A prospective in silico analysis of interdisciplinary and interobserver spatial variability in post-operative target delineation of high-risk oral cavity cancers: Does physician specialty matter?

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INTRODUCTION

Intensity modulated radiotherapy (IMRT) is a conformal radiation technique that enables the generation of steep dose gradients within complex geometries [1]. The widespread adoption of this modality has resulted in improved dose sparing of organs at risk, ultimately resulting in improved delivery of tumoricidal dose and dose-toxicity profiles. A shift from traditional two-dimensional (2D) treatment to use highly conformal IMRT treatment has greatly reduced concurrent and late-onset toxicity sequelae. However, this problem continues to be a challenge as even minor variability in treatment setup and/or execution may result in significant under...
dosage of at-risk areas and/or over dosage of surrounding normal tissues [2].

Modern evaluation and treatment of head and neck cancer (HNC) patients typically involves, and is dependent upon, the collective, coordinated expertise of multidisciplinary care teams with heavy input from radiologic, surgical, and radiation oncologic specialties. The multidisciplinary input in patient care has become widely accepted as “best practice,” having demonstrated measureable improvements in clinical quality indicators [3,4]. The teams are continuously challenged with effectively communicating at all stages of the process (diagnosis, staging, treatment, support, rehabilitation, and follow-up) to maximize benefit to the patient. While communication itself can be challenging, the process may be further complicated by differing use (or understanding) of specialty-specific vernacular and/or therapeutic decision making algorithms.

Furthermore, the radiation oncologist, particularly in a non-academic setting, is dependent upon the descriptive language of the surgeons and/or radiologists in the post-operative setting if adequate pre-operative imaging is not available for comparison. Given the potential for significant adverse patient outcomes based on a variable interdisciplinary understanding of fundamental radiation oncology treatment paradigms we consequently sought to investigate the variation in delineation of target volumes in post-operative HNC patients recommended to receive adjuvant radiation therapy by all parties involved in a typical case. We evaluated whether any discrepancy in nomenclature, particularly ‘post-operative tumor bed’ and ‘post-operative nodal bed’; between disciplines was present, necessitating the need to establish a standardized set of definitions. Fundamentally, we sought to determine whether, when specialist head and neck surgeons, radiologists and radiation oncologists discuss the ‘post-operative tumor bed’ they were actually talking about the same spatial region; furthermore, did the ‘surgical’, ‘radiological’ and ‘radiation oncological’ post-operative tumor bed mean the same within a specialty to differing physicians?

This study is a prospective in silico human performance evaluation to identify and quantify the intradisciplinary and interdisciplinairy observer variability in post-operative target volume delineation using a standardized case set and accepted spatial metrics as a surrogate for shared understanding of where radiation should be directed in high-risk cases.

Materials and Methods

Imaging and contouring of cases

Three standardized cases of patients with resected oral cavity cancers and recommended to receive post-operative radiation therapy (PORT) were selected for this study. Patients were randomly chosen from an Institutional Review Board (IRB) approved dataset and real patient data were extracted from patient records. The patients had a planning CT scan acquired (CTAqSim, Philips Medical Systems) without IV contrast utilizing immobilization devices, including tongue-depressing oral stent, and head and neck thermoplastic mask [5,6]. CT imaging was obtained from the vertex to the carina with 2 mm thickness slice thickness reconstruction [7]. Clinical information and planning CT images were anonymized and used for target delineation. After receiving a standardized set of explicit instructions [Appendix A], radiation oncologists (RO) specializing in HNC, head and neck surgeons (HNS), and head and neck radiologists (NR) contoured the post-operative tumor and nodal beds, respectively, using DICOM images in a commercial treatment planning/segmentation software (Pinnacle v9.0, Philips Medical Systems); expertise levels by specialty and years of experience are listed in Table 1. For users who were unfamiliar with the software interface (e.g. HNS and NR physicians, who do not use segmentation software daily), a skilled segmentation software user [BD/ASRM] was present throughout the initial contouring process to answer software interface questions only. Physicians were allowed access to all pertinent anonymized patient records including pre-operative imaging and any operative, pathologic or clinical note relevant to their task, excluding the actual delivered radiation treatment plan or planning notes. One radiation oncologist and one radiologist did not complete a majority (>50%) of contouring. Therefore their volumes were excluded from the analysis.

