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Interobserver variations in the delineation of target volumes and organs at risk and their impact on dose distribution in intensity-modulated radiation therapy for nasopharyngeal carcinoma

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A B S T R A C T

Objective: This study aimed to (a) assess the differences in the delineation of target volumes and organs-at-risk (OARs) by different physicians designing an intensity-modulated radiation therapy (IMRT) for nasopharyngeal carcinoma (NPC) and (b) analyze the impact of these differences on the treatment plan optimization.

Materials and methods: The planning target volumes (PTVs) and OARs for radiotherapy were manually delineated from computed tomography images of a patient with NPC, and a standard delineation was determined using the STAPLE algorithm of ABAS software. IMRT was designed using one standard plan and 10 individual plans based on the same constraints and field conditions. The maximum/minimum ratio (MMR) of the PTV and OAR volumes and the coefficient of variation (CV) for the different groups were evaluated and compared to the volume of the standard contour.

Results: Significant differences were seen in the PTVs of the nasopharynx (PTV_{nx}), neck lymph node (PTV_{nd}) and the OARs manually delineated by different physicians. Compared to the standard plan, the mean dose-related parameters of various OARs in different individual plans were not significantly different, while that of most organs in different individual plans were reduced. However, a significant difference in the dose at each organ was noted in different individual plans.

Conclusion: Significant differences were noted in the PTV and OAR delineations by different physicians in radiotherapy of NPC, and their dosimetric parameters were significantly different from the standard planned parameters. Therefore, multicenter trials should pay attention to the impact of these differences on the clinical evaluation.

1. Introduction

Intensity-modulated radiotherapy (IMRT) has better clinic outcomes in the treatment of head and neck cancer, achieving more accurate target dose distribution and better protection of normal tissues [1–3]. However, the premise is that the planning target volumes (PTVs) and organs at risk (OARs) must be accurately delineated. The treatment plan should be designed so that the prescribed dose can accurately

Abbreviations: ABAS, atlas-based automatic segmentation; CV, coefficient of variation; MMR, maximum/minimum ratio; PDC, prescription dose coverage; STAPLE, simultaneous truth and performance level estimation; NPC, nasopharyngeal carcinoma; TPS, treatment planning system

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cover the tumor target site, whereas the dose to the OARs does not exceed the established limit. For head and neck tumors, especially nasopharyngeal carcinoma (NPC), the shape of the treatment target is complex given the structures of the adjacent OARs. Thus, structure delineation is not only very time-consuming but is also significantly different for the same target area or organs when delineated by different physicians [4,5]. These differences will affect not only the optimization and quality of the treatment plan but also the curative evaluation and analysis of the treatment outcomes [6,7]. In recent years, image delineation software based on atlas-based automatic segmentation (ABAS) has been widely used for the automatic delineation of anatomical structures. Studies have demonstrated that the manual modification and confirmation based on the automatic delineation of the OARs using the ABAS software could save the physicians' time in OAR delineation, improve the efficiency of the planning design [8], and reduce the inter-physician variations in the delineation [9,10]. However, given the complex shape of the tumor target areas in NPCs and the significant differences in the target areas of different patients, it is difficult to establish a uniform atlas. The ABAS software can only be applied to the automatic delineation of OARs. Therefore, the delineation of PTVs must be manually performed by the physicians. Although a series of delineation guidelines for PTVs and OARs in radiotherapy have been published in recent years, the accuracy of the anatomical delineation for patients is highly dependent on the imaging skills and the clinical training experience of the physicians.

The purpose of this study was to evaluate differences in the delineation of PTVs and the surrounding OARs by different physicians while designing IMRT treatment plans for NPC. We also aimed to analyze the influence of these differences on the treatment plan and dose distribution to determine the deviation from the planned dose, which is expected to provide a reference for the design of optimal treatment plans and evaluation programs in clinical trials.

2. Material and methods

2.1. Clinical data of the patient

A 65-year old man undergoing IMRT for NPC was randomly selected. He had T2N2M0 stage disease and was diagnosed with an undifferentiated non-keratinized carcinoma by nasopharyngeal biopsy. The study was approved by the ethics committee of Sun Yat-sen University Cancer Center, and the patient provided informed consent for this study.

