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Enhanced head and neck radiotherapy target definition through multidisciplinary delineation and peer review: A prospective single-center study

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ABSTRACT

This study evaluates the benefit of weekly delineation and peer review by a multidisciplinary team (MDT) of radiation oncologists (ROs), radiologists (RXs), and nuclear medicine (NM) physicians in defining primary and lymph node tumor volumes (GTVp and GTVn) for head and neck cancer (HNC) radiotherapy.

This study includes 30 consecutive HNC patients referred for definitive curative (chemo)-radiotherapy. Imaging data including head and neck MRI, [18F]-FDG-PET and CT scan were evaluated by the MDT. The RO identified the 'undeniable' tumor as GTVp_core and determined GTVp_max, representing the maximum tumoral volume. The MDT delineation (MDT-D) by RX and NM physicians outlined their respective primary GTVs (GTVp_RX and GTVp_NM). During the MDT meeting (MDT-M), these contours were discussed to reach a consensus on the final primary GTV (GTVp_final). In the comparative analysis of various GTVp delineations, we performed descriptive statistics and assessed two MDT-M factors: 1) the added value of MDT-M, which includes the section of GTVp_final outside GTVp_core but within GTVp_RX or GTVp_NM, and 2) the part of GTVp_final that deviates from GTVp_max, representing the area missed by the RO. For GTVn, discussions evaluated lymph node extent and malignancy, documenting findings and the frequency of disagreements.

The average GTVp core and max volumes were 19.5 cc (range: 0.4–90.1) and 22.1 cc (range: 0.8–106.2), respectively. Compared to GTVp_core, MDT-D to GTVp_final added an average of 3.3 cc (range: 0–25.6) and spared an average of 1.3 cc (0–15.6). Compared to GTVp_max, MDT-D and -M added an average of 2.7 cc (range: 0–20.3) and removed 2.3 cc (0–21.3). The most frequent GTVn discussions included morphologically suspicious nodes not fixing on [18F]-FDG-PET and small [18F]-FDG-PET negative retropharyngeal lymph nodes.

Multidisciplinary review of target contours in HNC is essential for accurate treatment planning, ensuring precise tumor and lymph node delineation, potentially improving local control and reducing toxicity.

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1. Introduction

Head and neck cancer (HNC) most often presents at a locally advanced stage (III-IV) and ranks as the seventh most prevalent cancer worldwide. According to the 2020 Globocan cancer statistics, they account for more than 660,000 new cases and 325,000 deaths annually [1].

Over the past decades, multimodal treatment and a multidisciplinary approach have become the standard of care, directly impacting on disease free and overall survival [2]. This positive impact can be attributed to enhanced staging, improved target delineation through CT, MRI, and/or PET-scan technologies, and more precise treatment strategies. These advancements allow for treatment with minimized toxicity and morbidity, ultimately enhancing the quality of life for patients, while improving treatment outcomes. Furthermore, HNC being a complex disease it necessitates a multidisciplinary team (MDT) approach involving various specialized professionals such as surgeons, radiation and medical oncologists, pathologists, swallow and speech therapists, specialized nurses, dieticians, and psychologists [3].

Radiation therapy plays a pivotal role in the comprehensive management of advanced stage HNC, which often involves a combination of treatment modalities. The radiation therapy process is complex and comprises several crucial steps, including patient consultation, interpretation of diagnostic imaging, delineation of the target volumes, treatment planning, treatment administration, quality assurance, and patient follow-up. Accurate delineation of the tumor volume is of paramount importance to ensure the effectiveness and safety of radiotherapy. The responsibility for precise target volume delineation primarily rests with the radiation oncologist (RO), relying on clinical information and diagnostic imaging. This task requires extensive training, a comprehensive understanding of the anatomy, knowledge of disease spread patterns, adherence to established guidelines, and proficiency in modern imaging techniques. Accurately defining the primary tumor and regional lymph node metastasis is a critical and challenging step in HNC radiotherapy. While international delineation guidelines [4–8] offer valuable guidance, they may not always provide definitive answers to the complex decision-making ROs encounter in their daily practice. This explains the well-known interobserver variability in HNC target volume delineation [9,10]. This variability can substantially affect the quality and, consequently, the effectiveness of radiotherapy treatments [11–13]. With the noted variability among observers in defining target volumes for HNC, the importance of peer review quality assurance is emphasized.