Comparison of volumes

Contour information was subsequently exported and analyzed using the EvaluateSegmentation program and metrics as described by Taha and Hanbury [8]. Contours were compared for agreement. The Warfield’s simultaneous truth and performance level estimation (STAPLE) algorithm was used to generate a consensus contour representing the ‘ground truth’ volume. Warfield’s STAPLE is an algorithm which incorporates multiple unordered and assumed independent segmentations to create an estimate of the hidden true segmentation, enabling characterization of the performance level of each observer [9]. The STAPLE volume was compared to each observer’s volumes, allowing direct comparison between observers’ volumes and the ‘ground truth’ volume [9].

The following metrics were included in the analysis:

1. Dice similarity coefficient (overlap based) – measures the similarity between two sets of segmentations and is calculated using the formula DSC = 2(𝐴∩𝐵) ∕(𝐴+𝐵) [10]

   where A represents the observer dataset and B represents the STAPLE dataset [11] (Fig. 5).

2. Sensitivity and specificity (Information theoretic based) – Sensitivity, also known as the True Positive Rate (TPR), measures the voxels that are labeled positive by both the observer and STAPLE and is calculated by the formula: Sensitivity = TPR = TP ∕ (TP + FN) [8]

   where true positive (TP) represents positive voxels in STAPLE and observer and false negative (FN) represents the positive voxels in observer segmentation but not in STAPLE.

   Similarly, specificity, also known as True Negative Rate (TNR), measures the voxels that are labeled negative by both observer and STAPLE: Specificity = TNR = TN ∕ (TN + FP) [8], where TN represents true negative, and FP represents false negative.

3. Hausdorff distance (Spatial distance based) measures the maximum distance between contours and is measured from one point in one set of segmentation to the closest point in another set of segmentation [8].

| Table 1 | Observers and their corresponding specialty and years of experience. |
|---------|-----------------------------|
| Specialty               | Observer | Years of Experience |
| Radiation Oncology      | RadOnc_A   | 4                      |
|                        | RadOnc_B   | 22                     |
|                        | RadOnc_C   | 2                      |
| Head and Neck Surgery   | Surgeon_A  | 3                      |
|                        | Surgeon_B  | 10                     |
|                        | Surgeon_C  | 9                      |
|                        | Surgeon_D  | 5                      |
| Radiology               | Radiologist_A | 12                |
|                        | Radiologist_B | 5                   |
|                        | Radiologist_C | 8                   |
Statistical analysis

Individual and intradisciplinary results were concatenated and analyzed as a cohort using the JMP v.12.1.0 software package (SAS Institute; Cary, NC). The analyzed metrics for post-operative primary and nodal tumor bed delineation by all users were pooled according to user specialty. The non-parametric Steel-Dwass Method was used to compare all pairs of measurements whilst controlling the overall error rate [12]. A variability gauge modeled with main effect was generated and Bayesian analysis was performed to measure the variation in Dice coefficient similarity between observers and disciplines.

Results

Three patients with resected high-risk oral cavity tumors were chosen for this study. All three patients had T2-T3 N1-2 oral cavity squamous cell carcinomas resected with clear margins and were recommended to receive post-operative radiation therapy to improve locoregional control. A total of three ROs, four head and neck surgeons, and three radiologists completed all contours.

Interobserver variability

The volumes (in cc) contoured by each observer for each case are illustrated in Fig. 1. Dice similarity coefficients were used as a measure of conformity between observers. As demonstrated in Fig. 2, there was a high degree of variability existed between observers with an Acceptable Percent Measurement Variation of 99.7% (16.5% Repeatability and 83.5% Reproducibility). According to the proposed guidelines for acceptable Repeatability and Reproducibility percent by Barrentine [13], a measurement of <21% is acceptable, 21–30% is marginally acceptable and >30% is considered unacceptable.

Interdisciplinary variability

Table 2 summarizes the results for all metrics between disciplines. In summary, there were significant differences between disciplines for most metrics. Radiologists and radiation oncologists segmented relatively similar post-operative volumes compared to surgeons (Fig. 4). On review of individual contours, surgeons tend to delineate anatomical compartments whilst radiologists tend to contour the surgical bed. Radiation oncologists’ volumes were of an approximate average of surgeons and radiologists, but tend to be more similar to radiology colleagues, as demonstrated by the Hausdorff distance (Table 2), average volume contoured and Dice coefficient similarity (Fig. 3). The variability between interdisciplinary contours is depicted in Fig. 2 as well.