2.2. Acquisition of the simulated positioning image

A spiral CT (Somatom Sensation Open, Siemens AG)-enhanced scan was performed with the patient in a supine position, fixed with a head and neck mask. The scanning parameters included 140 kV voltage, 280 mA current, 3 mm thick scanning and reconstruction layer, and pitch of 1:1. The acquired positioned CT images were transmitted to a radiotherapy planning system (Monaco Version 3.2, Elekta AB) for contouring.

2.3. Delineation of PTVs and OARs

All target and OAR volumes were outlined slice by slice on the axial contrast-enhanced CT images referred to magnetic resonance imaging (MRI). The contours were defined in accordance with the International Commission on Radiation Units and Measurements Reports 50 and 62 [11,12] and following the protocol reported by Xiao et al. [13]. Gross tumor volume (GTV) was determined according to diagnostic CT and physical examination. The nasopharynx gross target volume (GTV_{nx}) and the positive neck lymph nodes (GTV_{nd}) were identified. Two clinical target volumes (CTVs) were delineated: CTV1 and CTV2. CTV1 was defined as the nasopharynx gross target volume plus a 5–10 mm margin (2–3 mm margin posteriorly) to encompass the high-risk sites of microscopic extension and the whole nasopharynx. CTV2 was defined as the CTV1 plus a 5–10 mm margin (2–3 mm margin posteriorly) to encompass the low-risk sites of microscopic extension, the level of the lymph node located, and the elective neck area (bilateral levels IIa, IIb, III, and Va are routinely covered for all N0 patients, whereas ipsilateral levels IV, Vb, or supraclavicular fossae were also included for N1 patients). The OARs to be contoured included the brain stem, spinal cord, lens, optic nerve and optic chiasm, pituitary gland, parotid gland, temporal lobe, temporomandibular joint (TMJ), and mandible. After delineation of the above target areas, the planning volumes for all GTVs, CTVs and the corresponding OARs (PTV_{nx}, PTV_{nd}, PTV1, PTV2 and PRVs) were generated automatically according to the immobilization and localization uncertainties, and the same PTV/PRV margins were used among those 8 centers.

A total of 10 junior radiation oncologists from eight hospitals, who had finished a three-year professional training program specialized for radiation treatment, independently and manually contoured each target area and OARs on the CT images to obtain 10 sets of individual contours, each containing the PTVs and PRVs. All volumes contoured must be reviewed by a senior physician (professor) in the consensual peer-review group, where the variations were picked up, discussed with the delineator and confirmed by the professor finally. The atlas-based automatic segmentation software (ABAS, Version 2.01, Elekta AB, Stockholm, Sweden) was used to establish a set of standard "true contours" using the simultaneous truth and performance level estimation (STAPLE) algorithm [14,15]. The individual contours from the above 10 physicians were fed into the ABAS software as a "combination template" to iteratively estimate the quality of the individual segmentations and compute the overall value by weighing the reliability scores using the STAPLE algorithm and the expectation- maximization (EM) technique of the software. The algorithm then computed a probabilistic estimate of the true contour from the 10 individual contours.

Simon et al. [14] have experimentally verified that STAPLE is capable of accurately estimating the most likely "true contour" from a set of independent structural contours. Therefore, based on the delineation results by the 10 physicians as the "standard" contour for the PTVs and OARs, we determined the most likely contour for this patient.

2.4. IMRT planning

For 11 sets of CT images containing the individual and standard contours of the PTVs and OARs, nine dynamic intensity-modulated radiotherapy (dIMRT) synchronous dosage plans were made. The same prescription dose and OAR dose constraints were applied to all plans with 6 MV X-ray irradiation in prescription doses of 70 Gy, 66 Gy, 60 Gy, and 54 Gy for PTV_{nx}, PTV_{nd}, $PTV_{1,}$ and PTV_2, respectively, and the irradiation was delivered 32 times. The calculation grid of the planned dose was 3 mm × 3 mm × 3 mm. Each plan that was optimized based on the 10 individual contours was defined as an individual plan, and a plan designed based on the standard contour was defined as the standard plan.

2.5. Differences in the planning volume and its impact on the quality of the IMRT program

Definition of the various parameters to evaluate the impact of each individual contour on the program

Maximum/Minimum Ratio (MMR): The volume differences in the target areas and OARs contoured independently by different physicians or the range of relative differences in the dosimetry parameters of the treatment plan due to the delineation differences were described using the PTV and OAR volume as well as the MMR of the dose parameters corresponding to these volumes. The MMR is expressed by the following equation: