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Review Article

Determination of Planning Target Volume in Radiotherapy - A Review

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Abstract
Treatment volume definitions used in three-dimensional radiotherapy treatment planning are essential in advancing treatment modalities. However, there are many sources of error during the treatment preparation and execution that limit the accuracy. Consequently, a safety margin is required to add to the target to ensure that the planned dose is delivered to the target. Multiple margins surround the tumour to reduce positional inaccuracy, such as Clinical Target Volume (CTV), Planning Target Volume (PTV), etc. The International Commission of Units and Measurement (ICRU) recommended margins in 1978. It was later reviewed in Reports 50 and 62 of ICRU, providing information on margins covering gross volume, clinical volume, and critical structures that should be eliminated as feasible. This article aims to discuss various techniques and methods that various authors have created.
Keywords: *Margin, Errors, GTV, CTV, ITV, PTV, ICRU 50, ICRU 62, Radiotherapy.*

1. Introduction

Radiotherapy treatment is performed by delivering a radiation beam using a radiotherapy machine from a distance or placing the source close to the target. In the case of External Beam Radiotherapy, to achieve the goal of the treatment, modern technologies use different imaging devices to achieve the patient's anatomical details and use a planning system, and the beams are arranged as per requirement. The main aim of the treatment is to eradicate cancerous cells with ionizing radiation and to spare normal healthy cells as much as possible. The International Commission of Units and Measurements (ICRU) published a report as “ICRU Report 29. Dose Specification for Reporting External Beam Therapy with Photons and Electrons.” in 1978, which addressed the issue of consistent volume and dose specification.[1,2]

The report defined the target volume as the volume containing tissue to be irradiated to a specified absorbed dose.

In External Beam Radiotherapy (EBRT), the patient is positioned and aligned correctly on a machine's couch. A safe and effective radiotherapy depends on the patient being positioned accurately. However, errors can come from various sources when treatment is planned and administered. The inability to consistently reproduce the patient in the same position for each treatment session results in error sources that need special attention. The International Commission of Units and Measurements (ICRU) published a report definition of target volumes in 1993, one of which, Planning Target Volume (PTV), takes into account the positional uncertainties caused by this random deviation in position.[3]

PTV is a safety margin to ensure that the recommended dose is administered to the Clinical Target Volume (CTV) while accounting for positional uncertainty. CTV to PTV margins can be calculated using various methods, including Van Herk's formula, Stroom's method, and ICRU 62. Σ and σ are the population systematic and population random error, respectively.[4,5,6]

This article will discuss the various target volume concepts and review different methods and formulas to calculate PTV margins.

2. Radiotherapy Treatment & Planning

Radiotherapy is a localized treatment for localized tumours analogous to surgery. The diagnostics Computed Tomography (CT) guides the tumour extension in different sites. A radiation oncologist defines the tumour localization and other normal organs, a medical physicist plans the treatment module, and the therapist treats the patient. Various Techniques of External Beam Radiotherapy (EBRT) like Three-Dimensional Conformal Radiotherapy (3D-CRT), Intensity Modulated Radiotherapy (IMRT), Volume Modulated Radiotherapy (VMAT), SRS/SRT require special care from the point of patient positioning. The treatment volumes are added to eliminate the errors in patient positioning as per recommendation from the ICRU. An excellent tool is Image Guided Radiotherapy (IGRT), which helps correct patient positioning and compare the errors from the origin—the imaging tool is integrated with the treatment isocentre. The user can compare the treatment position with the planned position acquired during the simulation.[7, 8]

Three fundamental axioms of radiotherapy provide pertinent background information for this discussion. First, the likelihood of local control is typically increased when the tumour receives a higher radiation dose. Second, by preventing metastatic spread from local recurrence, enhancing local control in the setting of a localized tumour improves the overall cure rate. Third, protecting normal tissues enhances the therapeutic ratio by improving the side-effect profile of radiotherapy. Conformal radiation is one example of an implementation that spares normal tissue and gives the option of increasing the dose while maintaining a consistent level of side effects or using the same dose but reducing it.[9]

Improvements in radiotherapy imaging have improved the definition and delineation of the visible tumour volume, facilitating the implementation of ICRU margins. However, the spread of microscopic disease cannot be detected using imaging techniques. Target volume definition has improved due to the application of the IGRT technique, which has reduced setup and organ-motion-related uncertainties.[1]

Accurate dose delivery to the patient during radiotherapy is paramount, and the proper delineation of target volumes plays a crucial role in achieving this goal. The meticulous identification and definition of target volumes are essential in targeting the tumour while minimizing radiation exposure to nearby normal tissues. Consequently, the concept of target volumes holds significant importance in ensuring the efficacy of radiotherapy by optimizing the therapeutic impact on the tumour while sparing surrounding healthy tissues.