Discussion

The cardinal principle in radiation oncology planning is ‘do not miss the tumor’. This rule is usually achievable when there is intact tumor with normal (usually undistorted) anatomy that can be easily visualized on planning scan. This proves to be rather challenging in post-operative cases where the gross tumor has been resected and the patient’s anatomy has been altered by removal of tissue (resection), addition of new tissue (reconstruction) or surgical hardware and/or inflammation (healing). In the post-operative setting, radiation oncologists rely heavily on pre-operative images and operative reports to delineate the tumor and/or nodal beds accurately with assistance from his/her diagnostic radiology and surgical colleagues to delineate the areas at risk or concern. It is recognized that in a pre-treatment setting, multidisciplinary team input has significant impact on patient’s treatment plan and potentially improving patients’ outcomes [4]. However, in the post-operative setting, it appears that these same multidisciplinary teams may have varied understanding or consensus of what consists of a ‘post-operative tumor bed’ and ‘post-operative nodal bed’. Our study investigated the interspecialty and intraspecialty consistency in delineation of target volumes in the post-operative setting for head and neck cancer patients.
Our results showed overall there were significant differences in segmentation between specialties. This translates to a difference in the understanding of the region treated in a post-operative setting. In a study with intact gross tumors, Horan et al. [14] reported good concordance of gross tumor delineation between radiologists and radiation oncologists, especially in head and neck tumor cases. When assessing interdisciplinary contouring variation, there was good consistency within each discipline, particularly among the surgeons. Within radiation oncology discipline, there was one person (RadOncB) with significantly different contours. This may be secondary to the experience of the clinician as Cardenas et al. [15] demonstrated that the experience of the treating radiation oncologist significantly affected the agreement between pre- and post-quality assurance segmentations. Previous studies evaluating interobserver variations in target delineation in head and neck cancer were predominantly in the definitive setting, comparing gross tumor volume delineation, between radiation oncologists with or without radiologists [14,16,17]. To our knowledge, this is the first prospective study comparing post-operative head and neck delineation. Studies in other disease sites have shown that when target volumes delineated by radiation oncologists were compared between institutions, a large discrepancy in target volumes was

![Image of variability gauge chart](image.png)

Table 2
Summary of metrics measurements and comparisons for each discipline. *depicts significant p-value (<0.05). Abbreviations: HNS – head and neck surgery; NR – radiology, RO – radiation oncology.

| Metric                           | Discipline | Median    | Range          | Nonparametric Comparison Pairs | P-value |
|---------------------------------|------------|-----------|----------------|-------------------------------|---------|
| Volume (in cc)                  | RO         | 116.3     | 22.1–179.1     | RO: HNS                       | 0.0316  |
|                                 | HNS        | 232.9     | 107.4–333.3    | RO: NR                        | 0.8569  |
|                                 | NR         | 206.6     | 36.9–173.6     | HNS: NR                       | 0.0025  |
| Sensitivity                     | RO         | 0.99      | 0.83–1         | RO: HNS                       | 0.6513  |
|                                 | HNS        | 0.98      | 0.43–1         | RO: NR                        | 0.0333  |
|                                 | NR         | 1.00      | 0.66–1         | HNS: NR                       | 0.0094  |
| Specificity                     | RO         | 0.99      | 0.99–1         | RO: HNS                       | 0.0099  |
|                                 | HNS        | 0.99      | 0.99–1         | RO: NR                        | 0.2520  |
|                                 | NR         | 0.99      | 0.99–1         | HNS: NR                       | <0.0001 |
| Dice Similarity Coefficient (Dice) | RO     | 0.56      | 0.03–0.91      | RO: HNS                       | 0.0196  |
|                                 | HNS        | 0.71      | 0.25–0.98      | RO: NR                        | 0.0623  |
|                                 | NR         | 0.33      | 0.14–0.60      | HNS: NR                       | <0.0001 |
| Hausdorff Distance (in mm)      | RO         | 49.38     | 19.21–257.18   | RO: HNS                       | 0.0029  |
|                                 | HNS        | 22.95     | 3.16–251.13    | RO: NR                        | 0.9083  |
|                                 | NR         | 43.32     | 19.24–243.13   | HNS: NR                       | 0.0060  |
observed \cite{18,19}. However, when target volumes were compared within an institution, there was good concordance in gross tumor delineation between radiation oncologists and radiologists \cite{17}, consistent with our findings. Despite no significant interobserver difference in gross tumor volume, these studies showed that the volumes on PET/CT images were the most consistent between observers compared to volumes on CT \cite{17,20,21} or MRI \cite{21}. The role of PET/CT imaging is limited in post-operative cases, as the gross tumor has been resected.

In this study, we have demonstrated that there is an interdisciplinary difference in understanding of ‘at risk’ tissue in a post-operative setting. This can have significant implication for patient management. For example, a surgeon may perform a smaller resection with the perception that the treating radiation oncologist will irradiate the whole anatomical compartment. In this case, if the surgeon did not communicate his or her concerns of areas at risk accurately, the surgical ‘high-risk’ area may be not be included in the high radiation dose region, thus placing the patient at higher risk of local recurrence. On the contrary, if the treating surgeon was not aware that the radiation oncologist would treat all areas perturbed by the surgeon, the surgeon may make an incision quite a distance away from the tumor (e.g. to achieve better cosmetic outcome) without realizing that the patient will subsequently be treated with a larger radiation field to encompass the surgically-perturbed area, thereby increasing treatment toxicities. Similarly, a mutual understanding of the high-risk post-operative area is imperative between radiation oncologists and radiologists. We have shown that radiologists delineated smaller volumes than radiation oncologists. This can be an issue especially in the post-treatment setting, whereby a lesion detected on radiological scan may be reported as favoring a recurrence rather than post-treatment inflammation-related changes as the radiologist may have thought that the lesion was located outside the radiotherapy fields. This may result in additional and likely unnecessary further investigations, some of which may be invasive, to the patient.

Our study demonstrated significant interobserver and interdisciplinary differences in tumor bed delineation, emphasizing that peer review quality assurance remained of utmost importance to ensure accurate target delineation \cite{22}. A recent single institution study by Cardenas et al. \cite{15} indicated that peer review quality assurance led to major plan changes in 14% of patients. In a central quality assurance review of 687 treatment plans for a large international phase 3 head and neck study, Peters et al. \cite{23} reported
that 25% of patients had noncompliant plans, and 47% of noncompliant plans may have resulted in a significant adverse tumor control outcome. Furthermore, patients who received treatment with major deficiencies in treatment plan had significantly poorer clinical outcome in terms of freedom from locoregional failure and overall survival compared to those who had a protocol compliant treatment plan. While quality assurance requires additional clinical and treatment planning time, a simulated study on a head and neck cancer study by the EORTC 22071–24071 [24] showed that a quality assurance program not only improved patient outcomes but was also cost-effective. Therefore, it is advocated that every radiation oncology center should implement a peer review program, adding to the quality of patient care. In addition, we advocate extending this paradigm, such that a radiation plan review might ideally (at some interval) also provides feedback and information to the treating surgeons and radiologists. We suggest that radiation oncology treatment plans be made readily available and easily accessible in every patient’s medical record, allowing other non-radiation oncology physicians to review and better understand the regions treated. This will also allow rapid assessment and determination if any future normal tissue complications or recurrences may or may not be within the radiotherapy fields.

This study has its own limitations. To recapitulate real-life clinical workflow, the observers were allowed to access anonymized patients’ records, imaging reports, and diagnostic images. As some observers were the direct treating physicians for some of these patients, a potential bias could be imposed due to prior knowledge or recall of the intricacies of the case. Furthermore, this is a single institution study in a high volume cancer center, possibly reducing the magnitude of segmentation differences between disciplines and radiation oncologists. A study across different institutions is required to understand the general interdisciplinary agreement and/or understanding of ‘post-operative bed’. Although each discipline may have their own anatomical and radiological definition of ‘post-operative bed’, it is of utmost importance that each clinician communicates clearly with their colleagues when it comes to treating post-operative patients as it may alter patients’ radiotherapy fields and consequently, dose to target and normal tissues, and potential side effects to patients.

