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Clinical Investigation: Head and Neck Cancer

Target Volume Delineation in Oropharyngeal Cancer: Impact of PET, MRI, and Physical Examination

Anuradha Thiagarajan, M.D.,* Nicola Caria, M.D.,* Heiko Schöder, M.D.,[†] N. Gopalakrishna Iyer, M.D.,[‡] Suzanne Wolden, M.D.,* Richard J. Wong, M.D.,[‡] Eric Sherman, M.D.,[§] Matthew G. Fury, M.D.,[§] and Nancy Lee, M.D.*

*From the Departments of *Radiation Oncology, [†]Radiology, [‡]Head and Neck Surgery, and [§]Medical Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY*

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Summary

In the era of high precision radiotherapy, accurate target delineation is crucial. Sole utilization of computed tomography scans in gross tumor volume delineation for head and neck cancers is subject to significant inter-observer variation. This paper demonstrates that magnetic resonance imaging and positron emission tomography add valuable complementary information, and that their combined use is recommended. In addition, it shows that thorough physical examination is invaluable in assessing superficial tumor extent in oropharyngeal malignancies, a dimension that is often missed or underestimated by imaging alone.

Introduction: Sole utilization of computed tomography (CT) scans in gross tumor volume (GTV) delineation for head-and-neck cancers is subject to inaccuracies. This study aims to evaluate contributions of magnetic resonance imaging (MRI), positron emission tomography (PET), and physical examination (PE) to GTV delineation in oropharyngeal cancer (OPC).

Methods: Forty-one patients with OPC were studied. All underwent contrast-enhanced CT simulation scans (CECTs) that were registered with pretreatment PETs and MRIs. For each patient, three sets of primary and nodal GTV were contoured. First, reference GTVs (GTVref) were contoured by the treating radiation oncologist (RO) using CT, MRI, PET, and PE findings. Additional GTVs were created using fused CT/PET scans (GTVctpet) and CT/MRI scans (GTVctmr) by two other ROs blinded to GTVref. To compare GTVs, concordance indices (CI) were calculated by dividing the respective overlap volumes by overall volumes. To evaluate the contribution of PE, composite GTVs derived from CT, MRI, and PET (GTVctpetmr) were compared with GTVref.

Results: For primary tumors, GTVref was significantly larger than GTVctpet and GTVctmr ($p < 0.001$). Although no significant difference in size was noted between GTVctpet and GTVctmr ($p = 0.39$), there was poor concordance between them (CI = 0.62). In addition, although CI (ctpetmr vs. ref) was low, it was significantly higher than CI (ctpet vs. ref) and CI (ctmr vs. ref) ($p < 0.001$), suggesting that neither modality should be used alone. Qualitative analyses to explain the low CI (ctpetmr vs. ref) revealed underestimation of mucosal disease when GTV was contoured without knowledge of PE findings. Similar trends were observed for nodal GTVs. However, CI (ctpet vs. ref), CI (ctmr vs. ref), and CI (ctpetmr vs. ref) were high (>0.75), indicating that although the modalities were complementary, the added benefit was small in the context of CECTs. In addition, PE did not aid greatly in nodal GTV delineation.

Conclusion: PET and MRI are complementary and combined use is ideal. However, the low CI (ctpetmr vs. ref) particularly for primary tumors underscores the limitations of defining GTVs using imaging alone. PE is invaluable and must be incorporated.

Keywords: GTV delineation, Head-and-neck cancer, Clinical examination, Contouring

Reprint requests to: Anuradha Thiagarajan, M.D., Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, New York, NY 10021. Tel: (212) 639-6800; Fax: (212) 717-3104; E-mail: anu_thiagarajan@hotmail.com

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Introduction

In recent years, intensity-modulated radiation therapy (IMRT) has found widespread use in the management of head-and-neck cancers because of its ability to create sharp dose−gradients between tumor volumes and neighboring critical structures. With the advent of such highly conformal radiation delivery techniques, precise delineation of target volumes has become critical. Even minor inaccuracies may lead to marginal misses of tumor or overdosage of surrounding normal tissues, results of which can be devastating.

It is well documented that the sole utilization of computed tomography (CT) simulation scans in contouring gross tumor volume (GTV) is subject to a large degree of interobserver variability. In fact, in a study that evaluated the degree of concordance among eight experienced physicians who contoured identical GTVs based on contrast-enhanced CT scans alone, the overlap in contoured volumes was only 53% (1).