3. Target Volume Concepts:

ICRU has published Report 50 and Report 62 to promote the use of a standard set of definitions and concepts for specifying and reporting the doses in radiotherapy and the volumes in which they are prescribed and delivered. According to ICRU Recommendation, different margins are described as: [2,3]

3.1 Gross Tumour Volume (GTV)

"*GTV is the gross palpable or visible /demonstrable extend and location of malignant growth.*"

It may consist of a primary tumour, metastatic lymphadenopathy, or other metastases. The GTV usually corresponds to those parts of the malignant where the density of the tumour cells is the highest.

Different diagnostic methods determine the GTV. Sometimes, multimodality imaging has led to the potential for improved localization of the tumour volume and, hence, a better definition of the GTV. Important psychological and functional information about the tumour can be obtained by applying Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI) in radiotherapy.

3.2 Clinical Target Volume (CTV)

"*The Clinical Target Volume is a tissue volume that contains a demonstrable GTV and subclinical microscopic malignant disease, which has to be eliminated. This volume does have to be treated adequately to achieve therapy's aim.*"

CTV is the most difficult of all margins as it requires the clinical assessment of microscopic disease extension, generally based on historical series. In certain situations, a second CTV may occur—for instance, in a regional lymph node, a clearly visible GTV may be absent. The diagnostic imaging tool aids in defining the tumour and facilitates the extraction of data regarding the tumour's spread and the location of local lymph node dissemination.[2] Pathological and imaging data have led to recommendations and guidelines for delineating the CTV and the involved node for some treatment sites, such as the head and neck area.

3.3 Internal Target Volume (ITV):

The Internal Target Volume is a margin added to the CTV to compensate for expected physiological movement and all variations in site, size, and shape of the organ and tissue adjacent to the CTV. They may result from respiration, different fillings of the bladder, different filling of the rectum, shallowing, heartbeat, movements of the bowel, etc.

In radiotherapy, generally patients breathe freely during irradiation (with few exceptions). GTVs and CTVs belonging to mobile organs will thus move during exposure following the respiratory cycle. Other organs like the small bowel, in which the lower jejunum and ileum loops roll continuously and change position. The filling of the rectum or urinary bladder varies during the day, creating a continuous change in volume and shape. The larynx structure moves vertically by a few centimetres at each deglutition. There are numerous examples. Because imaging for planning is usually done in a multi-slice CT, these movements are not accounted for when delineating the GTV, CTV and organs-at-risk (OAR) volumes. It is therefore necessary to add a margin around these structures that accounts for the variation of position, volume and/or shape during a multi-fraction treatment, called the ITV obtained by adding a margin to the CTV. In the current state of radiotherapy, this concept is still a matter of research, and there is no unambiguous answer to the problem.

3.4 Planning Target Volume (PTV):

"*Planning Target Volume is a geometrical concept, and it is defined to select appropriate beam sizes and beam arrangement, taking into* *consideration the net effect of all the possible geometrical variation, to ensure that the prescribed dose is absorbed in the CTV."*

The PTV and the beam are connected using fixed coordinates. This volume has nothing to do with the patient's anatomy but with the linear accelerator's isocenter. Because of this, the PTV may go beyond anatomical boundaries like bony margins and possibly outside the patient, accounting for every possible uncertainty in the planning, patient, and beam positions.[10]

4. Setup errors in radiotherapy

Errors and margins are important concepts in radiotherapy planning and delivery. Errors are deviations from the intended treatment that may occur due to various factors, such as patient positioning, organ motion, beam alignment, or dosimetry. Margins are safety distances added to the target volume to account for errors and ensure adequate tumour coverage. Examples of errors and margins in radiotherapy are:

- A patient with prostate cancer may have daily variations in the position and shape of his prostate due to bladder filling, bowel movement, or weight loss. Hence, PTV can be created by adding a 5–10 mm margin to the CTV in order to account for these inaccuracies.[11]
- A patient with lung cancer may have a respiratory motion that causes the tumour to move during treatment. To account for this error, a 5-11 mm margin may be added to the internal target volume (ITV) to create the PTV. Alternatively, a motion management technique, such as breath-hold, gating, or tracking, may reduce or compensate for the motion.[12]
- A patient with head and neck cancer may have setup errors due to misalignment of the lasers, couch, or immobilization device. The errors can be avoided by adding a 3-5 mm margin to the CTV to create the PTV. Additionally, a verification technique, such as portal imaging, cone-beam CT, or surface guidance, may be used to check and correct the setup before or during treatment.[13]

Margins can be calculated using different methods, such as the ICRU 62, van Herk formula, the Stroom formula, etc.

