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Original Article

Joint modeling of missing and mismeasured measurements for computing radiotherapy margins

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ABSTRACT

Purpose: Pelvic organs are naturally prone to positional and volumetric changes over time. These individual organ changes may result in variations in the clinical target volume (CTV) position and shape. Planning target volume (PTV) that encompasses the CTV with some margins to account for such uncertainties in patient positioning, organ motion, and beam geometry is universally accepted today in radiotherapy. Keeping this view in mind, the present study has been planned in order to determine the setup error (random and systematic) in patients of carcinoma cervix and rectum image-guided radiotherapy and to propose a population-based three-dimensional CTV to PTV margins in IGRT scenario.
Materials and methods: The mean margin displacements of 61 patients measured through different directions. The proposed method is used to estimate margins of displacement of specific CTV dosing. A further method is illustrated to simulate the dose received by the CTV. The margin distance compared with Van Herk model through consideration of systematic and random errors. Different site-wise displacements were measured and compared. The CTV performance dosimetry has been carried through proposed model and compared with the traditional margin for each of the datasets.
Results: The PTV margins obtained on lateral, longitudinal and vertical sides on Cervix site are 0.91, 1.93 and 0.96 [Van Hark's formula] and 0.84, 1.79 and 0.89 through proposed formula. It can be noted that in both the cases, the respective margin obtained through proposed method was lesser in comparison to that of Van Hark's method.
Conclusions: The presence of heterogeneity in patient's random error is natural. This random error is highly influential on radiotherapy margin widths of the patients. The Bayesian statistics are useful to deal with such a problem. In this article, a simple and well-defined model is adopted to deal with the patient's heterogeneity problem. It has been observed that the model accounted the variability in the margin estimation. The variation in margin can be extended from one cancer site to another cancer site.

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1. Introduction

The clinical target volume (CTV) is important to be considered during external beam radiotherapy. The margins are placed around the CTV to cover the daily movement in CTV position through repeated measurement. These margins are required to be large enough to avoid delivery of inadequate dose in CTV's position. However, larger amounts of margins can unnecessarily affect the healthy tissue to radiation and simultaneously increased toxicities. At various times, displacement arises between the assumed position of CTV during the planning and its actual position. This displacement can be divided into a systematic and random component.[1] The systematic part occurs due to the error during treatment planning and target delineation. The reason may be the use of a single delineated position of the tumor instead of a time-averaged CTV position. The random error occurs during the daily variation in tumor position due to organ movement relative to the reference markers used for beam alignment. The systematic error is defined as the standard deviation of the mean displacements of the CTV's across all patients. The standard deviation of the specific patient's CTV's displacements is defined as the random error.[2] The most widely adopted formula for calculating margins was introduced by Van Herk et al.[2]

The Van Herk margin formula is computationally simple and mathematically sophisticated. However, there are some mathematical assumptions about CTV displacements. It is assumed that mean displacements are normally distributed. Each patient's repeatedly measured fraction-to-fraction CTV displacements are assumed with the normal distribution, and there is no influential correlation in displacements between dimensions. It is also assumed that random error is constant for all patients.[3–10] However, some patient's CTV displacements become larger than others. It can be solved through heterogeneity modeling.[11] The repeatedly measured data are prone to be affected with missing observations. In IG-IMRT era, Cone Beam Computer Tomography's (CBCT) are performed on the regular basis throughout the treatment verification. Ideally, we should take CBCT every day to verify our treatment plan and to execute our treatment which may not be feasible practically due to huge patient's burden and the shortage of time. This is a kind of compromise in our image verification part and optimum execution of treatment. With less number of CBCT's, we decide our random and systematic error, and finally calculate the Planning target volume (PTV) margin which may not be accurate. We are using Van Herk's formula to calculate the PTV margins which overlook missing or mismeasured observation for PTV calculation. For example, in Ca-cervix, we usually deliver a total dose of 50.4 Gy in 28 fractions over five and half weeks. Ideally, CBCT should be performed in all those 28 days. If we consider CBCT for first three days and twice weekly for rest of the treatment, the total number of acquired CBCT's will be around 14. It is exactly half of the ideal required images to calculate the error and PTV margin. These attributes will highlight the new method of PTV calculation which will take missing and mismeasured observations into consideration that may further give the robust estimate of PTV margin. The presence of missing observation is inevitable in this type of study design. It is true that missing data are common in experiments with repeatedly measured observations. Three types of missing data are found in clinical data (i.e. missing completely at random (MCAR), missing at random (MAR), and non-ignorable missing (NIMR).[12] It is often found that the variable is affected through missing measurement.[13] The example of MAR is like, ''Male participants are more likely to attend all the visits, but it does not have any reason about their gender to attend for visits more''. It is better to consider MAR when we do not have any idea about the reason of occurrence of missing data. In this work, the MAR is considered for simplicity. However, the presence of missing observations has been overlooked in earlier studies in PTV measurement. There has been virtually no literature at all for handling missing and mismeasured data simultaneously, that is, modeling the longitudinal process while patients are repeatedly measured, and then also jointly attempt the approach modeling for missing and mismeasured data.

In this study, we propose a model to handle missing and mismeasured variable. The variable is considered as ''displacements''. Particularly displacement is separated with the random, systematic error and mismeasured error. This study is dedicated to evaluating the error in Ca-cervix and Ca-rectum patients undergoing radiotherapy. An optimum population-based CTV–PTV margin in carcinoma cervix and carcinoma rectum cancer patients will be obtained in patients undergoing conformal radiotherapy.

2. Methods

The mean margin displacements of 61 patients measured through four different directions (lateral, vertical, longitudinal and rotational) are detailed in Table 1. However, we concentrated on 3-dimensional displacement. The proposed method is used to estimate margins of displacement of specific CTV dosing. A further method is illustrated to simulate the dose received by the CTV. The margin distance is compared with Van Herk model through an assumption of systematic and random errors. Different site-wise displacements were measured and compared. The CTV performance dosimetry has been carried through proposed model and compared with the traditional margin for each of the datasets. The treatment planning with high geometrical accuracy can only deliver the

Table 1 – A summary of the patients cohorts used to mode day-to-day variation in CTV position.

Cohort	Treatment site	Number of patients	Averaged displacement			
			Lateral	Longitudinal	Vertical	Rotational
1	Cervix	44	0.47	0.65	0.27	0.14
2	Rectum	17	0.30	0.38	0.23	0.04