Supported by a growing body of clinical evidence, many oncological societies such as American College of Radiation Oncology and the World Health Organization have underlined the necessity of quality assurance programs in radiation oncology treatment planning, advocating for peer review as one of the most effective methods [14–16]. Peer review of treatment plans is a well-established practice in radiation oncology and during these sessions, members of the treatment team, including radiation oncologists, medical physicists, and dosimetrists, collaboratively review each case [17,18]. Some studies have demonstrated that involving neuro-radiologists in a collaborative delineation approach can have a significant clinical impact, particularly when dealing with challenging cases or disease patterns [19,20]. Routine head and neck radiologist input in radiotherapy peer review is feasible and can help avoid gross error in contouring [21]. However, there is a lack in the literature regarding the nuclear medicine physicians input in defining target volumes for head and neck cancer radiotherapy planning. While [18F]-FDG-PET-CT is increasingly being accepted for defining target volumes in HNC within the radiation oncology field, there is still no standardized method for contouring the GTV in the literature using this imaging technique [8]. The contouring of the PET-CT-based GTV, is difficult as representing a metabolic tumor volume and influenced by the choice of threshold level [22]. This underscores the importance of nuclear medicine physicians' expertise in enhancing the precision of radiotherapy planning for HNC [23,24].

Since 2017, our institute has implemented a weekly multidisciplinary peer review meeting, bringing together HNC dedicated ROs, radiologists (RXs), and nuclear medicine (NM) physicians. This meeting serves as a platform for discussing the imaging data of individual HNC patients, with the primary goal of enhancing the precision of target volume definition in radiotherapy.

To the best of our knowledge, this study represents the first attempt to assess the influence of multidisciplinary delineations and peer-review evaluations involving three distinct disciplines, RO, RX and NM, each with their unique backgrounds and perspectives. Consequently, our research aims to investigate the impact of this MDT delineation (MDT-D) and meeting (MDT-M) on the definition of the Gross Tumor Volume of the primary tumor (GTVp) and lymph nodes (GTVn) in patients undergoing definitive radiotherapy for HNC.

2. Materials and methods

2.1. Study population

HNC patients planned to undergo curative-intent definitive (chemo-) radiotherapy between December 2019 and August 2021 were included in this prospective study. As part of their evaluation, all patients underwent a clinical examination, endoscopy, and diagnostic imaging, including both a head and neck MRI and a [18F]-FDG-PET-CT scan. If patients had not undergone diagnostic imaging before arriving at our center, these examinations were performed in RT position. The [18F]-FDG-PET-CT was acquired 1 h post-injection on an EARL accredited GE Discovery 690 PET/CT (GE Healthcare, Milwaukee, WI, USA). Tumors were classified according to the Eighth Edition of AJCC Cancer Staging Manual. For treatment planning purposes, each patient underwent two CT scans, a first without contrast, immediately followed by a contrast-enhanced one. These scans were conducted with 2 mm axial sections, in supine position, using a five-point thermoplastic mask along with a head support to ensure effective immobilization. The contrast-enhanced planning CT scan served as the reference image set. A rigid co-registration of the region of interest (GTVp) was performed with [18F]-FDG-PET-CT and MRI sequences (including T1 gadolinium and T2 sequences) [25–27].

The MDT comprised two HNC dedicated ROs (ages 41 and 62, with 10 and 20 years of experience in HNC, respectively), two RXs (ages 42 and 64, with 15 and 24 years of experience in HNC, respectively), one NM physicians (age 48, with 10 years of experience in HNC), RO students, and members of the dosimetry and physics teams.

The **MDT-D** started with the RO. To optimize the radiation target volume delineation, a two-step procedure was implemented based on [18F]-FDG-PET-CT and MRI images, following the guidelines of the International Commission on Radiation Units and Measurements (ICRU) 83 [28]. As a first step, a GTVp_core contour, defined as undeniably being tumoral tissue, was created by the RO. At the same time, the RO defined the GTVp_max to encompass the maximum volume of tissue that could potentially be tumoral. An internal email was sent by the responsible RO to the RX and NM with the clinical case scenario and essential data such as the patient's ID, clinical and histological information, diagnostic imaging results, the indication for radiation therapy, and specific questions that the radiation therapy team intended to address during the meeting. The RX then delineated the GTVp_RX on the contrast-enhanced simulation CT based on the information derived from the MRI sequences. Simultaneously, the NM used the estimated threshold segmentation algorithm in PET VCAR (AW Server 3.2, GE Healthcare, Milwaukee, WI, USA) to contour GTVs on the [18F]-FDG-PET-CT. This process automatically delineated areas suspected to be the primary tumor or pathological lymph nodes (designated as GTVp_NM and GTVn_NM). Manual adjustments were made when surrounding areas exhibited high physiological uptake, such as the salivary glands and lymphoid tissue. All delineations were centralized within the

radiotherapy contouring MIM software version 7.1.3 (MIM incl, Cleveland, OH, USA), which also served as the platform for visualization and discussion during the MDT-M.

The **MDT-M** was conducted once a week at a fixed time slot, with a minimum presence requirement of at least two out of the three HNC dedicated ROs. A member of the dosimetry team ensured the quality of image fusions; the availability for visual evaluation of all previously described contours and eventually provided responses to any specific questions related to image processing. During the MDT-M review, the four GTVp contours were presented on a large-screen display. The independent contours were thoroughly discussed with the aim of reaching a final consensus, the GTVp_final. During the MDT-M, adjustments to GTVp in various anatomical compartments (cranio-caudal and lateral limits) and to lymph node extent and malignancy for GTVn (number and/or location) were documented. The peer review results were saved as GTVp_final (Fig. 1).

2.2. Data analysis

Quantitative assessments of volumetric information were conducted with the following objectives:

- **RO's confidence level (VR):** to assess the RO's confidence in contouring before discussion, a volumetric ratio (VR) between GTVp_core and GTVp_max was calculated. This ratio is expressed as:

$$VR = \frac{GTVp\_core}{GTVp\_max}$$

- **Contribution by multidisciplinary experts (RX and NM) (MDT-D)**: the value of the delineation by multidisciplinary experts was determined by identifying the portion of GTVp_final that was not initially included in GTVp_core by the RO but was considered tumor by the RX or NM. This is represented as:

$$MDT\text{-}D = GTVp\_final \cap (GTVp\_RX \cup GTVp\_NM) \backslash GTVp\_core$$

- **Addition by MDT-M**: to assess the impact of the MDT-M discussion, we calculated the part of GTVp_core and GTVp_max respectively:

$$\text{added by MDT-M} = GTVp\_final \backslash GTVp\_core$$

$$\text{added by MDT-M} = GTVp\_final \backslash GTVp\_max$$

These evaluations were designed to address the "do not miss" approach for target delineation, with a focus on the inclusion of volumes.

- **Sparing by MDT-M:** by reporting the portions of GTVp_core and GTVp_max that were outside the GTVp_final:

$$\text{removed by MDT-M} = GTVp\_core \backslash GTVp\_final$$

$$\text{removed by MDT-M} = GTVp\_max \backslash GTVp\_final$$

Descriptive information was collected to document the nature of modifications made during the MDT-M, including changes to GTVs, any involvement of anatomical structures like bone or soft tissue, and the inclusion or exclusion of lymph nodes in the GTVn. In the latter case, an interactive discussion was conducted to assess the extent and malignancy of lymph nodes, and the findings were documented (Fig. 2).

2.3. Ethics

This study was conducted at a single-center university hospital and received approval from the Ethics Committee (CE number: 3376). It adhered to the ethical standards outlined in the current version of the Declaration of Helsinki.

3. Results

We included 30 HNC patients of whom 15 patients (50 %) had oropharyngeal carcinoma, 7 (23 %) laryngeal carcinoma, 3 (10 %) nasopharyngeal carcinoma, 3 (10 %) hypopharyngeal carcinoma, 1 (3 %) oral cavity carcinoma, and 1 (3 %) cervical paraganglioma. Of the patients, 87 % were male, and 13 % were female, with Eastern Cooperative Oncology Group (ECOG) Performance Status scores ranging between 0 and 2. Among the patients, 20 (67 %) presented with locally advanced disease (clinical stage III–IV), while 10 (33 %) had stage I-II disease. Lymph node metastases in the neck (TNM 8th version, N1-3) were present in 21 patients (70 %).