5. PTV Determination

Setup margins significantly affect the overall dose administered to the target and are crucial in preventing unintentional doses to the organ at risk. When positioning radiation treatments, two errors can arise randomly and systematically. Random errors can cause the cumulative dose to be shifted from its correct location, whereas systematic errors lead to a dose distribution that diverges from the intended target area. Random errors tend to occur less frequently than systematic errors, which are particularly concerning since they can persist over multiple treatment sessions and potentially result in severe organ injury or tumour recurrence. Hence, the PTV margin must be determined accurately to minimize the setup errors during radiotherapy. Various authors have presented different methodologies to determine the PTV margin.[14]

5.1 ICRU Report 62:

ICRU Report 62 recommended that the PTV margin sizes can be total standard deviation (SD), which is calculated from the quadrature sum of the mean standard deviation of the systematic error (Σ) and the random error (σ). This recommendation is invalid because it assumes that systematic and random error uncertainties affect patient dose distribution equally. Thus, the linear addition of uncertainties should lead to an extensive PTV, compromising the tolerance of surrounding normal tissues.[4]

$$\boxed{\text{PTV margin mentioned in ICRU 62} = \Sigma+0.7\sigma}$$

5.2 Antolak's approach:

John A Antolak defined the PTV margin in his paper. He calculated the CTV-PTV margin by considering the physical position uncertainties. As per the paper, the CTV-PTV margin should ideally be determined solely by the magnitudes of the uncertainties involved, but practically, the CTV-PTV margins are decided clinically considering doses abutting healthy tissues.

Antolak described the CTV by independent Gaussian distribution in the three Cartesian directions. Three strategies were chosen to analyse the CTV-PTV margin based on 1: the probability that the CTV is completely enclosed, 2. There is a probability that the projection of the CTV in the beam's eye view (BEV) is entirely enclosed by the projection of the PTV. 3. The probability that a point on the edge of the CTV is within the PTV. Cumulative probability distribution is derived for each of the above strategies.

The article found that expansion of the CTV by one standard deviation (SD) in each direction results in CTV entirely enclosed within the PTV of 24%. Thus, it concludes that the PTV is calculated from the CTV using a margin of 1.65 SD in each direction, giving a dose greater than 95% of the minimum PTV dose. It is also mentioned that healthy structures can be spared by modifying the beam, not by adjusting the PTV.[4]

PTV margin as per J. Antolak et al. = $1.65\ \Sigma$

5.3 van Herk's Formula:

van Herk used the minimum cumulative CTV dose as a ‘gauze’ for geometrical misses. Based on dose population histograms, they derived a margin recipe to guarantee that 90% of patients receive a minimum cumulative dose of at least 95% of the prescribed dose. This margin is approximately 2.5 times the total SD of systematic plus 0.7 times the SD of random error.

PTV margin as per van Herk’s formula = $2.5\Sigma+0.7\sigma$

Van Herk's margin recipes and errors in radiotherapy are based on physical and biological considerations. However, it does not consider the rotational deviation.[6]

5.4 Stroom’s Formula:

Joep C. Stroom has developed a method for automatically calculating the PTV margin. Their model was demonstrated to be fast and accurate for prostate, cervix and lung cancer. The article used 12 parameters describing random and systematic deviations in their margin deviation. The patient’s CTV was described as a 3D matrix using the treatment room coordinate system. This matrix was convolved using the probability distribution of the random and systematic errors. The margin ensures at least 95% dose to the 99% of the CTV, which equals about two times systematic error plus 0.7 of random error.[5]

PTV margin as per Stroom’s formula = $2\Sigma + 0.7\sigma$

6. Conclusion

The article gives an overview of margins and error in radiotherapy treatment, emphasizing the need for accurate target volume delineation, patient positioning, radiotherapy planning and treatment delivery, including examples like daily setup errors in head and neck cancer, lung cancer with respiratory motion, and prostate cancer with daily variations. Target volumes are given margins to account for mistakes and ensure sufficient tumour coverage. By defining Gross Tumour Volume (GTV), Clinical Target Volume (CTV), and Planning Target Volume (PTV) and outlining various methods to calculate setup error, including ICRU Report 62, Antolak's approach, van Herk's formula, and Stroom's formula, the article highlights the significance of precise target delineation, accurate patient positioning, and margin determination in achieving successful radiotherapy outcomes while minimizing adverse effects to the normal structures.

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