Hence, attention has shifted to the incorporation of other imaging modalities such as magnetic resonance imaging (MRI) and more recently, positron emission tomography (PET), into the treatment planning process to clarify areas of tumor burden. MRIs offer several well recognized advantages over CTs. First, they provide superior soft-tissue contrast compared with CTs. Second, their multiplanar imaging capability permits better definition of the craniocaudal tumor extent. Third, although CTs are ideal at demonstrating cortical bone erosion, marrow infiltration is better appreciated on MRIs. Finally, MRIs are far less susceptible to image degradation caused by artifacts arising from dental amalgam (2−5). One recent study showed that the coregistration of MRI and planning CTs substantially improved interobserver variability in critical organ as well as target volume delineation, particularly in patients with intracranial tumor extension, heavy dental work, or contraindications to iodinated contrast agents (6).

The integration of PET into the treatment planning process has become increasingly popular across a variety of tumor subsites including head and neck. There are several theorized advantages of using PET for target volume delineation. These include standardization of GTV delineation by minimization of interobserver variation; reduction in the size of the GTV on the basis of PET-derived metabolic information, facilitating sparing of normal tissues in the immediate vicinity; identification of regions of tumor extension either missed by or not readily apparent on CT and MRI; localization of PET-avid subvolumes of tumor to direct dose escalation; and per-treatment modification of target volumes to account for tumor shrinkage in adaptive planning strategies (7−10).

Although the respective roles of PET and MRI in the target volume delineation of head-and-neck neoplasms are the subject of ongoing debate particularly in the context of contrast-enhanced CT simulation scans, it is undisputed that imaging plays a fundamental role in the initial workup of these patients and subsequently, in radiation treatment planning. What is considerably less appreciated is the role of careful physical examination in the assessment of disease extent in this anatomically complex subsite.

This study aims to assess the relative contributions of MRI and PET to GTV delineation in patients with oropharyngeal cancer and evaluate the role, if any, of physical examination.

Methods and Materials

This study was approved by the Memorial Sloan-Kettering Cancer Center institutional review board with a waiver of informed consent. Forty consecutive patients with oropharyngeal cancer treated at Memorial Sloan-Kettering Cancer Center were studied. Patient characteristics are shown on Table 1. All underwent contrast-enhanced CT simulation scans which were fused with pretreatment MRI and PET/CT scans obtained within 2 weeks of the date of simulation. All PET/CT scans were performed on a General Electric Discovery LS PET (Advance NXi)/CT (LightSpeed four-slice) scanner (GE HealthCare, Waukesha, WI) with an intrinsic resolution of 4.2-mm full-width at half maximum, using standardized image acquisition protocols that have been previously described (11). Fusion between the various datasets (CT/MRI and CT/PET) was performed using an in-house image registration software (ImgReg). This software uses a fully automated algorithm based on maximizing the mutual information in the respective image datasets, providing a rigid method of coregistration. The area over which fusion was performed was selected such that it centered over the area of interest (typically the GTV) and encompassed a wide area of soft tissue and bony structures as well as the periphery of the patient to provide as much information for the coregistration process as possible. For CT/MRI fusion, no distortion correction techniques were applied before coregistration as there is ample evidence to suggest that geometric inaccuracies arising from distortion from magnetic field inhomogeneities and nonlinearities in the MRI gradient are minimal in the head-and-neck region (4, 12).

The quality of the registrations was subsequently evaluated subjectively using the brain, spinal cord, and mandibular bone as references, with corrections made in the axial, sagittal, coronal, or rotational directions if required. If the registration was deemed suboptimal for planning purposes even after manual fine-tuning because of variations in neck position, for example, the case was excluded from this study.

For each patient, three sets of primary and nodal GTV were contoured. Reference "gold standard" GTVs (GTVref) were

Table 1 Patient and tumor characteristics

Age	
≤55	18 (45%)
>55	22 (55%)
Gender	
Male	31 (78%)
Female	9 (22%)
Site	
Tonsil	22 (55%)
Base of tongue	17 (43%)
Pharyngeal wall	1 (2%)
T stage	
T1	5 (13%)
T2	17 (43%)
T3	9 (22%)
T4	9 (22%)
N stage	
N0	3 (8%)
N1	9 (22%)
N2	26 (65%)
N3	2 (5%)
Stage group	
I	1 (2%)
II	1 (2%)
III	6 (15%)
IV	32 (81%)