The mean primary tumor volume delineated by the RO, represented by the GTV max, was the largest, while the GTV delineated by the RX was comparatively the smallest, as indicated in Table 1.

The confidence level (VR) varied between 51 % and 100 % with the average value of 87 % across the entire cohort (with 90 % confidence interval of 71.4 % and 99.1 %). The delineation alone (MDT-D) contributed a mean 1.6 cc addition (range: 0–16.8 cc) compared to the GTVp_core.

After the MDT-M, compared to GTVp_core and the GTVp_max, the volume of the GTVp_final was smaller in 4 and 18 cases, unchanged in 2 and 3, and larger in 24 and 9 cases, respectively (Fig. 3).

The MDT-M delineation contributed an average of 3.3 cc (range: 0–25.6) to the GTVp_final compared to the GTVp_core. Additionally, an average of 1.3 cc (0–15.6) of volume was spared by the MDT-M. In comparison to the GTVp_max, the MDT-M played a crucial role, without delineation and discussion, an average of 2.7 cc (range: 0–20.3) of the tumor volume would have been missed, while 2.3 cc (0–21.3) was removed prior reaching the GTVp_final (Fig. 4).

Regarding the GTVn, the most common discussions were about lymph nodes suspicious by nodal size and/or contrast enhancement patterns on CT and/or MRI, not corresponding to [18F]-FDG-PET findings (5/7); and about small [18F]-FDG-PET negative retropharyngeal lymph nodes (2/7). Two lymph nodes were pathologic on [18F]-FDG-PET and morphologically normal on CT scan. MDT-M resulted in the inclusion of 5 and the exclusion of 2 suspect lymph nodes, leading to changes in the elective clinical tumor volume.

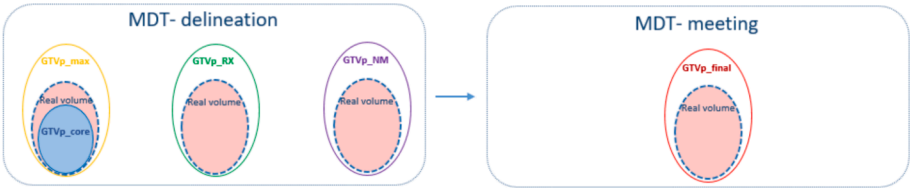

Fig. 1. Study workflow: MDT: multidisciplinary team; GTVp_max: maximum tumoral volume contoured by radiation oncologist; GTVp_core: undeniably tumoral volume contoured by radiation oncologist; GTVp_RX: tumoral volume contoured by radiologist, GTVp_NM: tumoral volume contoured by nuclear medicine specialist; GTVp_final: tumoral volume after MDT delineation and discussion.