Nonetheless, to our knowledge, our data represents the first prospective rigorously executed multi-disciplinary (surgery, radiology and radiation oncology) specialist assessment of quantitative differences in defining the post-operative tumor bed. At a technical level, the importance of quantification is innovative; however, more important is the observation that different specialties are often talking about different and distinctive regions when discussing “the post-operative bed”. We recommend that future cooperative group target delineation efforts include non-radiation oncologists when incorporating post-operative radiotherapy. The rise of minimally invasive transoral robotic surgery (TORS) trials, such as the ECOG-3311 trial (ClinicalTrials.gov Identifier: NCT1898494) necessitates this move. It would be poor form to over-irradiate unnecessarily in trials where surgery is designed as a radiation dose de-escalation strategy, based only on failed nomenclature for the target volumes. This effort represents a first step towards such approaches, and brings the imperative nature of multidisciplinary care not only to clinical practice, but into the realm of spatial, not just conceptual agreement.

**Conclusion**

Overall, our study demonstrated significant variations in inter-disciplinary target delineation, highlighting the importance of good communication and explicit description of ‘areas of concern’ amongst multidisciplinary care teams to ensure proper target delineation and adequate radiation coverage of at-risk post-operative areas. To our knowledge, this is the first prospective study comparing target delineation variations between all three main disciplines in post-operative oral cavity cases. As there were intra-discipline and inter-observer variations observed, peer-to-peer review of target delineation is recommended to ensure adequate target coverage while avoiding ‘over-contouring’ that may result in increased radiation-related acute and/or late toxicity to the patient. Although there are contouring guidelines available, post-operative cases target delineation can prove to be more difficult due to anatomical distortion. In these cases, peer-to-peer review is of utmost importance, in addition to communication with the treating surgical and radiological colleagues.

**Prior presentation**

Preliminary analyses and portions of this data were presented as a poster at the 2013 American Society of Radiation Oncology (ASTRO) Annual Meeting, September 22–25, 2013, Atlanta, GA, USA.

**Co-author specific contributions**

All listed co-authors performed the following:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work;
2. Drafting the work or revising it critically for important intellectual content
3. Final approval of the version to be published
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Specific additional individual cooperative effort contributions to study/manuscript design/execution/interpretation, in addition to all criteria above are listed as follows:

- SPN, BAD, MJA, ASRM, CDF - Manuscript writing, statistical analysis, oversight of all image segmentation, supervised statistical analysis.
- JKC, CC - Segmentation analysis.
- GBG, JP, MZ, JMD, CML, RRC, MEK, JH, BH, NGT, SL, DR, BH, JH - Image segmentation, contributory analytic support, clinical review and review of manuscript.
- CDF - Corresponding author; conceived, coordinated, and directed all study activities, responsible for data collection, project integrity, manuscript content and editorial oversight and correspondence; direct oversight of trainee personnel. Statistical analysis and guarantor of statistical quality.

**Conflict of interest**

None

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.ctro.2018.07.006.

References

[1] Brahme A. Design principles and clinical possibilities with a new generation of radiation therapy equipment. A review. Acta Oncol. 1987;26:403–12.
[2] Al-Mamgani A, van Rooij P, Verduijn GM, Mehillal R, Kerrebijn JD, Levendag PC. The impact of treatment modality and radiation technique on outcomes and toxicity of patients with locally advanced oropharyngeal cancer. Laryngoscope 2013;123:386–93.
[3] Back MF, Ang EL, Ng WH, See SJ, Lim CC, Tay LL, et al. Improvements in quality of care resulting from a formal multidisciplinary tumour clinic in the management of high-grade glioma. Ann Acad Med Singapore. 2007;36:347–51.
[4] Wheless SA, McKinney KA, Zanation AM. A prospective study of the clinical impact of a multidisciplinary head and neck tumor board. Otalaryngol Head Neck Surg. 2010;143:850–4.
[5] O’Daniel JC, Rosenthal DI, Garden AS, Barker JL, Ahamad A, Ang KK, et al. The effect of dental artifacts, contrast media, and experience on interobserver contouring variability in head and neck anatomy. Am J Clin Oncol. 2007;30:191–8.
[6] Wang H, Wang C, Tung S, Dimmitt AW, Wong PF, Edson MA, et al. Improved setup and positioning accuracy using a three-point customized cushion/mask/hite-block immobilization system for stereotactic radiosurgery of head and neck cancer. J Appl Clin Med Phys. 2016;17:180–9.
[7] Sturgeon JD, Cox JA, Mayo LL, Gunn GR, Zhang L, Balter PA, et al. Improved human observer performance in digital reconstructed radiograph verification in head and neck cancer radiotherapy. Int J Comput Assist Radiol Surg. 2015;10:1667–73.
[8] Taha AA, Hanbury A. Metrics for evaluating 3D medical image segmentation: analysis, selection, and tool. BMC Med Imaging 2015:15:29.
[9] Warfield SK, Zou KH, Wells WM. Simultaneous truth and performance level estimation (STAPLE): an algorithm for the validation of image segmentation. IEEE Trans Med Imaging 2004;23:903–21.
[10] Allozi R, Li XA, White J, Apet A, Tai A, Michalski JM, et al. Tools for consensus analysis of experts’ contours for radiotherapy structure definitions. Radiother Oncol. 2010;97:572–8.
[11] Kalpathy-Cramer J, Awan M, Taintor CA, Raich CR, Rosenthal DI, Fuller CD. Development of a software for quantitative evaluation radiotherapy target and organ-at-risk segmentation comparison. J Digit Imaging 2014;27:108–19.
[12] Steel RGD. Some Rank Sum Multiple Comparisons Tests. Biometrics 1961;17:539–52.
[13] Barrentine LB. Concepts for R&R Studies. ASQC Quality Press; 1991.
[14] Horan G, Roques TW, Curtin J, Barrett A. “Two are better than one”: a pilot study of how radiologist and oncologists can collaborate in target volume definition. Cancer Imaging 2006;6:16–9.
[15] Cardenas CE, Mohamed AS, Tao R, Wong AJ, Awan MJ, Kuruvila S, et al. Propective Qualitative and Quantitative Analysis of Real-Time Peer Review Quality Assurance Rounds Incorporating Direct Physical Examination for Head and Neck Cancer Radiation Therapy. Int J Radiat Oncol Biol Phys. 2016.
[16] Riegel AC, Berson AM, Destan S, Ng T, Tena LB, Mintsch RJ, et al. Variability of gross tumor volume delineation in head-and-neck cancer using CT and PET/CT fusion. Int J Radiat Oncol Biol Phys. 2006;65:726–32.
[17] Breen SL, Publicover J, De Silva S, Pond G, Brock K, O’Sullivan B, et al. Intraobserver and interobserver variability in GTV delineation on FDG-PET-CT images of head and neck cancers. Int J Radiat Oncol Biol Phys. 2007;68:763–70.
[18] Jeanneret-Sozzi W, Moeckli R, Valley JF, Zouhair A, Oszahin EM, Mirimannoff RO, et al. The reasons for discrepancies in target volume delineation: a SARSRO study on head-and-neck and prostate cancers. Strahlenther Onkol. 2006;182:450–7.
[19] Moeckli R, Sozzi WJ, Mirimannoff RO, Oszahin M, Zouhair A, Valley JF, et al. Physical considerations on discrepancies in target volume delineation. Z Med Phys. 2009;19:224–35.
[20] Berson AM, Stein NF, Riegel AC, Berson AM, Destan S, Ng T, Tena LB, et al. Variability of gross tumor volume delineation in head-and-neck cancer using PET/CT fusion. Part II: the impact of a contouring protocol. Med Dosim. 2009;34:30–5.
[21] Anderson CM, Sun W, Buatti JM, Maley JE, Polenci B, Mott SL, et al. Interobserver and intermodality variability in GTV delineation on simulation CT, FDG-PET, and MR Images of Head and Neck Cancer. Jacobs J Radiat Oncol. 2014;1:006.
[22] Christiennes M, Collette S, Overgaard J, Gregoire V, Kazmierska J, Castadot P, et al. Quality assurance of radiotherapy in the ongoing EORTC 1219-DAHANCA-29 trial for HPV/p16 negative squamous cell carcinoma of the head and neck: results of the benchmark case procedure. Radiother Oncol. 2017;123:424–30.
[23] Peters LJ, O’Sullivan B, Giralt J, Fitzgerald TJ, Trotti A, Bernier J, et al. Critical impact of radiotherapy protocol compliance and quality in the treatment of advanced head and neck cancer: results from TRACD 02.02. J Clin Oncol. 2010;28:2996–3001.
[24] Weber DC, Hurkmans CW, Melidis C, Budach W, Langendijk JH, Peters LJ, et al. Outcome impact and cost-effectiveness of quality assurance for radiotherapy planned for the EORTC 22071–24071 prospective study for head and neck cancer. Radiother Oncol. 2014;111:393–9.
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