy; 2 Gy/d
9	pT1N2b	Right base of tongue	Right base of tongue, left Level 2 nodes	70 Gy; 2 Gy/d
10	pT1N2b	Right tonsil	CTV only	66 Gy; 2 Gy/d

Abbreviations: Pt. No. = patient number; GTV = gross tumor volume; CTV = clinical target volume.

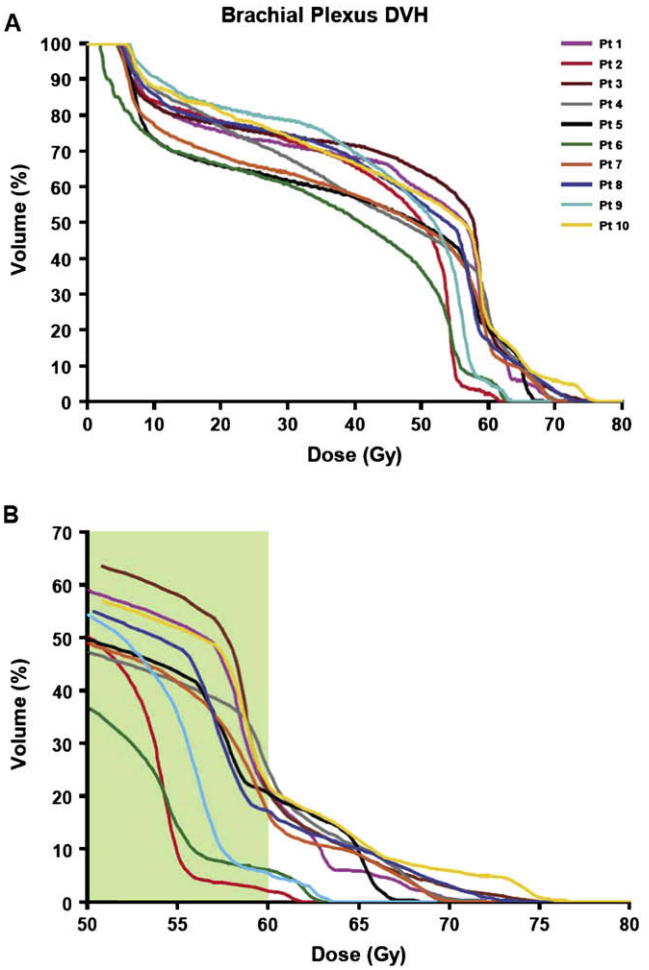

Fig. 3. (A) Brachial plexus (BP) dose–volume histogram (DVH) characteristics for 10 patients contoured for present study. All patients had some portion of BP receiving >60 Gy. In 3 patients, this volume was small; however, in 7 patients, approximately 20% of BP was treated to >60 Gy, with maximal dose of 70–80 Gy. (B) DVH from 50–80 Gy shown for all patients in study. Shaded area illustrates percentage of BP volume receiving <60 Gy. Of 10 patients, 60% received total dose of >65 Gy and 30% received >70 Gy.

in the OAR contour from patient to patient, the planning target volume contours for all 10 patients were finalized and approved by one of two experienced radiation oncologists (A.C. and S.N.) and were similar for all patients.

Several limitations of this study and the brachial plexus OAR contouring guidelines must be recognized. First, the brachial plexus is best imaged with gadolinium-enhanced T_1-weighted coronal and sagittal MRI sequences and generally cannot be visualized using CT. Additionally, axial MRI projections are typically inadequate for identification of the brachial plexus. As a result, these guidelines were based on a best approximation of the location of the brachial plexus in relation to structures that are easily delineated on standard axial projection radiotherapy planning CT scans. Acknowledging that the use of coronal and sagittal MRI, if available, might offer improved precision in delineating the brachial plexus, it is our belief that the proposed instructions serve as a highly accurate and clinically relevant surrogate using traditional treatment planning techniques with axial CT. Although the technique is easily applied in the setting of definitive treatment, contouring the OAR in postoperative patients is challenging and can be particularly difficult in patients who have undergone removal of the sternocleidomastoid muscle as a part of neck dissection. In circumstances in which visualization of the scalenes is not feasible, possibly because of edema or fibrosis, we relied on symmetry with the contralateral neck to determine the anatomic position. Clearly, additional research is needed to analyze the degree of variability among individuals and to determine the influence of such factors as shoulder/neck motion and weight loss on the delineation of this structure.

Another limitation of this contouring technique relates to the normal anatomic variation of the brachial plexus. In particular, 5–10% of individuals have a variant brachial plexus in which the first nerve root contributing to the plexus originates at the level of the 4th cervical vertebra (4). This variation cannot be elucidated with CT and could result in failure to contour the first nerve root of the brachial plexus. A second anatomic variation that can occur is the presence of fused C2

and C3 vertebrae (10). This variation can potentially lead to misidentification of the vertebral levels and, thus, initiation of the brachial plexus contour more inferior in the neck than its actual position.

CONCLUSIONS

Our results have shown that this basic technique provides a precise and accurate method for delineating the brachial plexus OAR on treatment planning CT scans. Our dosimetric analysis suggested that excellent agreement exists between the geometric and volumetric parameters when applying the new brachial plexus OAR contouring guidelines in several common head-and-neck IMRT treatment situations. Furthermore, our preliminary data have suggested that for patients undergoing whole-field IMRT for head-and-neck cancer, the brachial plexus could receive doses near to, or in excess of, historic and current Radiation Therapy Oncology Group dose recommendations. The clinical repercussions of this finding will form the basis for future studies at our institution.

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