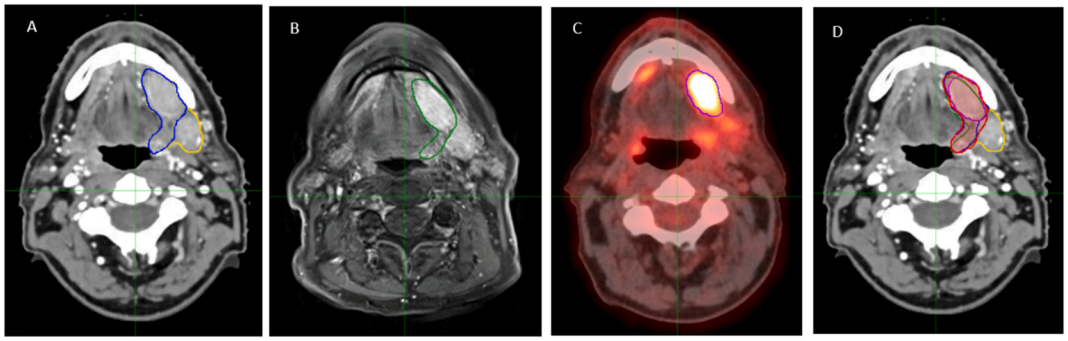

Fig. 2. Multidisciplinary team delineation (MDT-D) of an oropharyngeal tumor stage T4aN2cM0, p16- (TNM 8th edition): A: GTVp_core (blue): undeniably tumoral volume and GTVp_max (yellow): maximum tumoral volume contoured by radiation oncologist on simulation CT scanner. B: GTVp_RX (green): tumoral volume contoured by radiologist on MRI T1, gadolinium enhanced. C: GTVp_NM (purple): tumoral volume contoured by nuclear medicine specialist on PET CT scanner. D: all contours, including the GTVp_final (red): tumoral volume after MDT delineation and discussion on simulation CT scanner.

Table 1
Mean Volume of GTVs. GTVp_core: undeniably tumoral volume contoured by radiation oncologist; GTVp_max: maximum tumoral volume contoured by radiation oncologist; GTVp_RX: tumoral volume contoured by radiologist; GTVp_NM: tumoral volume contoured by nuclear medicine specialist; GTVp_final: tumoral volume after multidisciplinary delineation and discussion.

N = 30	Mean Volume in cc (Range)
GTVp_core	19.5 (0.4–90.8)
GTVp_max	22.1 (0.84–106.15)
GTVp_RX	14.4 (0.4–61.4)
GTVp_NM	16.36 (0.8–85.9)
GTVp_final	19.46 (0.6–65.4)

4. Discussion

Our study used a comprehensive approach by implementing a systematic review not only by dedicated HNC ROs but also HNC dedicated RXs and NM specialists. This integrated peer-review process involving these three distinct disciplines, had not been described or evaluated in previous clinical studies.

We observed the volume of GTVp_RX and GTVp_NM to be relatively smaller than the GTVp_max delineated by ROs. This is in line with the study conducted by Daisne et al., comparing the delineation of GTV using CT, MRI, and [18F]-FDG-PET in pharyngo/laryngeal squamous cell carcinoma [29]. They observed differences in the GTV volumes between these imaging modalities for different tumor locations. For oropharyngeal tumors, the average GTV delineated using CT was 32.0 cc, while 20.3 cc when using [18F]-FDG-PET, although the difference was not statistically significant ($p = 0.10$). In the case of laryngo/hypopharyngeal tumors, the average GTV delineated using CT was 21.4 cc, whereas 16.4 cc when delineated using [18F]-FDG-PET, with the difference being statistically significant ($p = 0.01$). There are several reasons to explain this difference. Firstly, ROs often are on the side of caution when delineating tumor volumes, opting for a conservative approach in case of uncertainty. This tendency to "play it safe" can result in relatively larger delineated volumes. Secondly, these differences can also be attributed to the inherent variations in the primary purpose of the imaging techniques used by different specialists. RXs and NM specialists may rely on specific imaging modalities highlighting certain aspects of the tumor, global tumor size and invasion patterns. They are rarely asked to delineate the exact tumor boundaries.

Our study illustrates the significant impact of the MDT-D on the final delineated gross tumor volume (GTVp_final). Following the multidisciplinary meeting, a comprehensive assessment was conducted, revealing nuanced adjustments in GTV_final compared to both GTV_core and GTV_max. Notably, GTV_final presented a reduction in size in a subset of

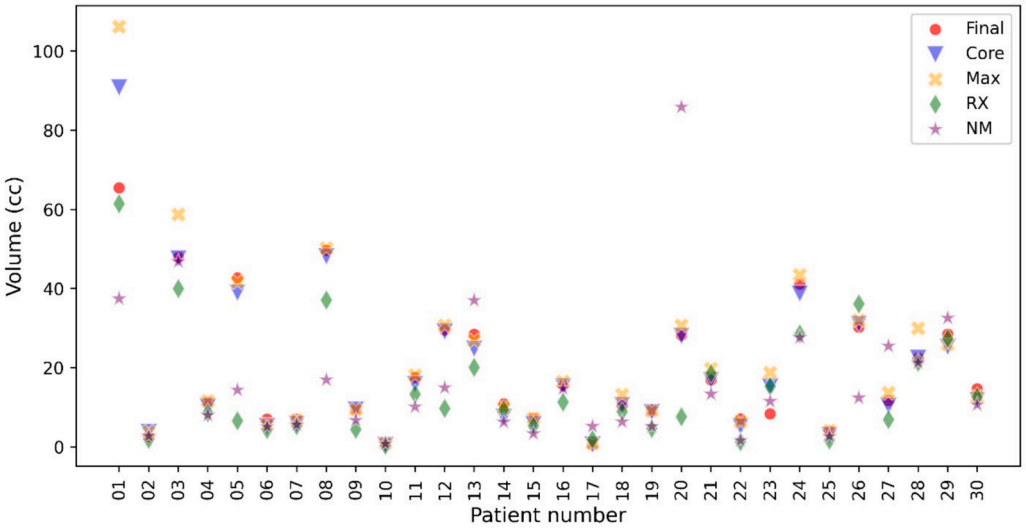

Fig. 3. GTV volume variations for each patient. GTVp_final (red): tumoral volume after multidisciplinary delineation and discussion; GTVp_core (blue): undeniably tumoral volume contoured by radiation oncologist; GTVp_max (yellow): maximum tumoral volume contoured by radiation oncologist; GTVp_RX (green): tumoral volume contoured by radiologist; GTVp_NM (purple): tumoral volume contoured by nuclear medicine specialist.

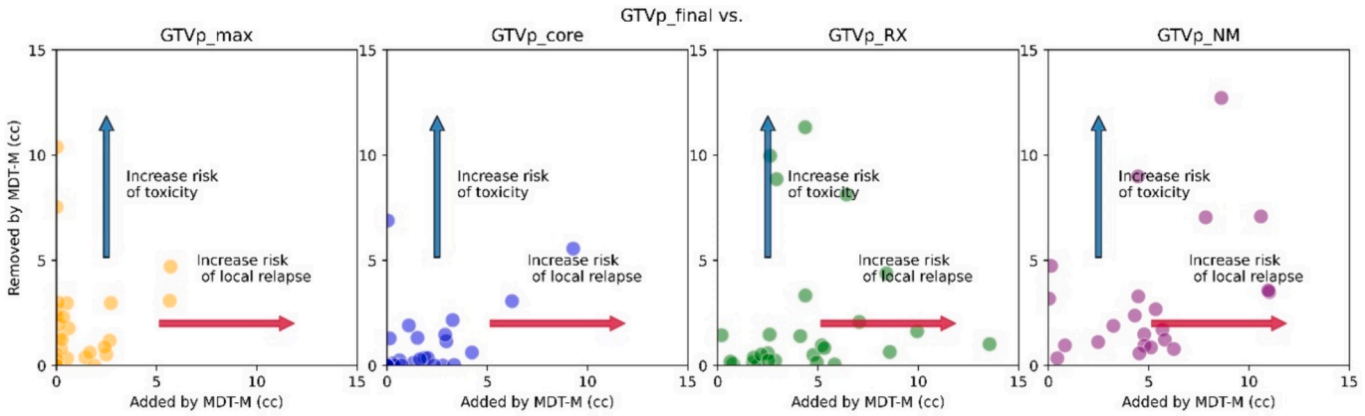

Fig. 4. GTVp_max changes (exclusion and inclusion) compared to GTVp_final. GTVp_final (red): tumoral volume after multidisciplinary delineation and discussion; GTVp_core (blue): undeniably tumoral volume contoured by radiation oncologist; GTVp_max (yellow): maximum tumoral volume contoured by radiation oncologist; GTVp_RX (green): tumoral volume contoured by radiologist; GTVp_NM (purple): tumoral volume contoured by nuclear medicine specialist.

cases (4/30) when contrasted with GTV_core, highlighting the refined precision achieved through collaborative deliberations. Conversely, a larger proportion of cases (24/30) observed an expansion in GTV_final relative to GTV_core, underlining the complexity inherent in tumor delineation and the necessity for meticulous analysis. Furthermore, the evaluation in contrast to GTV_max revealed a distinct pattern, with GTV_final demonstrating a reduction in size in a significant number of cases (18/30), implying a refined delineation process that prioritizes clinical accuracy. The expertise of each specialist contributed to the final decision by adding or extracting certain contoured areas of the GTV. Furthermore, the range of values observed in our study (0–25.6 cc for contributions and removals in different comparisons) highlights the variability and potential complexity involved in delineating tumor volumes. These findings underscore the dynamic nature of treatment planning, where interdisciplinary insights shape and optimize therapeutic strategies, ultimately enhancing patient care and outcomes. During the MDT-M, discussions regarding GTVp were often more challenging in cases of oropharyngeal carcinoma, particularly those involving the base of tongue. These discussions revolved around disagreements on the boundaries between tumor and inflammation, lymphoid tissue invasion, and cranio-caudal limits. In five out of 15 patients with oropharyngeal cancer, different areas related to primary tumor extension were either excluded or included. For laryngeal carcinoma, the discussion was mainly about cartilaginous invasion and the superior/inferior limits of the tumor. In one (out of seven) patient with laryngeal carcinoma, the MDT-M even resulted in a significant decision regarding cartilaginous invasion, ultimately changing the disease stage and treatment approach. Our MDT-M was beneficial by changing the status of 7 (23 %) patients in terms of GTVn delineation. Challenges included a mismatch between CT/MRI and [18F]-FDG-PET, as well as small [18F]-FDG-PET negative RPLN. MRI has been proven to better detect small nodes and metastasis in RPLN compared to CT [30]. Although PET imaging is generally more accurate than CT/MRI in identifying lymph node metastasis, its sensitivity for pathological lymph nodes smaller than 5 mm is only 23 % [31]. This is particularly relevant for suspect RPLN, which tend to be small, often less than 1.5 cm [32]. In general, [18F]-FDG-PET is less effective in providing soft tissue contrast and resolution compared to CT/MRI, making it challenging to identify small positive lesions and susceptible to false positives due to tissue inflammation. The involvement of experienced NM physicians and RXs in discussions helps to improve image interpretation and delineation consistency.

The MDT-M discussions can influence how imaging is interpreted, potentially leading to clinical adjustments in target volumes. This process may result in “down staging,” where the GTVp_final becomes smaller than initially anticipated. This can lead to changes like omitting prophylactic lymph node areas or even all lymph node areas in very early-stage tumors, improving organ at risk preservation and reducing toxicity. Conversely, “upstaging” may occur, leading to an enlargement of the elective CTV by including nodal or presumed subclinical disease areas, potentially affecting adjacent organs at risk. In some cases, these changes might necessitate higher doses to certain nearby organs, prompting a shift in treatment strategy, such as the initiation of induction therapy or surgery. A systematic review of 11 studies on peer review practices in radiation oncology revealed that, on average, 10.8 % of treatment plans were modified. Among these modifications, 45.2 % involved changes in target volume delineation [33]. These findings underscoring the importance of meticulous delineation strategies, like the multidisciplinary discussion, in accurately capturing the tumor volumes.

To our knowledge, this is the first head and neck cancer specific study on multidisciplinary delineation and peer review for radiation therapy contours. The limitation of this report include that the study was conducted at a single-center university hospital, which may restrict the generalizability of the findings to other medical institutions with varying resources, expertise, and patient populations. Additionally, the study featured a relatively small sample size of HNC patients. While the research aimed to address inter-observer variability, it did not explore intra-observer variability within each discipline, which could also impact target volume delineation. These limitations should be taken into consideration when interpreting the study’s results and may serve as guidance for future research in this field.

It is worth noting that currently, MDT-D and -M play a crucial educational role in our department, actively involving young ROs in training. The weekly MDT-M sessions have also contributed to our RX and NM teams gaining more experience and better understanding of the challenges involved in the radiation oncology decision-making process and the impact of their imaging (quality) on it.

5. Conclusion

The complexity of target definition in HNC emphasizes the need for a multidisciplinary meeting dedicated to review/discuss target contours before treatment planning. The process of delineating primary tumor and pathological lymph node volumes, both before and during the MDT-M, can result in important modifications in GTVs as well as CTV, possibly influencing local control and toxicity. Our structured and collaborative approach to review radiation therapy target delineation ensures the most accurate utilization of diagnostic imaging in the context of HNC radiation oncology treatment planning.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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